PANCREATIC CANCER NEWS & UPDATES – AUGUST 2011

PANCREATIC CANCER ACTION NETWORK AND COMMUNITY NEWS

Pancreatic Cancer Action Network – AACR 2012 grants program: Now accepting applications
http://www.pancan.org/section_research/research_grants_program/apply_for_a_grant.php
A record high of more than $3.1 million will be distributed this year! Please click above for eligibility requirements and information on deadlines. Spread the word!

Save the date: AACR Pancreatic Cancer Special Conference
http://www.aacr.org/home/scientists/meetings--workshops/special-conferences/pancreatic-cancer.aspx
Save the date: the AACR Pancreatic Cancer Special Conference will be June 18-21, 2012, in Lake Tahoe, NV. The Pancreatic Cancer Action Network is a proud lead supporter of this meeting, and looks forward to the opportunity to convene a diverse group of investigators in the field to discuss the current status and future of pancreatic cancer research.

Grantee receives prestigious mentored clinical scientist development award
http://oncology.surgery.duke.edu/research/institutes-and-labs/white-lab
Rebekah White, MD (2007 Seena Magowitz – Pancreatic Cancer Action Network – AACR Career Development Award) was awarded a National Cancer Institute K08 grant for her project titled, "RNA Therapeutics for Pancreatic Cancer". Congratulations, Dr. White, and good luck with your research!

Thomas Jefferson University receives $1 million to study uncharted 98 percent of human genome
http://www.newswise.com/articles/thomas-jefferson-university-receives-1-million-to-study-uncharted-98-percent-of-human-genome-and-its-role-in-diseases
The W.M. Peck Foundation has awarded $1 million to the Computational Medicine Center at Thomas Jefferson University, to continue its work on pyknons and their role in human disease, including pancreatic cancer. Pyknons are sequences of DNA that repeat more frequently than expected by chance. The collaborative team includes Jefferson researcher Jonathan Brody, PhD (2010 Skip Viragh – Pancreatic Cancer Action Network – AACR Career Development Award) and MD Anderson collaborator George Calin, MD, PhD (2009 Seena Magowitz – Pancreatic Cancer Action Network – AACR Pilot Grant).

National Cancer Institute releases requests for applications for Provocative Questions
http://provocativequestions.nci.nih.gov/rfa
The R01 (http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-11-011.html) and R21 (http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-11-012.html) RFAs have been announced. Harold Varmus, MD, Director of the NCI, launched his Provocative Questions initiative last year, and is now seeking grant proposals to address these specific topics.

Pancreatic cancer blog: Ralph Hruban, MD

http://apps.pathology.jhu.edu/blogs/pancreas/?p=131

Dr. Hruban (Emeritus Scientific Advisory Board) describes exciting new discoveries in pancreatic cancer genetics in this Johns Hopkins blog entry.

PCRT elects new Executive Board members

http://www.tgen.org/news/index.cfm?newsid=1990

The Pancreatic Cancer Research Team (PCRT) at Translational Genomics Research Institute (TGen) elected. Dr. Ramesh K. Ramanathan is the new Chairman of the Executive Board, and eight elected Board Members were also announced, including Vincent Picozzi, MD (Medical Advisory Board).

BIOLOGY OF CANCER

Hallmarks of cancer: the next generation

http://www.ncbi.nlm.nih.gov/pubmed/21376230

This was published a few months ago, but recently featured in a *NY Times* article: http://www.nytimes.com/2011/08/16/health/16cancer.html?_r=3&pagewanted=all. The original "Hallmarks of Cancer" came out in 2000, written by Bob Weinberg, PhD and Doug Hanahan, PhD (2007 Pancreatic Cancer Action Network Pilot Grant). In the original article (http://www.ncbi.nlm.nih.gov/pubmed/10647931), Drs. Hanahan and Weinberg established six features characteristic of cancer cells. Now, the authors came together again to discuss and expand upon their findings from 11 years ago. Modifications include the cells' ability to evade the immune system, changes in metabolic functions, and interrelationship between the tumor and normal bystander cells.

Pancreatic cancer

http://www.ncbi.nlm.nih.gov/pubmed/21620466

This review in *Lancet* includes Joe Herman, MD (2008 Blum-Kovler – Pancreatic Cancer Action Network – AACR Career Development Award) and Ralph Hruban, MD (Emeritus Scientific Advisory Board) as authors.

Cellular features of senescence during the evolution of human and murine ductal pancreatic cancer

http://www.ncbi.nlm.nih.gov/pubmed/21860420

This *Oncogene* paper is out of Dave Tuveson, MD, PhD (Chair, Scientific Advisory Board and 2003 Pancreatic Cancer Action Network – AACR Career Development Award)'s lab at Cancer Research UK, with collaboration from Anirban Maitra, MD (Scientific Advisory Board and 2004 Pancreatic Cancer Action Network – AACR Career Development Award) and Ralph Hruban, MD (Emeritus Scientific Advisory Board) at Johns Hopkins. These researchers looked at oncogene-induced senescence (OIS) in premalignant pancreatic lesions in mice and humans. Their findings suggested that senescence-associated beta-galactosidase (SAb-gal) served as a marker for OIS in pancreatic intraepithelial neoplasia (PanIN) and acinar to ductal metaplasia (ADM), suggesting further uncertainty concerning the hierarchy of precancerous lesions and the cell of origin for PanIN and pancreatic ductal adenocarcinoma.

A novel 3D culture system uncovers growth stimulatory actions by TGFb in pancreatic cancer cells
http://www.ncbi.nlm.nih.gov/pubmed/21613822
Lorenzo Sempere, PhD (2008 Laurie and Paul MacCaskill – Pancreatic Cancer Action Network – AACR Career Development Award) and colleagues published this *Cancer Biology & Therapy* paper. In order to recapitulate tumor-microenvironment interactions, the researchers cultured pancreatic cancer cells embedded in Matrigel (components similar to the stroma), above a layer of soft agar. They found that treatment of 3D-cultured pancreatic cancer cells with TGFb and EGF led to increased growth, and that inhibition of each receptor with SB431542 and erlotinib, respectively, inhibited growth and improved sensitivity to cytotoxic therapies.

c-Met is a marker of pancreatic cancer stem cells and therapeutic target
http://www.ncbi.nlm.nih.gov/pubmed/21864475
This *Gastroenterology* paper involves two of our recent grant recipients: lead author Diane Simeone, MD (2010 The Randy Pausch Family – Pancreatic Cancer Action Network – AACR Innovative Grant and Scientific Advisory Board member) and Marina Pasca di Magliano, PhD (2009 Paul Mitchell – Pancreatic Cancer Action Network – AACR Career Development Award). Since c-Met is known to be a marker of stem and progenitor cells in normal mouse pancreas, the authors determined whether c-Met is also indicative of pancreatic cancer stem cells. Data from human pancreatic cancer cells sorted into c-Met-high and c-Met-negative populations suggested that c-Met expression leads to increased tumorigenicity, metastatic potential, and that c-Met can potentially be therapeutically targeted.

A critical role for autophagy in pancreatic cancer
http://www.ncbi.nlm.nih.gov/pubmed/21494085
Shenghong Yang, PhD and Alec Kimmelman, MD, PhD (2010 Pancreatic Cancer Action Network – AACR Career Development Award) wrote this *Autophagy* article as a punctum to their exciting *Genes and Development* study published a few months ago (http://www.ncbi.nlm.nih.gov/pubmed/21406549). Here, Drs. Yang and Kimmelman discuss varying roles for autophagy in pancreatic cancer, and hypothesize that autophagy initially serves to suppress tumor growth, but later plays a pro-survival role in the context of cellular stresses.

MT1-MMP cooperates with KrasG12D to promote pancreatic fibrosis through increased TGFb signaling
http://www.ncbi.nlm.nih.gov/pubmed/21856775
A co-author on this study is Paul Grippo, PhD (2007 Nancy Daly Riordan – Pancreatic Cancer Action Network – AACR Career Development Award). Published in *Molecular Cancer Research*, the authors sought to understand the role of membrane type-1 matrix metalloproteinase (MT1-MMP) in the dense fibrotic reaction surrounding pancreatic tumors. They found that MT1-MMP promotes fibrosis by activating TGFb, and acts in concert with mutant Kras.

Disruption of nuclear NFATc2 protein stabilization loop confers pancreatic cancer growth suppression
http://www.ncbi.nlm.nih.gov/pubmed/21628454
Martin Fernandez-Zapico, MD (2007 Carole and Bob Daly – Pancreatic Cancer Action Network – AACR Career Development Award) is an author on this *JBC* article. Breast and pancreatic cancer cells were tested *in vitro* and *in vivo* for response to zoledronic acid. Zoledronic acid was found to disrupt the

NFATc2 stabilization pathway through two mechanisms, namely GSK-3B inhibition and induction of HDM2 activity.

Impact of APE1/Ref-1 redox inhibition on pancreatic tumor growth
http://www.ncbi.nlm.nih.gov/pubmed/21700832
This *Molecular Cancer Therapeutics* paper represents a collaborative, multi-institutional effort, with authors including Mircea Ivan, MD, PhD (2005 Pancreatic Cancer Action Network – AACR Career Development Award) at Indiana University and Anirban Maitra, MD (2003 Pancreatic Cancer Action Network – AACR Career Development Award and Scientific Advisory Board) at Johns Hopkins. Since reduction-oxidation (redox) mechanisms may play a role in pancreatic cancer development and progression, the authors explored functions of AP endonuclease1/Redox effector factor 1 (APE1/Ref-1). A specific inhibitor of APE1/Ref-1's redox function, E3330, blocks pancreatic cancer cells' growth *in vitro* and *in vivo*.

SMURF1 amplification promotes invasiveness in pancreatic cancer
http://www.ncbi.nlm.nih.gov/pubmed/21887346
Anirban Maitra, MD (2003 Pancreatic Cancer Action Network – AACR Career Development Award and Scientific Advisory Board) contributed to this *PLoS One* publication. Kwei, *et al* discovered a region of amplification on chromosome 7q21-22 in pancreatic cancer cell lines, and found that SMURF1, an E3 ubiquitin ligase, included in that amplicon. Further analysis showed SMURF1 amplification in about four percent of human pancreatic cancer cases. Down-regulation of SMURF1 via RNAi led to reductions in cell invasion and anchorage-independent growth.

CDK5 is amplified and over-expressed in pancreatic cancer and activated by mutant K-Ras
http://www.ncbi.nlm.nih.gov/pubmed/21825040
This *Clinical Cancer Research* study's senior author is Tony Hollingsworth, PhD (Scientific Advisory Board). The investigators found that amplification of the cyclin dependent kinase 5 (CDK5) gene, or either of its main activators, p35 and p39, was observed in 67 percent of human pancreatic ductal adenocarcinoma. Inhibition of CDK5 activity led to decreased invasion and migration of pancreatic cancer cell lines, and higher levels of CDK5 activity were observed in cells carrying a mutant K-Ras.

Decreased zinc and downregulation of ZIP3 zinc uptake transporter in pancreatic adenocarcinoma
http://www.ncbi.nlm.nih.gov/pubmed/21613827
University of Maryland, Baltimore press release:
http://www.oea.umaryland.edu/communications/news/?ViewStatus=FullArticle&articleDetail=14015
This *Cancer Biology & Therapy* article picked up some media attention. The authors evaluated zinc expression in pancreatic cancer cells, and determined that zinc is significantly decreased in ductal and acinar epithelium of pancreatic adenocarcinoma cells, as compared to normal pancreas epithelium. Additionally, the zinc uptake transporter ZIP3 was found to be genetically silenced in pancreatic cancer. Zinc was found to be toxic to a pancreatic cancer cell line.

Angiotensin II type 2 receptor blockade inhibits fatty acid synthase production through AMPK
http://www.ncbi.nlm.nih.gov/pubmed/21801966
Media attention: http://www.eurekalert.org/pub_releases/2011-08/tju-bri081011.php
Research out of Hwyda Arafat, MD, PhD's lab at Thomas Jefferson University suggests that angiotensin II type 2 receptor treatment increased fatty acid synthase expression and promoter activity in pancreatic cancer cells. Drugs that inhibit angiotensin II type 2 receptor and/or activate AMPK showed a chemopreventive and antilipogenic mechanism.

Tumor-specific expression and alternative splicing of the COL6A3 gene in pancreatic cancer
http://www.ncbi.nlm.nih.gov/pubmed/21719059
A similar team of Jefferson researchers also published this *Surgery* article last month. Collagen makes up a significant part of the dense desmoplastic reaction surrounding pancreatic tumors. Here, the authors look at collagen type VI, specifically COL6A3, and its alternatively spliced variants. They report that several exons of COL6A3 are alternatively spliced in pancreatic cancer tumor samples and cell lines. The relevance of this event in relation to signaling and diagnostics need to be further evaluated.

Tumor-infiltrating neutrophils in pancreatic neoplasia
http://www.ncbi.nlm.nih.gov/pubmed/21822201
Ralph Hruban, MD (Emeritus Scientific Advisory Board) contributed to this *Modern Pathology* paper. The authors examined the presence of tumor-infiltrating neutrophils in pancreatic cancer and precancerous lesions. Larger studies will be needed to investigate the association between tumor-infiltrating neutrophils and pancreatic neoplasms and their role in their clinical behavior.

The efficacy of IGF-I receptor monoclonal antibody against human gastrointestinal carcinomas
http://www.ncbi.nlm.nih.gov/pubmed/21642381
A monoclonal antibody against insulin-like growth factor I receptor (IGF-IR), figitumumab (CP-751,871), was tested in six GI cancer cell lines, including pancreatic. Figitumumab was found to block autophosphorylation of IGF-IR and its downstream signals, and suppressed tumorigenicity and proliferation. Encouragingly, the effects of figitumumab were independent of k-ras mutation status.

IGF1-R signals through the RON receptor to mediate pancreatic cancer cell migration
http://www.ncbi.nlm.nih.gov/pubmed/21565828
A team of UCSD scientists investigated the relationship between RON tyrosine kinase and insulin-like growth factor-1 receptor (IGF-1R). RON has been previously shown to be over-expressed in pancreatic cancer. Here, the authors demonstrate that IGF-1R activation leads to phosphorylation of RON, but not the reciprocal. Further, the IGF-1 ligand induces pancreatic cancer cell migration, in a manner dependent on RON activation.

MUC6 mucin expression inhibits tumor cell invasion
http://www.ncbi.nlm.nih.gov/pubmed/21851820
Here, the authors sought to determine whether the mucin MUC6 contributes to the etiology and/or progression of pancreatic cancer. Their results suggest that MUC6 may inhibit the invasion of pancreatic cancer cells through the basement membrane of the pancreatic duct.

Assessment of tumor vascularization in pancreatic adenocarcinoma using perfusion CT imaging
http://www.ncbi.nlm.nih.gov/pubmed/21765297
Delrue, *et al* utilized 128-slice perfusion computed tomography (CT) imaging to measure blood volume and blood flow in pancreatic tumors, compared to normal pancreas. They found that tumor tissue had 60 percent lower blood flow and blood volume than normal tissue of the pancreas.

Deficiency of the macrophage growth factor CSF-1 disrupts PNET development
http://www.ncbi.nlm.nih.gov/pubmed/21822305
Cornell researchers looked at tumor-associated macrophages in relation to pancreatic neuroendocrine tumors (PNET) progression. To measure the role of tumor-associated macrophages, CSF-1-deficient mice were crossed with a mouse model of PNET; CSF-1 deficiency leads to decreased macrophages. Results suggested that absence of CSF-1 reduced angiogenesis and tumor number, but not tumor growth itself. Further, other cytokines were up-regulated to compensate for the absence of CSF-1 and low number of macrophages.

Pancreatic cancer stem cells: new insights and perspectives
http://www.ncbi.nlm.nih.gov/pubmed/21698355
This review article describes pancreatic cancer stem cells' diverse functions, including self-renewal, differentiation, immune system evasion, and multidrug resistance, and discusses the possibility of therapeutically targeting this subset of cells.

ETIOLOGY

Pancreatic ductal adenocarcinoma in the setting of mutations in the CFTR gene
http://www.ncbi.nlm.nih.gov/pubmed/21809164
Researchers at Thomas Jefferson, including Jonathan Brody, PhD (2010 Skip Viragh – Pancreatic Cancer Action Network – AACR Career Development Award), published this *Journal of Gastrointestinal Surgery* subject review. Mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene are known to lead to CF as well as pancreatitis. Individuals with homozygous CFTR mutations are unlikely to live long enough to develop pancreatic ductal adenocarcinoma, but heterozygous mutation carriers may be. The authors conclude that patients with CFTR mutations, who also have other risks for the development of pancreatic cancer such as a family history of the disease, should undergo screening and be educated about their risks.

Insulin-like growth factor axis gene polymorphisms modify risk of pancreatic cancer
http://www.ncbi.nlm.nih.gov/pubmed/21852217
MD Anderson investigators looked at insulin-like growth factor (IGF)-axis genetic variants to determine if they affect the risk of pancreatic cancer. There were several examples of polymorphic variants of IGF-axis genes that were found to act alone or jointly with other risk factors to affect susceptibility to pancreatic cancer.

Mitochondrial DNA copy number and pancreatic cancer in the ATBC prevention study
http://www.ncbi.nlm.nih.gov/pubmed/21859925
To determine how mitochondrial DNA (mtDNA) copy number may impact pancreatic cancer risk, Lynch, *et al* conducted a nested case-control study in the Alpha-Tocopherol Beta Carotene Cancer Prevention

(ATBC) Study cohort. Their results demonstrated that higher mtDNA copy number was significantly associated with increased pancreatic cancer risk.

PREVENTION

Inhibition of chronic pancreatitis and PanIN by capsaicin in LSL-KrasG12D/Pdx1-Cre mice
http://www.ncbi.nlm.nih.gov/pubmed/21859833
Capsaicin, a component of chili peppers, has been shown to have some cancer preventive mechanism in other cancer types. Here, researchers at Northwestern looked at a K-Ras driven mouse model of pancreatic cancer. Upon treatment with caerulein and subsequent administration of capsaicin, the results suggested that capsaicin blocked inflammation (pancreatitis) and also inhibited the progression of PanIN lesions.

EARLY DETECTION, DIAGNOSIS, AND PROGNOSIS

Diagnosis and treatment of cystic pancreatic tumors
http://www.ncbi.nlm.nih.gov/pubmed/21397725
A team of Indiana University researchers, including Max Schmidt, MD, PhD (2003 Pancreatic Cancer Action Network – AACR Career Development Award), review approaches to the diagnosis and management of serous and mucinous cystic pancreatic tumors.

A single-institution review of patients presenting with benign & malignant tumors of ampulla of Vater
http://www.ncbi.nlm.nih.gov/pubmed/21801957
Research out of the Wash-U St. Louis lab of William Hawkins, MD (2005 Skip Viragh – Pancreatic Cancer Action Network – AACR Career Development Award) sought to determine the best surgical strategy for patients with T1 localized tumors: endoscopic removal of pancreaticoduodenectomy. The best predictors of malignancy were larger tumors and jaundice. The authors conclude that pancreaticoduodenectomy is recommended for any patient with biopsy proven adenocarcinoma who is a suitable candidate for surgery.

Differentiation of pancreatic cysts with optical coherence tomography imaging: an ex vivo pilot study
http://www.ncbi.nlm.nih.gov/pubmed/21833374
Media attention: http://www.eurekalert.org/pub_releases/2011-08/osoa-nis081711.php
Iftimia, *et al* investigated the use of optical coherence tomography (OCT) to diagnose pancreatic cysts. Their *ex vivo* findings suggest that OCT can reliably distinguish between morphologic features of low risk pancreatic cysts (e.g., pseudocysts and serous cystadenomas) and high risk pancreatic cysts (e.g., mucinous cystic neoplasms and intraductal papillary mucinous neoplasms). The investigators will next work on developing and implementing a probe that would attach to a pancreas biopsy needle, and allow for *in vivo* analyses of cysts.

Claudin-4 expression predicts survival in pancreatic ductal adenocarcinoma
http://www.ncbi.nlm.nih.gov/pubmed/21837532
This *Annals of Surgical Oncology* paper reports the prognostic value of claudin-4 in pancreatic ductal adenocarcinoma. Overall, the authors found that increased expression of claudin-4 predicted for better survival in pancreatic cancer patients.

Prognostic significance of erythropoietin in pancreatic adenocarcinoma
http://www.ncbi.nlm.nih.gov/pubmed/21829709
Published in *PLoS One*, this article explores patients' endogenous serum levels of erythropoietin (sEpo), hemoglobin, and tissue Epo and Epo receptor expression. The authors' data suggest that higher levels of sEpo protect from anemia, but represent a poor prognostic indicator for pancreatic ductal adenocarcinoma patients.

Detection of KRAS gene mutations in endoscopic ultrasound-guided fine-needle aspiration biopsy
http://www.ncbi.nlm.nih.gov/pubmed/21876563
The authors proposed adding mutational analyses of KRAS to biopsies taken via endoscopic ultrasound-guided fine-needle aspiration. Wang and colleagues demonstrated that KRAS mutation status, or KRAS mutation in addition to CA19-9 value, showed a significantly higher detection rate and specificity than CA19-9 alone.

EUS is still superior to multidetector computerized tomography for detection of PNETs
http://www.ncbi.nlm.nih.gov/pubmed/21067742
A team of Johns Hopkins researchers, including Ralph Hruban, MD (Emeritus Scientific Advisory Board), performed a retrospective single-center cohort study to compare endoscopic ultrasound (EUS) to computerized tomography (CT) in the detection of pancreatic neuroendocrine tumors (PNETs). Although CT scanning has improved over time, EUS is still superior at detecting suspected insulinomas.

UH pancreatic cancer study focuses on early tumor detection
http://www.cleveland.com/healthfit/index.ssf/2011/08/uh_study_looks_to_improve_dete.html
Researchers at University Hospitals Seidman Cancer Center in Cleveland are exploring a synthetic version of the protein secretin to aid in pancreatic cancer diagnosis. The company Repligen Corp. has developed a synthetic secretin called RG1068. RG1068 "tricks" the pancreas into functioning as if naturally produced secretin was present. That means more blood flow to the pancreas and, it is hoped, a way to facilitate spotting tumors, even the smallest ones.

Prognosis in Palliative care Study predictor models to improve prognostication in advanced cancer
http://www.ncbi.nlm.nih.gov/pubmed/21868477
A prospective multicenter observational cohort study spearheaded by St. George's University of London looked at developing a composite model to predict which advanced (metastatic or locally advanced, no longer receiving curative treatment) cancer patients were likely to survive for days, weeks, or months. The investigators conclude that, in patients with advanced cancer no longer being treated, a combination of clinical and laboratory variables can reliably predict two week and two month survival.

TREATMENT

Brivanib is active both first and second line against mouse pancreatic neuroendocrine tumors
http://www.ncbi.nlm.nih.gov/pubmed/21622725
The senior author of this *Clinical Cancer Research* paper is Doug Hanahan, PhD (2007 Pancreatic Cancer Action Network Pilot Grant). Brivanib, a dual VEGF/FGF inhibitor, was tested preclinically in a mouse model of pancreatic neuroendocrine cancer. Effects of brivanib were compared to drugs which only block either VEGF or FGF signaling. Dr. Hanahan and colleagues found that brivanib produced enduring

tumor stasis and angiogenic blockade, as both first and second line treatment following the failure of other anti-angiogenic drugs.

A pilot clinical study of treatment guided by personalized tumorgraft in patients with advanced cancer
http://www.ncbi.nlm.nih.gov/pubmed/21673092
This *Molecular Cancer Therapeutics* article follows another paper published in the same journal earlier this year (http://www.ncbi.nlm.nih.gov/pubmed/21135251), which described using a mouse xenograft of a patient's pancreatic tumor to select treatment options for the patient. Here, the authors collected tissue from 14 patients who underwent surgery for refractory, advanced cancer, and implanted specimens into mice. Four of the 14 patients had been diagnosed with pancreatic ductal adenocarcinoma. The investigators found a significant correlation between xenografted tumors' response to treatment, and the corresponding patients' sensitivity to the same drug.

Armed and targeted measles virus for chemovirotherapy of pancreatic cancer
http://www.ncbi.nlm.nih.gov/pubmed/21701532
This study out of the German Cancer Research Center was published in *Cancer Gene Therapy*. Measles virus targeted to PSCA (prostate stem cell antigen; prevalent on the surface of pancreatic cancer cells), expressing the prodrug convertase purine nucleoside phosphorylase, was tested in a pancreatic cancer xenograft mouse model. Beneficial therapeutic effects were shown.

Impact of KRAS mutations on clinical outcomes in pancreatic cancer patients
http://www.ncbi.nlm.nih.gov/pubmed/21862683
This *Molecular Cancer Therapeutics* article describes retrospective analysis of pancreatic cancer patients treated with gemcitabine and erlotinib or gemcitabine alone, and their responses in relation to KRAS mutation status. They found that KRAS-mutant patients treated with gemcitabine/erlotinib showed a poorer response to treatment than those with wild-type KRAS. There was not an association between KRAS mutation and response to gemcitabine alone. Prospective studies will be necessary before personalized medicine recommendations can be made.

Adjuvant gemcitabine versus NEOadjuvant gemcitabine/oxaliplatin plus adjuvant gemcitabine
http://www.ncbi.nlm.nih.gov/pubmed/21831266
Heinrich, *et al* describe a prospective, randomized multi-center phase III trial abbreviated NEOPAC: adjuvant gemcitabine versus NEOadjuvant gemcitabine/oxaliplatin plus adjuvant gemcitabine in resectable PAncreatic Cancer. This study will provide insight into the efficacy of adjuvant chemotherapy and patients' overall survival following surgery of tumors in the pancreatic head.

The use of GTX as 2nd-line chemotherapy for metastatic pancreatic cancer: a retrospective analysis
http://www.ncbi.nlm.nih.gov/pubmed/21850466
Duke researchers retrospectively analyzed the use of GTX (gemcitabine, docetaxel, and capecitabine) regimen for second-line treatment of metastatic pancreatic cancer patients. GTX showed activity in this patient population, and individuals with better performance status and who showed a decrease in CA19-9 showed better survival.

Combining betulinic acid and mithramycin A effectively suppresses pancreatic cancer
http://www.ncbi.nlm.nih.gov/pubmed/21673052
This *Cancer Research* paper represents a collaborative, international effort. Gao, *et al* look at mouse pancreatic cancer xenografts treated with betulinic acid, mithramycin A, and the combination. Treatment with either drug alone led to toxicity, but a combination of both drugs at a nontoxic dose was tolerable and led to inhibitory effects on cell proliferation, invasion, and angiogenesis. As both drugs function through Sp1 inhibition, over-expression of Sp1 blocked the inhibitory effects of the combined treatment.

New approaches to treatment of pancreatic cancer: from tumor-directed therapy to immunotherapy
http://www.ncbi.nlm.nih.gov/pubmed/21815696
This review is co-written by Maeve Lowery, MD and Eileen O'Reilly, MD (Medical Advisory Board) from Sloan-Kettering. Drs. Lowery and O'Reilly discuss recent advancements in pancreatic cancer therapy and promising agents, focused on immune-directed treatments and vaccines.

New strategies & designs in pancreatic cancer research: guidelines report from European expert panel
http://www.ncbi.nlm.nih.gov/pubmed/21810728
This report offers a consensus strategy from multidisciplinary panel of experts from different European institutions and collaborative groups involved in pancreatic cancer. Ways to improve clinical trials and reminders to focus on the tumor microenvironment, in addition to the cancer cells themselves, are described.

An ultrasonically-powered implantable micro oxygen generator (IMOG)
http://www.ncbi.nlm.nih.gov/pubmed/21824840
Media attention: http://www.eurekalert.org/pub_releases/2011-08/pu-tog083111.php
Research out of Babak Ziaie, PhD's lab at Purdue explored the idea of adding oxygen to tumors to improve the effectiveness of radiation therapy. They performed experiments in a mouse model of pancreatic cancer, as the disease is notoriously hypoxic. Their ultrasonically-powered IMOG device is capable of in situ tumor oxygenation through water electrolysis.

FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer
http://www.ncbi.nlm.nih.gov/pubmed/21864184
Researchers at the Regina Elena National Cancer Institute in Rome, Italy wrote this correspondence to the *NEJM* in response to Conroy, *et al*'s paper describing the study comparing FOLFIRINOX to gemcitabine in metastatic pancreatic cancer (http://www.ncbi.nlm.nih.gov/pubmed/21561347).

Surgical management of neuroendocrine tumors of the gastrointestinal tract
http://www.cancernetwork.com/gastrointestinal-cancer/content/article/10165/1921828
Commentary: Neuroendocrine Tumors: a Heterogeneous Set of Neoplasms: http://www.cancernetwork.com/gastrointestinal-cancer/content/article/10165/1921838?GUID=4205A703-5E76-43B8-BA2D-20A552A43187&rememberme=1&ts=18082011
This review article by Stanford researchers and commentary by Dr. Kooby at Emory discuss the surgical management of gastrointestinal neuroendocrine tumors, including the preoperative control of hormonal

symptoms, extent of resection required, postoperative outcomes, and differing management strategies as determined by whether the tumor has arisen sporadically or as part of a familial disorder.

Infinity reports second quarter 2011 financial results
http://www.marketwatch.com/story/infinity-reports-second-quarter-2011-financial-results-2011-08-09?reflink=MW_news_stmp
Infinity Pharmaceuticals, Inc is testing its Hedgehog inhibitor IPI-926 in pancreatic cancer, hoping to complete enrollment of their Phase 2 trial (IPI-926 in combination with gemcitabine) by the second half of this year. Infinity also announced an expanded investigator-sponsored trial combining IPI-926 with FOLFIRINOX in previously untreated advanced pancreatic cancer patients. This trial is sponsored by Andrew Ko, MD (2003 Pancreatic Cancer Action Network – ASCO Career Development Award) at UCSF.

Clavis Pharma second quarter and first half report 2011
http://pharmalive.com/News/index.cfm?articleid=800285&categoryid=36%2C61
Clavis Pharma, a Norwegian cancer drug development company, has several pancreatic cancer drugs in ongoing clinical trials. CP-4126, a gemcitabine analog, is being compared to gemcitabine in their expanded "LEAP" study. They also embarked on an open-label Phase II study of CP-4126 in gemcitabine-refractory pancreatic cancer patients. Finally, Clavis is retrospectively analyzing hENT1 (human Equilibrative Nucleoside Transporter 1) levels to define criteria for high/low expression, to determine hENT1's predictive value in response to nucleoside analog treatments.

U.S. scrambling to ease shortage of vital medicine
http://www.nytimes.com/2011/08/20/health/policy/20drug.html?_r=4
This *NY Times* article describes an alarming shortage of many potentially lifesaving drugs, including those for certain types of cancer, and discusses possible short- and long-term solutions.

SURVIVORSHIP

Early endoscopic ultrasound-guided celiac plexus neurolysis to prevent pain progression
http://www.ncbi.nlm.nih.gov/pubmed/21844506
This *JCO* article discusses a randomized, double-blind, controlled trial of early endoscopic ultrasound-guided celiac plexus neurolysis (EUS-CPN) to prevent pain progression in patients with newly diagnosed, painful, inoperable pancreatic cancer. They found that early EUS-CPN at diagnosis relieved pain and somewhat decreased morphine usage, compared to patients receiving conventional pain management. There was no change in survival or quality of life score.

Feasibility of a pancreatic cancer surveillance program from a psychological point of view
http://www.ncbi.nlm.nih.gov/pubmed/21857231
High-risk individuals participating in an endoscopic ultrasonography-magnetic resonance imaging-based pancreatic cancer surveillance program received a questionnaire assessing experiences with each imaging modality, reasons to participate, psychological distress, and benefits and barriers of surveillance. Overall, the large majority patients reported that the advantages of surveillance outweighed the disadvantages.

Music interventions for improving psychological and physical outcomes in cancer patients

http://www.ncbi.nlm.nih.gov/pubmed/21833957

NY Times write-up:

http://www.nytimes.com/2011/08/16/health/research/16regimens.html?_r=2&ref=research

Drexel University researchers retrospectively analyzed data from randomized controlled trials and quasi-randomized trials of music interventions for improving psychological and physical outcomes in patients with cancer. Their findings suggest that musical interventions may be beneficial for cancer patients, in regard to anxiety, pain, mood, and quality of life, with potential improvements in respiration, heart rate, and blood pressure.