PANCREATIC CANCER NEWS & UPDATES – DECEMBER 2011

PANCREATIC CANCER ACTION NETWORK AND COMMUNITY NEWS

AACR Special Conference – Pancreatic Cancer: Progress and Challenges – registration is open
The first AACR special conference on pancreatic cancer will take place June 18-21, 2012 at the Hyatt Regency Lake Tahoe, Nevada. Registration is now open. The deadline for abstract submission and award application is Wednesday, April 11, and advance registration closes on Monday, May 7.

Pancreatic Cancer Action Network receives $1.4 million from Daniel and Janet Mordecai Foundation
The Daniel and Janet Mordecai Foundation have generously donated $1.4 million to support the Pancreatic Cancer Action Network 2012 research grants program. Their investment will provide funding for one Pathway to Leadership Grant and four Career Development Awards.

Ranked nonprofits: national cancer
http://www.myphilanthropedia.org/top-nonprofits/national/cancer
The Pancreatic Cancer Action Network was named as one of the top high-impact cancer nonprofit organizations in US. Based on a survey of experts in the field, Philanthropedia determined the top 16 most outstanding cancer nonprofit organizations in the country. The Pancreatic Cancer Action Network was tied for seventh place!

Pancreatic Cancer Research video: Jordan Berlin
http://www.youtube.com/watch?v=reD9sji_uRk
Through the Vanderbilt Health You Tube site, Jordan Berlin, MD (Chair, Medical Advisory Board) is featured in this video describing pancreatic cancer research and the importance of clinical trials.

Clinical Cancer Advances 2011: Annual Report on Progress Against Cancer From ASCO
http://jco.ascopubs.org/content/30/1/88.full
The Journal of Clinical Oncology published this year-end report describing progress in the fight against cancer. Newly approved drugs to treat pancreatic neuroendocrine tumors are discussed as a major accomplishment in 2011.

WebMD: 2011’s Great Health Race
WebMD revealed that “pancreatic cancer symptoms” was the top-trending search in 2011, surrounding the death of Steve Jobs.
Fund A Cure makes donation to Thomas Jefferson University Hospital
The nonprofit Fund A Cure raised $30,000 at the annual Newtown Run Over Cancer 5K, and have donated the money to the pancreatic cancer research team at Thomas Jefferson University Hospital, co-led by Charlie Yeo, MD and Jonathan Brody, PhD (2010 Skip Viragh Career Development Award).

Thomas Jefferson University receives Science Center’s QED award for pancreatic cancer research
http://www.newswise.com/articles/thomas-jefferson-university-receives-science-center-s-qed-award-for-pancreatic-cancer-research
This award is named QED to stand for Quod Erat Demonstrandum, or “proven as demonstrated.” A team of researchers at Thomas Jefferson University received this $200,000 award to devote to developing a diagnostic test for pancreatic cancer. In addition to the monetary prize, the team will gain access to one year of business guidance from the Science Center entrepreneurs.

BIOLOGY OF CANCER
A novel FoxM1-Caveolin signaling pathway promotes pancreatic cancer invasion and metastasis
Craig Logsdon, PhD (Scientific Advisory Board) and Daoyan Wei, PhD (2006 Career Development Award) are authors on this Cancer Research publication. Caveolin-1 (Cav-1) is a principal component of caveolar membrane domains, and is transcriptionally regulated by FoxM1. Here, the authors demonstrate that increased expression of Cav-1 leads to epithelial-to-mesenchymal transition, invasion, and metastasis of pancreatic cancer cells in a mouse model or human tissue samples. Up-regulation of FoxM1 had the same effects, and both could be inhibited by appropriate siRNAs.

Pancreatic ductal cells in development, regeneration, and neoplasia
This Journal of Clinical Investigation review is coauthored by Max Reichert, MD and Anil Rustgi, MD (Scientific Advisory Board) at University of Pennsylvania. Drs. Reichert and Rustgi describe the three major cellular lineages of the pancreas, with particular emphasis on pancreatic ductal cells.

Constitutive K-RasG12D activation of ERK2 specifically regulates 3D invasion of pancreatic cancer cells
Anil Rustgi, MD (Scientific Advisory Board) is also an author on this article. A 3D model of pancreatic cancer cell invasion is created using pancreatic ductal epithelial cells on a basement membrane. When K-Ras is mutated to its active form in these cells, invasion takes place. The invasion was found to be dependent on the activity of Erk2 and MMP1.

Cathepsin B promotes the progression of pancreatic ductal adenocarcinoma in mice
This study is out of the laboratory of Dave Tuveson, MD, PhD (2003 Career Development Award and Chair, Scientific Advisory Board). Dr. Tuveson and colleagues crossed a mouse with a Kras mutation specific to its pancreas with a mouse deficient for cathepsin B, to see effects on the development pancreatic intraepithelial neoplasia (PanIN). This same experiment was also conducted in mice with
both Kras and p53 mutations to evaluate the role of cathepsin B in pancreatic ductal adenocarcinoma formation. The absence of cathepsin B indeed slowed the development of disease in both experimental models, and conferred a growth advantage to the mice.

**Genome-wide CpG island profiling of intraductal papillary mucinous neoplasms of the pancreas**
Ralph Hruban, MD (Emeritus Scientific Advisory Board) contributed to this *Clinical Cancer Research* paper. The authors looked at CpG island methylation profiling of pancreatic precursor lesions, intraductal mucinous neoplasms (IPMNs). They found multiple sites of hypermethylation, including one gene, BNIP3, whose methylation status may be clinically useful in evaluating aggressiveness of IPMNs.

**Key contribution of CPEB4-mediated translational control to cancer progression**
*Nature Medicine* published this article describing the expression and function of cytoplasmic polyadenylation element binding protein 4 (CPEB4) in cancer progression, using pancreatic adenocarcinoma as a model. CPEB4, an RNA-binding protein, is over-expressed in pancreatic cancer, and its activity leads to tumor growth and invasion through translational activation of silenced mRNAs.

**Immune recognition of mucin MUC1 by a fully synthetic aberrantly glycosylated tripartite vaccine**
The mucin MUC1 is often expressed on the surface of epithelial cancer cells, including pancreatic. As opposed to normal cells, the cancer version of MUC1 is aberrantly glycosylated with truncated O-linked saccharides. These authors are striving to capitalize on this MUC1 by developing a vaccine specific for the aberrantly glycosylated version of MUC1. Preliminary data suggest that the vaccine elicits an immune response in mice and leads to shrinking of the tumor.

**Mucin 16 is a functional selectin ligand on pancreatic cancer cells**
Chen *et al* wrote this *FASEB Journal* article analyzing mucin 16 (MUC16) in metastatic pancreatic cancer cells. They found that MUC16 is over-expressed, and, upon sialofucosylation, binds E- and L-selectin. Turning off MUC16 expression by siRNA led to decreased association with E- and L-selectin, and could perhaps interfere with invasion and metastasis of pancreatic cancer cells.

**The desmoplastic stroma plays an essential role in the accumulation, modulation of immune cells**
*Clinical and Developmental Immunology* published this paper to characterize how the desmoplastic stroma influences the infiltrating immune cells around a pancreatic tumor. Modulating the stroma to attract dendritic cells or promote the conversion of monocytes into dendritic cells could help train the immune system to fight the tumor.
N-cadherin haploinsufficiency increases survival in a mouse model of pancreatic cancer
Investigators at Thomas Jefferson University sought to determine the role of the cell adhesion factor N-cadherin in pancreatic cancer progression. They utilized a previously described mouse model of pancreatic cancer, and found that, when there was decreased expression of N-cadherin (due to only one functional copy of the N-cadherin gene, rather than two), the mice lived longer. This finding implicates N-cadherin as a potential therapeutic target in the treatment of pancreatic cancer.

Recruitment of HDAC1 and HDAC2 by the transcriptional repressor ZEB1 downregulates E-cadherin
A ZEB1-HDAC pathway enters the epithelial to mesenchymal transition world in pancreatic cancer
Gut published this article and accompanying commentary. Aghdassi et al evaluated primary pancreatic cancer tissue specimens and cell lines, and established that histone deacetylases HDAC1 and HDAC2, when activated by the zinc-finger transcription factor ZEB1, were responsible for down-regulation of E-cadherin expression characteristic of epithelial-to-mesenchymal transition.

Whole-exome sequencing, characterization of genomic instability caused by MLH1 haploinsufficiency
Genome Research published this study out of Japan, looking at how copy number of the DNA repair gene MLH1 influences mutation rates in pancreatic cancer cells. The authors found that hemizygous or complete deletion of MLH1 led to an increase in the rate of small insertion/deletion mutations.

Selective radiosensitization of p53 mutant pancreatic cancer cells by inhibition of Chk1 and PARP1
Members of the Radiation Oncology team at University of Michigan prepared this Cell Cycle publication. The authors opted to inhibit both Chk1 (to block homologous recombination repair, and to specifically radiosensitize p53-mutant cells) and PARP1 (to radiosensitize cells with double-strand break repair defects) in pancreatic cancer cells. Per their hypothesis, they found that combined inhibition of Chk1 and PARP1 selectively radiosensitized p53-mutant pancreatic cancer cells.

Targeting the hedgehog signaling pathway with interacting peptides to Patched-1
This Journal of Gastroenterology manuscript describes a novel strategy to target the protein Patched-1 (Ptch1) in pancreatic cancer. Within the hedgehog signaling pathway, Ptch1 serves as a repressor. Its activity is inhibited by over-expression of hedgehog ligands, such as sonic hedgehog (Shh), in cancer cells. In this study, the authors designed seven peptides to bind and block the Shh binding site on Ptch1, and found three compounds that impeded pancreatic cancer cell proliferation, and decreased the expression of Gli1, a transcription factor downstream of Shh signaling.
Dual combination therapy targeting DR5 and EMMPRIN in pancreatic adenocarcinoma
Xenograft mouse models of two pancreatic cancer cell lines were established, and treated with anti-DR5 antibody, anti-EMMPRIN antibody, both, or neither. Kim and colleagues demonstrated that the additive effects of combination treatment suppressed tumor growth in both xenograft model systems.

Emodin reverses gemcitabine resistance in pancreatic cancer via mitochondrial apoptosis pathway
A gemcitabine-resistant pancreatic cancer cell line was created by constantly exposing the cells to increasing concentrations of gemcitabine. The authors then demonstrated that pretreatment with emodin, a natural chemical supplement that is extracted from the root of the Turkish rhubarb plant, caused the cells to be sensitive to gemcitabine treatment, via a mitochondrial apoptotic pathway.

The dual PI3K/mTOR inhibitor NVP-BGT226 induces cell cycle arrest and regulates Survivin expression
This *Tumour Biology* article describes experiments testing the dual PI3K/mTor inhibitor NVP-BGT226 in various pancreatic cancer cell lines. The authors observed G0/G1 cell cycle arrest in the cells, as well as a decrease in the expression of Survivin. These effects appeared to be mediated only by inhibition of mTor, and not PI3K.

Omega-3-polyunsaturated fatty acids suppress pancreatic cancer cell growth in vitro and in vivo
A team of researchers in Korea sought to determine the relationship between omega-3-polyunsaturated fatty acids and beta-catenin in pancreatic cancer cells. Exposure to the omega-3-fatty acids docosahexaenoic acid and eicosapentaenoic acid inhibited cell growth and induced cell death, mediated by the Wnt/b-catenin signaling pathway.

MicroRNAs associated with mitogen-activated protein kinase in human pancreatic cancer
Ikeda *et al* looked at the connection between expression of microRNAs and activity of the mitogen-activated protein kinase (MAPK) pathway in pancreatic cancer cells. They found four microRNAs differentially expressed based on MAPK signaling; one was up-regulated by active MAPK and three were down-regulated.

Pancreatic cancer cells & normal pancreatic duct epithelial cells express autocrine catecholamine loop
To better understand the mechanism by which smoking is associated with pancreatic cancer risk, these University of Tennessee researchers studied the effects of nicotine on pancreatic cancer cell lines. Their data suggested an autocrine catecholamine loop activated by nicotinic acetylcholine receptors alpha-3, alpha-5, and alpha-7.
The proline TP53 variant stimulates likely lymphangiogenesis in an orthotopic mouse model
This *British Journal of Cancer* publication describes an effort to re-express wild type p53 in mutant-p53 pancreatic cancer cells that were used in a subcutaneous xenograft mouse model. Although primary tumor weight decreased, the re-expression of p53 led to increased vascularization and subsequent development of micro-metastases. Further experimentation in other model systems is warranted.

**ETIOLOGY**

**ATM** mutations in patients with hereditary pancreatic cancer
http://cancerdiscovery.aacrjournals.org/content/early/2011/12/23/2159-8290.CD-11-0194.abstract?sid=dfa81427-d56c-40d5-8046-d4beb1613269
This collaborative study features Gloria Petersen, PhD (Scientific Advisory Board) from the Mayo Clinic, and Ralph Hruban, MD (Emeritus Scientific Advisory Board) and Jim Eshleman, MD, PhD (2011 Innovative Grant) from Johns Hopkins. The authors performed next generation sequencing on patients with familial pancreatic cancer, compared to healthy spouse controls. Mutations in the ataxia telangiectasia mutated (ATM) gene were found in several cases, indicating that ATM might represent a predisposition gene for pancreatic cancer.

Pancreatic cancer risk and levels of trace elements
NY Times article: *Patterns: Trace Elements and Pancreatic Cancer Risk*
This Gut article picked up a great deal of media attention, as evidenced by the *NY Times* story posted above. Scientists at the Spanish National Cancer Research Centre detected trace elements in the toenails of pancreatic cancer patients and controls. Their results suggest that individuals with high levels of cadmium, arsenic, or lead were at increased risk of developing pancreatic cancer. By contrast, elevated levels of selenium or nickel were inversely correlated with pancreatic cancer risk. The authors do not recommend changes in dietary supplementation in response to these results.

*Molecular Carcinogenesis* Special Issue: Epidemiology & Etiological Mechanisms in Pancreatic Cancer
Gloria Petersen, PhD (Scientific Advisory Board) is among the editors of this special edition of *Molecular Carcinogenesis* devoted to pancreatic cancer epidemiology and etiology. Click above to see the individual articles, all of which are open-access.

Genome-wide association study identifies five loci associated with susceptibility to pancreatic cancer
*Nature Genetics* reports on a large genome-wide association study searching for susceptibility loci to pancreatic cancer in Chinese populations. Upon validation in an easier larger population, the researchers identified five new pancreatic cancer susceptibility loci at chromosomes 21q21.3, 5p13.1, 21q22.3, 22q13.32, and 10q26.11, as well as 13q22.1, which had previously been detected in individuals with European ancestry.
Is dietary fat, vitamin D, or folate associated with pancreatic cancer?
Sanchez and colleagues at the NCI and George Washington University review the relationship between pancreatic cancer and some lesser-known potential risk factors, such as dietary fat (particularly from animal sources), vitamin D, or folate intake.

Mitochondrial DNA sequence variation and risk of pancreatic cancer
Published in Cancer Research, this paper describes how variations in mitochondrial DNA (mtDNA) could be associated with risk of pancreatic cancer. Data from a San Francisco Bay Area pancreatic cancer case-control study suggested that aggregated common and rare variants, and singleton variants of mtDNA contribute to pancreatic cancer risk.

Coffee, tea and sugar-sweetened carbonated soft drink intake and pancreatic cancer risk
A collaborative team of researchers undertook a pooled analysis of 14 prospective cohort studies evaluating the association between adult intake of coffee, tea, and sugar-sweetened carbonated beverages, and pancreatic cancer. The results suggested no relationship involving coffee or tea, and potentially a modest increase of pancreatic cancer risk from sugar-sweetened beverage consumption.

Routine testing PALB2 mutations in familial pancreatic, breast cancer families with pancreatic cancer
The European Journal of Human Genetics published this article describing the prevalence of PALB2 mutations in a Dutch cohort of non-BRCA2 mutant familial pancreatic or familial breast cancer (with at least one instance of pancreatic cancer) populations. Their data suggest that PALB2 mutation does not have a major causal role in this group of patients, and screening is therefore not indicated.

EARLY DETECTION, DIAGNOSIS, AND PROGNOSIS
Whole-exome sequencing of neoplastic cysts of the pancreas reveals recurrent mutations
Authors on this PNAS paper include Anirban Maitra, MD (2004 Career Development Award and Scientific Advisory Board), Jim Eshleman, MD, PhD (2011 Innovative Grant), and Ralph Hruban, MD (Emeritus Scientific Advisory Board) at Johns Hopkins, as well as Max Schmidt, MD, PhD (2003 Career Development Award) from Indiana University. The investigators performed whole-exome sequencing of samples of the four major types of pancreas cysts: serous cystadenomas (SCAs), intraductal papillary mucinous neoplasms (IPMNs), mucinous cystic neoplasms (MCNs), and solid pseudopapillary neoplasms (SPNs). The data suggest that each type of neoplastic cyst has characteristic mutational profiles, and that all involve mutations in components of ubiquitin-dependent pathways.
Histologic tumor involvement of superior mesenteric vein/portal vein predicts poor prognosis
Huamin Wang, MD, PhD (2007 Skip Viragh Career Development Award) is the final author and Jason Fleming, MD (Medical Advisory Board) is also an author on this Cancer publication. The researchers evaluated 225 consecutive patients with stage II pancreatic adenocarcinoma who received neoadjuvant chemoradiation and pancreaticoduodenectomy with or without superior mesenteric vein/portal vein (SMV/PV) resection. Histologic tumor involvement of SMV/PV proved to be a poor prognostic indicator, warranting complete histological analysis of the SMV/PV in patients with pancreatic cancer.

A pilot study to explore circulating tumour cells in pancreatic cancer as a novel biomarker
Khoja et al wrote this British Journal of Cancer article exploring circulating tumor cells (CTCs) in pancreatic cancer. Blood samples of pancreatic cancer patients were analyzed by CellSearch, which exploits immunomagnetic capture of CTCs expressing epithelial markers, or isolation by size of epithelial tumor cells (ISET), a marker independent, blood filtration device. The results showed that ISET detects more CTCs than CellSearch and allows for biological characterization of the samples.

Identifying patients with pancreatic cancer in primary care: derivation and validation of algorithm
http://www.ingentaconnect.com/content/rcgp/bjgp/2012/00000062/00000594/art00022
This story picked up a good amount of media attention last month. Researchers at the University of Nottingham utilize the QResearch® primary care database to develop a risk prediction algorithm for identifying those at risk for pancreatic cancer. This algorithm can be used by clinicians to point out patients that might require further screening, and is also available on the internet for the general population (http://www.qcancer.org/pancreas/).

Serum HSP70: A novel biomarker for early detection of pancreatic cancer
Published in Pancreas, this collaborative study explores whether HSP70 is detectable in pancreatic cancer patients’ serum. Their results demonstrated that serum HSP70 was statistically significantly higher in pancreatic cancer patients’ serum, compared to serum of individuals with chronic pancreatitis or healthy controls.

New-onset diabetes patients need pancreatic cancer screening?
A team of researchers at Sungkyunkwan University in Seoul, Korea evaluated whether patients with new-onset diabetes should be screened for pancreatic cancer. Their findings suggest that patients with recent adult-onset diabetes, who are elderly, suffered weight loss, and no family history of diabetes, should be screened for the possibility of pancreatic cancer.
Pharmacokinetically stabilized cystine knot peptides that bind alpha-v-beta-6 integrin for detection
Kimura and colleagues at Stanford designed highly stable cystine knot peptides to bind specifically and with high affinity to alpha-v-beta-6-integrin for detection of pancreatic cancer. Imaging via PET demonstrated that these peptides quickly and specifically accumulate in tumor tissue, with impressive tumor-to-muscle ratios. Further optimization will be necessary.

Prognostic factors for survival and resection in patients with initial nonresectable pancreatic cancer
A team of researchers from the University of Southern Denmark looked for clues of which patients diagnosed with nonresectable, locally advanced pancreatic cancer would best benefit from chemoradiation. Patients who were ultimately able to undergo surgical resection fared better, and those with Stage III disease showed low likelihood of sufficient tumor regression to allow surgery. Patients who received gemcitabine treatment before chemoradiotherapy had a better prognosis, and patients with increasing tumor volume and/or abnormal hemoglobin levels had worse outcomes.

CA 19-9–EUS pancreatic cancer screen debated
Gastroenterology & Endoscopy News featured this article discussing the findings published a few months ago in “Screening for pancreatic cancer in a high-risk population with serum CA 19-9 and targeted EUS: a feasibility study” (http://www.ncbi.nlm.nih.gov/pubmed?term=21704809). Zubarik and colleagues reported that a screening protocol of measuring CA19-9 followed by targeted endoscopic ultrasound (EUS) could be beneficial to detect pancreatic cancer in high-risk individuals. Vince Picozzi, MD (Medical Advisory Board) is quoted in the article as unconvinced.

CA 19-9 in pancreatic cancer: retrospective evaluation of patients with suspicion of pancreatic cancer
CA19-9 is also discussed in this Tumour Biology paper. Here, suspected pancreatic cancer patients in Barcelona had CA19-9 measurements taken. Patients with pancreatic adenocarcinoma had significantly higher levels of CA19-9 than those without malignant disease or neuroendocrine tumors. Further, CA19-9 levels correlated with larger tumors and metastatic spread, particularly to the liver. When the patient also presented with jaundice, CA19-9 was an especially useful diagnostic test.

Repligen sends pancreatic diagnostic to FDA
Repligen Corporation is seeking FDA approval on their compound SecreFlo, a synthetic version of the intestinal hormone secretin. Phase 3 studies of SecreFlo plus MRI showed promising results in the detection of pancreatic duct abnormalities. They are hoping to eventually develop SecreFlo as a diagnostic for pancreatic cancer.
**TREATMENT**

**FOLFIRINOX: A great leap forward, but for whom?**

http://jco.ascopubs.org/content/30/1/114.2.full?cmpid=jco_etoc_1January2012#ref-list-1

Andrew Ko’s reply: http://jco.ascopubs.org/content/30/1/115.full?cmpid=jco_etoc_1January2012

*JCO* received this letter to the editor in response to an article written by Andrew Ko, MD (2003 Career Development Award). Dr. Ko’s original article can be found here: http://jco.ascopubs.org/content/29/28/3727.full?ijkey=342cea5da766b03274afe1acc94e5048af48edd9 &keytype2=tf_ipsecsha. Dr. Ko also wrote a response to dos Santos *et al*. The authors are discussing the potential of FOLFIRINOX to become a new standard of care for pancreatic cancer patients.

**Genomics and pharmacogenomics of pancreatic adenocarcinoma**


Maeve Lowery, MD and Eileen O'Reilly, MD (Medical Advisory Board) wrote this feature review in *The Pharmacogenomics Journal*. Current treatment options of pancreatic cancer are discussed, as well as successes and failures in trials of novel drugs and combinations. New knowledge of the genetics and pharmacogenomics show promise in leading to more effective treatments.

**Downstaging in pancreatic cancer: matched analysis of patients resected following systemic treatment**


Eileen O'Reilly, MD (Medical Advisory Board) also participated in this study out of Memorial Sloan-Kettering Cancer Center. The study was designed to evaluate patients diagnosed with stage III pancreatic cancer whose tumors were initially deemed unresectable. These patients responded well enough to chemotherapy or chemoradiation, allowing them to become surgical candidates. After resection, the initially unresectable patients were able to achieve the same overall survival rates as stage III patients who were able to undergo surgery immediately upon diagnosis.

**GOFURTGO Study: AGITG Phase II Study of gemcitabine-oxaliplatin integrated with 5FU, radiotherapy**


The *British Journal of Cancer* reports a clinical trial sponsored by the Australasian Gastro-Intestinal Trials Group (AGITG). Patients with inoperable localized pancreatic cancer were treated with gemcitabine-oxaliplatin chemotherapy with sandwich 5-fluorouracil (5FU) and three-dimensional conformal radiotherapy (3DCRT). The GOFURTGO trial established feasibility and efficacy of this treatment regimen, suggesting that a Phase III trial may be warranted.

**Phase II study of gemcitabine in combination with regional arterial infusion of nafamostat mesilate**


Investigators at the Jikei University School of Medicine in Tokyo underwent a clinical trial of advanced pancreatic cancer patients, testing the synthetic serine protease inhibitor nafamostat mesilate in combination with gemcitabine. The authors deemed this regimen as attractive based on patient survival, clinical benefit, and cost effectiveness.
Phase II open-label study of erlotinib in combination with gemcitabine in pancreas adenocarcinoma
This study took place in Spain, and assessed the relationship between skin rash and overall survival in unresectable and/or metastatic pancreatic cancer patients treated with erlotinib and gemcitabine. Patients who experienced a grade 1 rash showed better progression-free survival than patients with no rash, whereas patients with at least a grade 2 rash had the best progression-free and overall survival, confirming the relationship between development of a rash and improved responsiveness to erlotinib plus gemcitabine.

The molecular and cellular heterogeneity of pancreatic ductal adenocarcinoma
Published in Nature Reviews Gastroenterology & Hepatology, this article considers the failure of drugs to date to treat pancreatic cancer, and the promise of genetic characterization of patients’ tumors leading to individualized care.

A genome-wide association study of survival in patients treated with gemcitabine in CALGB 80303
This Cancer and Leukemia Group B (CALGB) study was published in Clinical Cancer Research. The group conducted a randomized phase III study of advanced pancreatic cancer patients, treated with gemcitabine alone or plus bevacizumab. Germline DNA was collected and the authors conducted a genome-wide association study to identify single nucleotide polymorphisms (SNPs) that were associated with overall survival. A potentially relevant SNP was found in the gene for interleukin 17F.

Intensity-modulated radiotherapy for pancreatic adenocarcinoma
A team of Radiation Oncology researchers at Stanford evaluated intensity-modulated radiotherapy (IMRT) in pancreatic cancer patients. All patients were treated with 5-FU as well. They were able to achieve durable disease control in several adjuvant patients, but prognosis remained poor. The IMRT regimen was better tolerated than three-dimensional conformal radiotherapy.

Potential contribution of preoperative neoadjuvant concurrent chemoradiation therapy
This Journal of Gastrointestinal Surgery paper describes a retrospective analysis of borderline-resectable pancreatic cancer patients who were treated with chemoradiation therapy prior to pancreatectomy. The results suggested that neoadjuvant chemoradiation may be beneficial towards achieving a margin-negative surgical resection.

Neuroendocrine pancreatic tumors: Guidelines for management and update
Burns and Edil describe the current clinical management of pancreatic neuroendocrine tumors, also known as islet cell tumors.
Could vaccines help in the fight against pancreatic cancer?
This local news piece features Bill Hawkins, MD (2005 Skip Viragh Career Development Award) from the Siteman Cancer Center at Washington University, St. Louis. Dr. Hawkins describes the promise of vaccine trials underway to treat pancreatic cancer.

RTOG initiates a phase I trial testing the therapy ganitumab for locally advanced pancreatic cancer
http://www.rtog.org/News/tabid/72/articleType/ArticleView/articleId/28/RTOG-1102-for-Advanced-Pancreatic-Cancer-Open-for-Accrual.aspx
The Radiation Therapy Oncology Group (RTOG) announced their 1102 clinical trial of ganitumab, a fully-human monoclonal antibody antagonist of the insulin-like growth factor-1 receptor, along with standard chemoradiation, in locally advanced pancreatic cancer patients. Chris Crane, MD (Medical Advisory Board) is the principle investigator of this trial in Houston, and is quoted in the article.

TGen seeking pancreatic-cancer patients for trial
The Translational Genomics Research Institute (TGen) is announcing the opening of enrollment for the Seena I trial. In the course of this trial, pancreatic cancer patients will be treated with gemcitabine and nab-paclitaxel (Abraxane) for a maximum of 6 months, followed by a combination of four drugs: 5-FU (fluorouracil), Leucovorin, Oxaliplatin, and Irinotecan (FOLFIRINOX) for a maximum of 6 months. In the third treatment, the patient’s tumor will be biopsied and analyzed using molecular profiling to determine the next most appropriate treatment.

Oncolytics Biotech® Inc. announces Phase 2 clinical trial of REOLYSIN® reaches primary endpoint
Oncolytics Biotech Inc. is undergoing a Phase 2 clinical trial of REOLYSIN, their proprietary formulation of the human reovirus, in combination with gemcitabine in patients with advanced pancreatic cancer. Their primary endpoint was defined as seeing at least eight of 33 evaluable patients show a response to the drug combination. Upon evaluating 13 patients, Oncolytics has already observed eight patients with stable disease for 12 weeks or longer. Due to these promising results, Oncolytics will continue enrolling patients in this study and testing REOLYSIN with other chemotherapies in pancreatic cancer patients.

VAXIMM starts clinical study of first oral cancer vaccine
VAXIMM AG, a Swiss-German biotech company, has started its first clinical trial of its investigational oral vaccine, VXM01. VXM01 stimulates the patients’ immune system to attack tumor-associated blood vessels. The Phase I study aims to enroll up to 45 pancreatic cancer patients at Heidelberg University in Germany, and will test VXM01 plus standard care, compared to standard care alone.
AngioDynamics completes enrollment in European NanoKnife® System trial (ONC-208)
AngioDynamics has completed patient enrollment in its European prospective NanoKnife® System trial (ONC-208) for the treatment of locally advanced unresectable pancreatic cancer. The trial’s primary endpoint (safety) and secondary endpoint (efficacy) will be evaluated at 90 days post-treatment.

Cyclacel provides update on clinical progress with sapacitabine in solid tumors including activity
Cyclacel Pharmaceuticals, Inc. reports data from ongoing clinical trials. A Phase I trial of sapacitabine, a nucleoside analogue, and seliciclib, a CDK inhibitor is underway in patients with advanced cancers, including pancreatic. Three patients total, including one with advanced pancreatic cancer, have achieved a partial response. All responders are carriers of BRCA mutations, consistent with sapacitabine’s enhanced activity against cancer cells that are deficient in the homologous recombination DNA repair pathway.

Threshold Pharmaceuticals announces update to TH-302 pancreatic data to be presented
The CEO of Thresholds Pharmaceuticals, Inc. was invited to give an update at the Oppenheimer 22nd Annual Healthcare Conference in New York City on the company’s corporate and clinical development, including progress on their TH-302 trial in pancreatic cancer. In regions of hypoxia, TH-302 is activated by conversion into its active form as a potent DNA alkylator. Threshold expects to report the primary analysis of their Phase 2 study of TH-302 in pancreatic cancer patients in February 2012.

CANCER CONTROL, SURVIVORSHIP, AND OUTCOMES RESEARCH
Surveillance of pancreatic cancer patients after surgical resection
Researchers at University of Texas evaluated the follow-up of a large population of patients after curative-intent surgery for pancreatic cancer diagnoses, using Surveillance, Epidemiology, and End Results (SEER) data. They found a lack of consistency or structure in the monitoring of patients post-surgery. Those who were treated by a cancer specialist underwent more frequent screenings than patients treated by primary care physicians.

URMC study: Most cancer-related blood clots occur in outpatients
Blood clots are a potentially life-threatening complication of cancer (both the disease itself, and as a side effect from chemotherapy). Researchers at the University of Rochester Medical Center presented recent findings at the American Society of Hematology (ASH) meeting in San Diego (please see scientific abstract here: http://ash.confex.com/ash/2011/webprogram/Paper37320.html). They found that over three-quarters of incidences of blood clots occurred in an outpatient setting, shifting the previous focus from only those patients currently hospitalized.