PANCREATIC CANCER ACTION NETWORK AND COMMUNITY NEWS

Share your federal funding experiences: Help our advocacy efforts

http://www.pancan.org/section_research/resources_for_scientists/form_funding_experiences.php

Have you struggled to receive grants from the NCI or other federal institutions? Have you been successful? We’re looking for information to help us understand what is working well for pancreatic cancer researchers and what could be improved (including, but not limited to, funding levels). We will use this information in our public policy efforts. Please click above and share your stories (they can be submitted anonymously).

Support of the Cancer Genome Atlas Program (TCGA): Funding opportunity

http://www.fdbdo.com/s12-335/

Financial support is available for submissions to the TCGA pancreas project. Please see the note from Kenna Shaw, PhD of the TCGA Program Office:

“Because of the poor prognosis and overall public health impact, pancreatic ductal adenocarcinoma has been selected to be studied by TCGA. However, the pancreatic cancer project might end before it even begins unless more collaborators provide tissue samples. The collapse of this research project would be a lost opportunity for the pancreatic cancer community ... If you have frozen, untreated samples in your tissue bank accompanied by blood, please help by providing them, either retrospectively or prospectively, to TCGA.”

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. Registration is now open. The deadline for abstract submission and award application is Wednesday, April 11, and advance registration closes on Monday, May 7.

BIOLOGY OF CANCER

Constitutive K-RasG12D activation of ERK2 specifically regulates 3D invasion via MMP-1


Anil Rustgi, MD (Scientific Advisory Board) contributed to this Molecular Cancer Research publication. The authors cultured pancreatic ductal epithelial cells in a three-dimensional model with a basement membrane analog. Expression of mutant K-Ras induces cell invasion, in a fashion that is dependent on ERK2, but not ERK1. Additionally, MMP-1 is necessary for K-Ras induced cell invasion, suggesting that ERK2 and/or MMP-1 may be viable therapeutic targets in pancreatic cancer.
Protein kinase C iota regulates pancreatic acinar-to-ductal metaplasia
This *PLoS One* article out of the Mayo Clinic, Jacksonville describes the signal transduction involved in pancreatic acinar-to-ductal metaplasia (ADM). In mouse models, ADM can be induced by pancreas-specific expression of mutant K-ras or TGF-alpha. In either case, ADM development is mediated by protein kinase C iota (PKC), and inhibition of PKC disrupts signaling via K-ras, MMP7, and Notch.

Losartan slows pancreatic tumor progression and extends survival of SPARC-null mice
Scientists at UT Southwestern wrote this *PLoS One* article looking at the complex relationship between SPARC and TGF-beta in pancreatic cancer progression. SPARC is a matricellular protein involved in extracellular matrix formation in tumorigenesis. In SPARC-null mice implanted with pancreatic cancer cells in an orthotopic model, TGF-beta levels were increased and tumor progression was also increased. Treatment with losartan, an angiotensin II type 1 receptor antagonist that blocks TGF-beta expression and activation, led to increased survival of the mice, implicating TGF-beta as inducing disease progression in the absence of SPARC.

EGCG enhances the therapeutic potential of gemcitabine and CP690550 by inhibiting STAT3 signaling
This *PLoS One* paper out of the University of Kansas Cancer Center describes the effects of treating pancreatic cancer cells with epigallocatechin gallate (ECGC) to inhibit signal transducer and activator of transcription 3 (STAT3) signaling. The investigators found that ECGC treatment inhibited growth and migration of pancreatic cancer cells and induced apoptosis, via STAT3 inhibition. Moreover, co-administration with gemcitabine or CP690550 (JAK2 inhibitor) had a synergistic effect on blocking pancreatic cancer cell growth.

Identification of anti-malarial compounds as novel antagonists to chemokine receptor CXCR4
Published in the same issue of *PLoS One*, this article describes a screen for anti-CXCR4 candidate drugs. The authors discovered that NSC56612 from the National Cancer Institute’s (NCI) Open Chemical Repository Collection appeared to inhibit CXCR4. NSC56612 has structural similarity to anti-malarial drugs chloroquine and hydroxychloroquine, implicating another mechanism by which these drugs might be effective in the treatment of pancreatic cancer.

The RalB small GTPase mediates invadopodia formation through the RalBP1/RLIP76 effector
This *Molecular and Cellular Biology* paper out of Channing Der’s lab at UNC looks at Ral small GTPases in pancreatic cancer cells. RalB was found to be more important for invadopodia formation than RalA. Surprisingly, these effects were independent of RalB’s GTPase activity, and instead dependent on the protein’s ATPase function.
Keratin 8 phosphorylation regulates keratin reorganization and migration of epithelial tumor cells
A collaborative team of researchers from Germany and Michigan produced this Journal of Cell Science article. Using pancreatic and gastric cancer cells as a model, the authors found that phosphorylation of keratin 8 induced by sphingosylphosphorylcholine is necessary and sufficient to cause cytoskeletal reorganization, leading to enhanced cell migration.

PALB2 interacts with KEAP1 to promote NRF2 nuclear accumulation and function
Also published in Molecular and Cellular Biology, this study describes how PALB2 function could be a link between oxidative stress and the development of cancer and Fanconi anemia.

S100P-binding protein, S100PBP, mediates adhesion through regulation of cathepsin Z
This team of researchers from Queen Mary University of London had previously identified S100P binding protein (S100PBP), with no homology to known proteins or known function. Here, the authors further analyzed expression of S100PBP, and found it in the nuclear/perinuclear compartments of healthy pancreas, translocated to the cytoplasm in early precancerous lesions, and low expression in pancreatic cancer specimens. S100PBP was further shown to act via cathepsin Z and avb5 integrin, to mediate cell adhesion.

K-Ras mutation-mediated IGF-1-induced feedback ERK activation contributes to the rapalog resistance
Drugs targeting the mammalian target of rapamycin complex 1 (mTORC1), known as rapalogs, have thus far been unsuccessful in the treatment of pancreatic adenocarcinoma. Wei and colleagues therefore looked at combinatory treatment, such as blocking expression of mutant K-Ras, to overcome the failure of rapalog therapeutics.

Hedgehog-EGFR cooperation response genes determine the oncogenic phenotype
Researchers at the University of Salzburg in Austria studied cooperation between the hedgehog and EGFR pathways in tumor-initiating pancreatic cancer cells and basal cell carcinoma.

An orally active LPA receptor antagonist attenuates pancreatic cancer invasion and metastasis in vivo
Komachi et al submitted this Cancer Science manuscript to describe an orally active lysophosphatidic acid (LPA) receptor antagonist to treat mice inoculated with pancreatic cancer cells. Their compound, Ki16198, was found to block invasion and metastasis in these disease models, seemingly via inhibiting LPA-induced MMP production.

Knock-down of plasminogen-activator inhibitor-1 enhances expression of E-cadherin
Published in the Journal of Cellular Physiology, this paper looks at effects of knock-down of plasminogen activator inhibitor-1 (PAI-1) expression in pancreatic cancer cells. PAI-1 has been previously shown to be
a poor prognostic marker in pancreatic cancer, and knock-down by shRNA led to an increase in epithelial marker mRNAs, suggesting that PAI-1 is associated with epithelial-to-mesenchymal transition.

**RGD-conjugated albumin nanoparticles as a novel delivery vehicle in pancreatic cancer therapy**
Researchers at Fudan University Shanghai Cancer Center devised a nanoparticle drug delivery strategy to target treatment to cells expressing integrin avb3. The arginine-glycine-aspartic acid (RGD) peptide, specific for avb3 integrin, was conjugated to an albumin nanoparticle, and used to deliver gemcitabine to pancreatic cancer cells.

**Small cell and large cell neuroendocrine carcinomas of the pancreas are genetically similar and distinct**
This research took place in the laboratory of Christine Iacobuzio-Donahue, MD, PhD (2007 Pilot Grant and member, Scientific Advisory Board), with collaboration from Anirban Maitra, MD (2004 Career Development Award and member, Scientific Advisory Board) and Ralph Hruban, MD (Emeritus Scientific Advisory Board). The researchers analyzed the differences between poorly differentiated neuroendocrine carcinomas and well differentiated neuroendocrine tumors of the pancreas. They found that small and large cell neuroendocrine carcinomas of the pancreas had similarities with each other, but were dissimilar from well-differentiated pancreatic neuroendocrine tumors.

**Suppression of tumor invasion and metastasis by concurrent inhibition of c-Met and VEGF signaling**
[http://cancerdiscovery.aacrjournals.org/content/early/2012/02/20/2159-8290.CD-11-0240.abstract?sid=9d2d46e4-1118-447c-abc3-b07de643559d](http://cancerdiscovery.aacrjournals.org/content/early/2012/02/20/2159-8290.CD-11-0240.abstract?sid=9d2d46e4-1118-447c-abc3-b07de643559d)
This Cancer Discovery article evaluated whether VEGF inhibition alone would increase invasion and metastasis in pancreatic neuroendocrine tumors, and whether inhibition of c-Met could reverse that unwanted effect, while slowing the growth of the tumor.

**ETIOLOGY**
**Colorectal and other cancer risks for families with a DNA mismatch repair gene mutation**
This JCO paper attracted a lot of media attention, including this Reuters article: [http://www.reuters.com/article/2012/02/15/us-mutations-idUSTRE81E1YM20120215](http://www.reuters.com/article/2012/02/15/us-mutations-idUSTRE81E1YM20120215). In the prospective cohort study, a large collaborative team of researchers looked at families with DNA mismatch repair (MMR) gene mutations. Unaffected relatives who are carriers of MMR mutations had increased risk for several cancer types, including pancreatic, but relatives without the mutation were not seen to have increased risk for developing any type of cancer.

**Concentrations of IGF-I and IGFBP-3 and pancreatic cancer risk**
This British Journal of Cancer article describes an analysis of the relationship between insulin-like growth factor (IGF-1) and IGF binding protein (IGFBP-3) levels and risk of pancreatic cancer, using the European Prospective Investigation into Cancer and Nutrition. Their data suggest that measurements of IGF-1, IGFBP-3, and their ratio were not statistically significantly linked to pancreatic cancer risk. However,
individuals with very high levels of IGF-1 and very low levels of IGFBP-3 appeared to be at greater risk for pancreatic cancer.

**A single nucleotide polymorphism of the cholecystokinin-B receptor predicts risk for pancreatic cancer**

Scientists at Penn State Hershey Medical Center describe the discovery of a single nucleotide polymorphism (SNP) in an alternatively spliced isoform of cholecystokinin B receptor (CCKBR), known as CCKCR, that predicts risk for pancreatic cancer.

**The associations of advanced glycation end products, soluble receptor with pancreatic cancer risk**

This large collaborative study utilized data from the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort. The research team looked at the association between advanced glycation end products (AGE) and their receptors (RAGE) and pancreatic cancer risk. The results of this study suggest that there is not an association between AGE, RAGE, and pancreatic cancer, although further experiments will be necessary to understand the function of these molecules.

**The functional cytotoxic T lymphocyte-associated protein 4 49G-to-A genetic variant and risk**

Published in *Cancer*, this paper looks at cytotoxic T lymphocyte-associated protein 4 (CTLA4), a negative regulator of T-cell activity and thus an immune-suppressive molecule in pancreatic cancer. The authors evaluated the small nucleotide polymorphism 49G>A in CTLA4, and how this genetic change influences patient risk to pancreatic cancer. The individuals with the 49G>A polymorphism carried a higher risk of developing pancreatic cancer, and that risk was increased even further in the presence of smoking or high alcohol consumption.

**Genetic variants in carcinogen-metabolizing enzymes, cigarette smoking and pancreatic cancer risk**

A research team at Cancer Care Ontario in Toronto investigated pancreatic cancer risk associated with cigarette smoking. Increased risk of pancreatic cancer was found to be associated with current smoking, many years of smoking, or long periods of smoking. Further, they found that variants of carcinogen metabolism genes are independently associated with pancreatic cancer risk and may modify the risk posed by smoking.

**Association of type O blood with pancreatic neuroendocrine tumors in Von Hippel-Lindau syndrome**

Researchers from the Endocrine Oncology Section at the NCI evaluated the relationship between ABO blood type and risk of pancreatic neuroendocrine tumors (PNETs), in patients with Von Hippel-Lindau syndrome (already at higher risk for developing PNETs). Their data suggest that Von Hippel-Lindau patients with type O blood were at higher risk for PNET.
PREVENTION
Chemoprevention of pancreatic cancer – one step closer
Dr. Volker Fendrich of Philipps University Marburg in Germany wrote this review article to discuss recent advancements in the chemoprevention of pancreatic cancer, made possible by mouse models that recapitulate disease progression through PanIN lesions.

EARLY DETECTION, DIAGNOSIS, AND PROGNOSIS
Early mortality risk score: Identification of poor outcomes following upfront surgery
This Journal of Gastrointestinal Surgery paper is out of the lab of Joe Herman, MD (2008 Blum-Kovler Career Development Award), and also features Ralph Hruban, MD (Emeritus Scientific Advisory Board). The authors looked to assess an early mortality risk score (EMRS) to predict which pancreatic cancer patients were at highest risk of early death following pancreaticoduodenectomy. EMRS was calculated based on the patient’s age, tumor size, differentiation, and co-morbid disease. In retrospective analysis, EMRS predicted for early death of pancreatic cancer patients, regardless of adjuvant treatment. Prospective analyses will be necessary to validate these results.

Clinicopathological characteristics and molecular analyses of multifocal IPMNs of the pancreas
The senior author on this study is Ralph Hruban, MD (Emeritus Scientific Advisory Board), and other authors include Mimi Canto, MD (Medical Advisory Board), Jim Eshleman, MD, PhD (2011 Innovative Grant), and Anirban Maitra, MD (2004 Career Development Award and Scientific Advisory Board). Dr. Hruban and colleagues sought to understand clinicopathological features of multifocal intraductal papillary mucinous neoplasms (IPMNs) and determine likelihood of synchronous or metachronous relationship between clones.

Vascular invasion in infiltrating ductal adenocarcinoma of the pancreas can mimic PanIN
This project is also out of the lab of Ralph Hruban, MD (Emeritus Scientific Advisory Board), with collaboration from Joe Herman, MD (2008 Blum-Kovler Career Development Award). This histopathologic study revealed that microscopic vascular invasion is a poor prognostic indicator and can histologically mimic pancreatic intraepithelial neoplasia (PanIN).

Quantitative molecular profiling of biomarkers for pancreatic cancer: Functionalized quantum dots
Anirban Maitra, MD (2004 Career Development Award and Scientific Advisory Board) collaborated on this Nanomedicine: Nanotechnology, Biology and Medicine paper. The authors use functionalized quantum dots (QD) to assess biomarkers on the cell surface of pancreatic cancer. This technique allowed the researchers to quantify expression of biomarkers on individual cells.
Identification of glycoprotein markers for pancreatic cancer CD24+CD44+ stem-like cells
Diane Simeone, MD (2010 The Randy Pausch Family Innovative Grant and member, Scientific Advisory Board) collaborated with Dr. Dave Lubman on this Journal of Proteome Research paper. The authors used lectin microarray to discover a differentially expressed subset of glycoproteins between CD24+CD44+ pancreatic cancer stem cells, compared to cells expressing CD44 but not CD24. These glycoproteins could provide therapeutic targets and/or prognostic markers for pancreatic cancer.

Multiplex targeted proteomic assay for biomarker detection in plasma: A biomarker case study
Ru Chen, PhD (2006 Career Development Award) and others worked with Teri Brentnall, MD (Emeritus Scientific Advisory Board) for this Journal of Proteome Research publication. The researchers discuss an SRM (select reaction monitoring) proteomic approach to detect candidate plasma biomarkers that may aid in the detection of pancreatic cancer. Three of the five candidate proteins, including gelsolin, lumican, and tissue inhibitor of metalloproteinase 1, carried statistical significance in differentiating plasma from individuals with pancreatic cancer, chronic pancreatitis, and healthy controls.

Clinical calculator of conditional survival estimates for resected and unresected survivors
Jason Fleming, MD (Medical Advisory Board) is among the authors on this Archives of Surgery paper. The authors created an internet browser-based calculator to determine conditional survival estimates for patients with pancreatic adenocarcinoma. A patient’s unique clinicopathological features could be translated into a personalized conditional survival estimate that is more accurate than prognostic predictions made at diagnosis.

Fluid biopsy in patients with metastatic prostate, pancreatic and breast cancers
Included among the authors on this Physical Biology paper is Andrew Ko, MD (2003 Career Development Award). The research team developed a fluid-based biopsy that can detect and isolate circulating tumor cells that are “high definition” enough for pathological analyses. Half of the metastatic pancreatic cancer patients evaluated were found to have at least five high-definition circulating tumor cells per milliliter of blood.

Statistical considerations of optimal study design for human plasma proteomics, biomarker discovery
The authors of this Journal of Proteome Research article took plasma samples from healthy volunteers or pancreatic cancer patients, and searched for biomarkers by mass spectrometry. Their analyses suggested that a minimum of six samples per group (such as, by stage or treatment history) were needed to confirm protein changes of at least two-fold.
Diagnostic accuracy of cyst fluid amphiregulin in pancreatic cysts
Expression of the EGFR ligand amphiregulin was looked at in pancreatic cyst fluid, to determine whether it could differentiate different types of cysts. Amphiregulin was significantly more highly expressed in cancerous or high-grade dysplasia cysts, suggesting that its expression could serve as a marker for more aggressive disease.

EUS-guided FNA for diagnosis of solid pancreatic neoplasms: A meta-analysis
Published in Gastrointestinal Endoscopy, this study sought to determine the accuracy of endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) for diagnosing pancreatic cancer. The authors performed a meta-analysis of the literature from 1997 to 2009, and observed that EUS-FNA is a highly accurate method to detect solid tumors of the pancreas.

Fate of the pancreatic remnant after resection for an intraductal papillary mucinous neoplasm
Researchers at the Virginia Mason Medical Center in Seattle performed a longitudinal level II cohort study of patients who underwent partial pancreatic resection for intraductal papillary mucinous neoplasm (IPMN). They found via follow-up CT scanning that eight percent of patients had a subsequent IPMN lesion arise in their partially-resected patient within 40 months, with additional lesions expected to occur as more time elapses.

Ack1 tyrosine kinase activation correlates with pancreatic cancer progression
This American Journal of Pathology paper demonstrates that activated Ack1 could serve as a prognostic marker for early or advanced pancreatic cancer. Moreover, inhibition of Ack1 was shown to decrease cell growth by arresting the cells in G-phase, because AKT does not get phosphorylated.

Transient receptor potential melastatin-related 7 channel is overexpressed, regulates cell migration
Rybarczyk, et al evaluated the melastatin-related transient receptor potential 7 channel (TRPM7) expression and activity in pancreatic cancer. High expression of TRPM7 was found to be a poor prognostic indicator for pancreatic cancer patients, and the protein was also found to play a role in cellular migration.

Asuragen launches miRInform® Pancreas Test for fine needle aspirate specimens of pancreatic masses
The Austin, Texas-based company Asuragen, Inc. issued this press release about their miRInform® Pancreas Test to distinguish benign from malignant disease from fine needle aspirate (FNA) samples. Their test is based on miRNA analyses, and is analyzed in a CAP-accredited CLIA-certified lab. miRInform is designed to analyze samples with “inconclusive” diagnoses from FNA cytology.
Incidental detection of pancreatic neuroendocrine tumors: An analysis of incidence and outcomes
Researchers at the Moffitt Cancer Center looked at incidental diagnosis of pancreatic neuroendocrine tumors, compared to patients who are diagnosed because they experience symptoms. Incidental diagnoses revealed many tumors in early stages, leading to a much higher overall survival rate.

TREATMENT

Gamma secretase inhibition promotes hypoxic necrosis in mouse pancreatic ductal adenocarcinoma
Dave Tuveson, MD, PhD (2003 Career Development Award and Emeritus Scientific Advisory Board) is the senior author on this Journal of Experimental Medicine paper. This article received a great deal of media attention, such as: http://www.bbc.co.uk/news/health-17095753. Dr. Tuveson and colleagues tested the gamma secretase inhibitor MRK003 (to block Notch signaling) in a genetically engineered mouse model of pancreatic cancer. Although MRK003 alone did not extend the mice’s survival, there was a benefit in combination with gemcitabine.

nab-paclitaxel potentiates gemcitabine activity by reducing cytidine deaminase levels
http://cancerdiscovery.aacrjournals.org/content/early/2012/02/23/2159-8290.CD-11-0242.abstract?sid=0d419529-0cd8-4f00-9f1a-db9695c635
This study also took place in the laboratory of Dave Tuveson, MD, PhD (2003 Career Development Award and Emeritus Scientific Advisory Board). Although early clinical data of treating pancreatic cancer patients with nanoparticle albumin-bound (nab) paclitaxel in combination with gemcitabine have been encouraging, the mechanism of action is not yet known. Therefore, these researchers at Cancer Research UK used a genetically engineered mouse model to determine that nab-paclitaxel treatment leads to a decrease in the gemcitabine-metabolizing enzyme cytidine deaminase, leading to higher concentrations of gemcitabine in the pancreatic tumor.

A phase II trial of nab-paclitaxel as second-line therapy in patients with advanced pancreatic cancer
This American Journal of Clinical Oncology paper describes the results of a phase II trial of nab-paclitaxel mono-therapy in previously gemcitabine-treated advanced pancreatic cancer patients. Nineteen patients were tested, and preliminary evidence suggests activity of the drug in some of the patients, with good tolerability.

A live-attenuated listeria vaccine and a vaccine expressing mesothelin for advanced cancers
Among the contributors to this study is Liz Jaffee, MD (Emeritus Scientific Advisory Board). These data also picked up some media attention, like: http://www.marketwatch.com/story/clinical-results-from-aduros-phase-1-trials-published-in-clinical-cancer-research-2012-02-07. Phase I results are reported on a live-attenuated listeria vaccine (ANZ-100) and a live-attenuated listeria vaccine expression mesothelin (CRS-207) tested in a variety of advanced cancers, including pancreatic. The investigators observed that both vaccines were well tolerated, and sparked immune responses.
Mesothelin-targeted agents in clinical trials and in preclinical development
Scientists at the NCI wrote this review to discuss mesothelin as a target for anti-cancer therapeutics. Mesothelin is highly expressed on the cell surface of several cancer types, including pancreatic, with lower expression on normal tissue, making it an attractive target.

Does preoperative therapy optimize outcomes in patients with resectable pancreatic cancer?
Rebekah White, MD (2007 Seena Magowitz Career Development Award) is the senior author on this study published in Journal of Surgical Oncology. The authors conducted a retrospective study of pancreatic cancer patients treated with either preoperative chemoradiation therapy or surgery first. Patients who underwent preoperative chemoradiation and then surgery had a significantly longer overall survival than those who had surgery first. Even patients who never were able to have surgery had a comparable survival as surgery-first patients. Dr. White and colleagues therefore deem preoperative chemoradiation a viable option for patients diagnosed with resectable pancreatic cancer.

Vascular surgery collaboration during pancreaticoduodenectomy with vascular reconstruction
This Annals of Vascular Surgery paper is also out of the lab of Rebekah White, MD (2007 Seena Magowitz Career Development Award). Dr. White and colleagues wanted to test whether the previous dogma that patients with portal venous involvement were unresectable was still true. Their analyses showed that patients whose surgery included vascular reconstruction did just as well as patients who had surgery without venous involvement. It is recommended to involve a vascular surgeon in the vascular reconstruction procedure.

Clinical Trials Network aims to strengthen cancer immunotherapy pipeline
http://www.cancer.gov/ncicancerbulletin/022112/page6
A new NCI-funded initiative, the Cancer Immunotherapy Trials Network (CITN) will launch its first clinical trials later this year. Among the early drugs to be tested will be CP-870,893, a Pfizer compound that targets the CD40 antigen, as presurgical treatment in patients with operable pancreatic cancer. This trial is led by Scientific Advisory Board member Bob Vonderheide, MD, DPhil.

EUS or percutaneously guided intratumoral TNFerade biologic with 5-fluorouracil and radiotherapy
A multidisciplinary, multi-institutional team of investigators, including Mimi Canto, MD (Medical Advisory Board), participated in this Phase I/II study of TNFeradeBiologic with 5-FU and radiation in previously untreated, locally advanced pancreatic cancer patients. TNFeradeBiologic, a replication deficient adenoviral vector expressing TNF-alpha, was injected directly into tumors by endoscopic ultrasound guidance. An appropriate dose was selected, and preliminary evidence suggests effectiveness in the treatment of locally advanced pancreatic cancer, in combination with chemoradiation approaches.
BioSante’s pancreas cancer vaccine shows over 60% survival increase in newly presented study
BioSante Pharmaceuticals, Inc. announced presentation of results from a Phase Ib clinical study that show its GVAX Pancreas cancer vaccine, in combination with ipilimumab, increased the median survival of pancreatic cancer patients with previously treated, locally advanced or metastatic pancreatic adenocarcinoma, as well as led to an increase in one year survival.

Phase 1 study of rigosertib, an inhibitor of the phosphatidylinositol 3-kinase and polo-like kinase 1
Ma and colleagues published this Clinical Cancer Research paper describing a Phase 1 trial testing rigosertib, an inhibitor of the phosphatidylinositol 3-kinase and polo-like kinase 1 pathways, combined with gemcitabine, in patients with advanced solid tumors, including pancreatic. The goals were to determine a recommended Phase 2 dose, and perform additional pharmacokinetic studies on pancreatic cancer patients treated with this drug combination.

A phase I/II, non-randomized, feasibility/safety, efficacy study of everolimus, cetuximab, capecitabine
Researchers at the Academic Medical Center Amsterdam tested combination treatment of everolimus (inhibits mTor pathway), cetuximab (inhibits EGFR), and capecitabine in patients with advanced pancreatic cancer. Early results showed significant toxicity and poor efficacy, suggesting that this is not a beneficial or appropriate treatment regimen for this patient population.

Multicentre phase II trial of trastuzumab and capecitabine in patients with HER2 pancreatic cancer
Harder and colleagues report testing the HER2 antibody trastuzumab in combination with capecitabine in patients with IHC confirmed HER2-positive advanced pancreatic cancer. Patients’ progression free- and overall survival were not improved compared to chemotherapy alone.

Gemcitabine alone versus combination of gemcitabine and cisplatin
A retrospective study looked at the combination of gemcitabine and cisplatin in the treatment of patients with locally advanced and/or metastatic pancreatic cancer. Progression free survival was slightly better in the gemcitabine-cisplatin combination arm of trials, but those data did not reach statistical significance. There was no difference between overall survival in the two groups. Patients treated with cisplatin experienced more toxicity.

Radiation-inducible immunotherapy for cancer: Senescent tumor cells as a cancer vaccine
This Molecular Therapy study out of the University of Chicago explored the potential of using senescent cancer cells as a vaccine to induce an immune response against a tumor. Senescence was induced in a pancreatic cancer mouse model by treatment with ionizing radiation and veliparib, a poly(ADP-ribose) polymerase (PARP) inhibitor.
Epigenetic approach to pancreatic cancer treatment: Prospective role of histone deacetylase inhibitors
Tinari and colleagues describe therapeutic strategies involving histone deacetylase inhibitors, alone and in combination, in the fight against pancreatic cancer.

The management of EGFR inhibitor adverse events: A case series and treatment paradigm
Researchers at the NYU School of Medicine explored skin-related side effects of EGFR inhibition in patients treated for cancer, including pancreatic.

Threshold Pharmaceuticals announces positive Phase 2b clinical trial results of TH-302
Threshold Pharmaceuticals, Inc issued this press release after its Phase 2b clinical trial of TH-302 in previously untreated advanced pancreatic cancer patients reached its primary endpoint. Threshold describes TH-302 as “converted selectively to the drug’s active form, dibromo isophoramide mustard, a potent DNA alkylator, within hypoxic tumor cells.” The results to date suggest that treatment with TH-302 and gemcitabine leads to a significantly improved progression free survival, compared to gemcitabine alone. The drug has been well tolerated, also.

Merck KGaA to pay Threshold up to $525 million for drug
Merck will pay Threshold Pharmaceuticals up to $525 million for the rights to jointly develop and sell TH-302, a drug in testing for pancreatic cancer and soft tissue sarcoma. TH-302 is specifically active in tissues in the presence of hypoxia, a hallmark of pancreatic cancer. If all of the developmental milestones decided upon by the two companies are met, Threshold will receive $525 million.

Nuvilex reports encapsulated living cells technology for pancreatic cancer treatment
The Cell Line Development and Engineering Asia Event in Shanghai included a presentation by SG Austria on behalf of Nuvilex, Inc. The companies’ Cell-in-a-Box® and Bac-in-a-Box™ technologies allow both living eukaryotic and bacterial cells to be encapsulated in order to protect, store, isolate, and transport them. The companies are hoping to utilize these technologies in the treatment of pancreatic cancer.

New method makes it easier to treat prostate and pancreatic cancer
http://www.eurekalert.org/pub_releases/2012-02/lu-nmm021512.php
Researchers in atomic physics at Lund University in Sweden are working to utilize photodynamic therapy (laser light in combination with drugs) to treat pancreatic or prostate cancer. Previously, a limitation to using this type of approach on solid tumors in internal organs (as opposed to skin cancer) was the inability to carefully measure the amount of laser light getting to the tumor. To circumvent this, the team is partnering with the company SpectraCure to develop software allowing optical fibers to both deliver the light, and measure the light reaching the tumor.
Targovax secures NOK 13 million series A funding for TG01 pancreatic cancer vaccine development
Targovax, an oncology biopharma company in Norway, received NOK 13 million (equivalent to $2.2 million in US dollars) to develop their pancreatic cancer vaccine, TG01. TG01 is the company’s lead compound, and is a vaccine that specifically targets cells expressing mutant Ras.

Tiltan Pharma commences Phase 2 clinical study of anti-angiogenic treatment for pancreatic cancer
The Jerusalem-based company Tiltan Pharma LTD is launching a Phase 2 study of their anti-angiogenic drug TL-118. TL-118 will be tested in combination with standard-of-care chemotherapy, and compared to chemo alone. Preclinical studies in mouse models showed effectiveness of TL-118, and Phase 1 study in patients demonstrated a good safety profile of the drug.

BSD Medical Corporation reports the initiation of a Phase III pancreatic cancer study
A randomized, multi-center Phase III clinical trial of BSD Medical Corporation’s BSD-2000 Hyperthermia System in combination with chemotherapy has been initiated. Patient accrual will begin April 1. Encouraging Phase II results showed a 16.9-month overall survival with BSD-2000 and chemotherapy treatment, compared to 6 months for patients treated with chemo alone.

DARA BioSciences signs exclusive agreement with Uman Pharma for U.S. rights to gemcitabine
Since gemcitabine went off patent in 2011, DARA Biosciences, Inc was able to sign an exclusive agreement with Uman Pharma Inc for exclusive US rights to the drug. Uman plans to file an Abbreviated New Drug Application (ANDA) for gemcitabine with the U.S. Food and Drug Administration (FDA) later this year.

Well-differentiated pancreatic neuroendocrine tumors: From genetics to therapy
Anirban Maitra, MD (2004 Career Development Award and Scientific Advisory Board) and Ralph Hruban, MD (Emeritus Scientific Advisory Board) were authors on this Nature Reviews Gastroenterology and Hepatology review. The authors highlight recent findings in the genetics and treatment of pancreatic neuroendocrine tumors.

New strategies for advanced neuroendocrine tumors in the era of targeted therapy
This Clinical Cancer Research review article highlights recent successes in the targeted treatment of pancreatic neuroendocrine tumors, such as attacking the mTor pathway or blocking VEGF signaling.
A new era for the systemic therapy of neuroendocrine tumors
The *Oncologist* published this review article, which also describes the implications of targeted therapies on the course of pancreatic neuroendocrine tumors, and discusses the future of the treatment of this disease.

**CANCER CONTROL, SURVIVORSHIP, AND OUTCOMES RESEARCH**

European cancer mortality predictions for the year 2012
This *Annals of Oncology* paper reports on statistics for cancer incidence and death rates in the European Union. Although cancer deaths overall are expected to continue to fall, rates for pancreatic cancer seem to be stable, or even increasing.