PANCREATIC CANCER ACTION NETWORK AND COMMUNITY NEWS

Be a Hero: Volunteer for Progress
http://www.knowitfightitendit.org/
In preparation for November Awareness Month, we’ve kicked off our “Volunteer for Progress” campaign. Check back regularly to see updated videos, and encourage folks in your community to join the fight! The current video features Kimberly Kelly, PhD (2007 Laurie and Paul MacCaskill – Pancreatic Cancer Action Network – AACR Career Development Award).

Steve Jobs, Apple founder, dies
Pancreatic Cancer Action Network official statement:
Steve Jobs passed away from respiratory arrest associated with pancreatic neuroendocrine cancer on October 5, 2011. Mr. Jobs was diagnosed in 2003, and underwent a liver transplant in 2009. He was 56 when he died. Mr. Jobs co-founded Apple in 1976, and stepped down as CEO in August of this year.

Medical expert discusses pancreatic cancer
Anitra Talley, Director of Patient Services and Medical Relations at the Pancreatic Cancer Action Network, live-chatted with Washington Post readers to address questions about pancreatic cancer following Steve Jobs’ death.

Cancer kills Nobel physician before he hears of prize
http://www.reuters.com/article/2011/10/03/us-nobel-medicine-idUSTRE79213M20111003
Ralph Steinman, MD passed away from pancreatic cancer before learning that he was a co-recipient of the 2011 Nobel Prize in Physiology or Medicine. Although Nobel prizes are not granted posthumously, this was a unique situation since the committee was not aware of his death when the announcement was made. While at Rockefeller University, Dr. Steinman discovered dendritic cells and their role in adaptive and innate branches of the immune system. Dr. Steinman reportedly received dendritic cell-based vaccine therapy as part of his pancreatic cancer treatment regimen. Dr. Steinman shares this award with Drs. Bruce Beutler and Jules Hoffman, also immunologists.

Famed pianist Roger Williams dies at 87
Roger Williams, nicknamed “pianist to the presidents”, passed away from pancreatic cancer. His diagnosis had been announced in March of this year.
Pancreatic Cancer Action Network welcomes prestigious members to its Scientific Advisory Board
This official press release went out in October to announce the addition of several new members to our organization’s Scientific Advisory Board.

Pancreatic Cancer Action Network grant recipient receives impressive award
We are delighted to announce that Dave Dawson, MD, PhD (2008 Seena Magowitz – Pancreatic Cancer Action Network – AACR Career Development Award) has been selected to receive an American Cancer Society Research Scholars Grant, totaling $720,000 over three years. Dr. Dawson will continue his focus on the regulation and therapeutic targeting of Wnt signaling in pancreatic cancer. Congratulations Dr. Dawson and good luck on your research project!

Abstract submission now open for the AACR Annual Meeting 2012
http://www.aacr.org/home/scientists/meetings--workshops/aacr-annual-meeting-2012/abstracts.aspx
Next year’s AACR Annual Meeting will take place March 31 – April 4, 2012 in Chicago, IL. The online abstract submitter for the AACR Annual Meeting 2012 is now available. The deadline for abstract submission was Tuesday, November 15, 2011.

American Pancreatic Association offers Mini-Sabbatical Fellowship
The APA Mini-Sabbatical fellowship is a program, offered to young pancreatologists, to allow them to spend up to two months with a reputable pancreatic research center to gain or expand skills in practice or research under the guidance of experts in the field. The mini-sabbatical can last from one week to two months, and is available to APA members who are students, trainees, and junior faculty. Application deadlines are April 15, August 15, and December 15 each year.

UNMC researchers to study role of tumor microenvironment in pancreatic cancer
http://app1.unmc.edu/PublicAffairs/TodaySite/newsreleases/view_t1.cfm?match=8565
Scientists at University of Nebraska Medical Center were awarded a $4.2 million grant from the NCI to study the microenvironment’s role in pancreatic cancer progression. Tony Hollingsworth, PhD (Scientific Advisory Board) is one of the project leaders on this grant.

NHL, NHLPA partner with cancer organizations
http://www.nhl.com/ice/news.htm?id=595487&print=true
The National Hockey League® and National Hockey League Players Association have partnered with several cancer advocacy groups, including Pancreatic Cancer Action Network, for Hockey Fights Cancer Awareness Month. Their contribution to our organization will go towards funding innovative research.
Department of Defense funding opportunities


The deadlines for these grants have passed, but please keep these two mechanisms in mind for the future, as they specifically welcome applications pertaining to pancreatic cancer.

**Save the date: AACR Special Conference – Pancreatic Cancer: Progress and Challenges**


Abstract submission and registration for the meeting are scheduled to open sometime in December – stay tuned!

**Pancreatic Cancer Action Network research newsletter content**

**Researcher Story: Max Schmidt**


Learn about the current progress of one of our first grant recipients, C. Max Schmidt, MD, PhD, MBA, FACS (2003 Pancreatic Cancer Action Network – AACR Career Development Award). Dr. Schmidt is the Surgical Director of the Indiana University Pancreas Cyst and Cancer Early Detection Center ([http://pancyst.org/](http://pancyst.org/)).

**Researcher Story: Jim Eshleman**


Meet recent grant recipient, James Eshleman, MD, PhD (2011 Pancreatic Cancer Action Network – AACR Innovative Grant), who has established nine cell lines from patients with hereditary pancreatic cancer. Dr. Eshleman plans to compare the genome of these cell lines in comparison to normal somatic DNA from each patient, to identify genetic changes associated with the tumor formation and progression.

**Tempur-Pedic® CEO meets with grant recipients**


Mark Sarvary, CEO and President of Tempur-Pedic International Inc. met with Zeshaan Rasheed, MD, PhD (2010 Tempur-Pedic® Retailers – Pancreatic Cancer Action Network – AACR Pathway to Leadership Grant), Ken Olive, PhD (Tempur-Pedic® Retailers – Pancreatic Cancer Action Network – AACR Career Development Award), and Julie Fleshman, JD, MBA, President and CEO of Pancreatic Cancer Action Network. It was a great opportunity for the grantees to showcase their work and express their gratitude to Tempur-Pedic for being a Corporate Champion for the Pancreatic Cancer Action Network.

**Grantees and board members interact at Scientific Session**


Over the weekend of the Pancreatic Cancer Action Network Evening with the Stars gala, early-career grant recipients had the opportunity to present their progress to the organization’s Scientific and Medical Advisory Boards and Board of Directors.
**BIOLOGY OF CANCER**

Cyclin-dependent kinase inhibitor dinaciclib (SCH727965) inhibits pancreatic cancer growth


Authors on this article include Zeshaan Rasheed, MD, PhD (2010 Tempur-Pedic® Retailers – Pancreatic Cancer Action Network – AACR Pathway to Leadership Grant) and Anirban Maitra, MD (2004 Pancreatic Cancer Action Network – AACR Career Development Award and Scientific Advisory Board member). The investigators tested dinaciclib (SCH727965), a novel small molecule multi-CDK inhibitor, in human pancreatic cancer cells *in vitro* and *in vivo*. SCH727965 was effective at blocking cells’ growth, motility, and anchorage independenc, and xenograft experiments showed synergy with gemcitabine.

Oncogenic transcription factors: cornerstones of inflammation-linked pancreatic carcinogenesis


This *Gut* review is co-written by Martin Fernandez-Zapico, MD (2007 Carole and Bob Daly – Pancreatic Cancer Action Network – AACR Career Development Award) at the Mayo Clinic, and researchers at Philipps-University of Marburg in Germany. The authors look at how inflammation drives activity of transcription factors in pancreatic cancer that lead to gene expression changes promoting growth, proliferation, and progression of the cancer cells. They also discuss current strategies to potentially target oncogenic transcription factors.

Molecular determinants of retinoic acid sensitivity in pancreatic cancer


This research took place primarily in the laboratory of Anirban Maitra, MD (2004 Pancreatic Cancer Action Network – AACR Career Development Award and Scientific Advisory Board). Dr. Maitra and colleagues sought to identify a predictive molecular “signature” for sensitivity to retinoic acid in pancreatic cancer. Their data suggest that all-trans retinoic acid (ATRA) treatment might be most appropriate in patients with biopsy-proven fatty acid binding protein 5 (FABP5)-negative tumors and positive for expression of cellular retinoic acid binding protein 2 (CRABP2). Combined treatment with a chromatin modifying agent can also serve to induce re-expression of CRABP2.

Cyclin-dependent kinase 5 is amplified and overexpressed and activated by mutant K-Ras


This *Clinical Cancer Research* paper is out of the lab of Tony Hollingsworth, PhD (Scientific Advisory Board). Dr. Hollingsworth and colleagues examined human pancreatic adenocarcinoma samples and found increased expression of cyclin-dependent kinase 5 (CDK5) or its activators p35 or p39. Further experiments suggested that mutant K-Ras stimulates the cleavage of p35 to its more active form, suggesting a potential role for CDK5 in early progression of pancreatic cancer. Inhibition of CDK5 with dominant negative or the drug roscovitine blocked migration and invasion of pancreatic cancer cells.

RAS oncogenes: weaving a tumorigenic web


*Nature Reviews Cancer* published this article lead-authored by Dafna Bar-Sagi, PhD (2008 Pancreatic Cancer Action Network – AACR Pilot Grant and Scientific Advisory Board). Dr. Bar-Sagi and colleagues discuss the activation and outcome of RAS signaling in cancer initiation and progression.
Mast cells in tumor microenvironment promote the in vivo growth of pancreatic cancer
Craig Logsdon, PhD (Scientific Advisory Board) is a co-author on this Clinical Cancer Research article. Among inflammatory cells, mast cells have been shown to be present and active in other cancer types. Therefore, Chang et al sought to determine levels of mast cells in pancreatic cancer. In genetically engineered mouse model of the disease, there was an influx of mast cells into the pancreatic cancer microenvironment. When pancreatic cancer cells were orthotopically implanted into mice deficient for mast cell production, disease progression was slowed, but restored upon addition to mast cells. Presence of mast cells in the tumor microenvironment proved to be a poor prognostic marker in human pancreatic cancer patients.

Vitamin E (delta)-tocotrienol augments the anti-tumor activity of gemcitabine and suppresses NFkB
Researchers in Mokenge Malafa, MD (Medical Advisory Board)’s laboratory at Moffitt Cancer Center undertook this study to determine whether vitamin E compounds have any anti-cancer properties in pancreatic cancer cells. Delta-tocotrienol was found to be the most bioactive for pancreatic cancer, augmenting gemcitabine administration and suppressing constitutive activation of NFkB.

Pancreatic cancer: Fibroblast co-conspirators
Review of: Inhibiting Cxcr2 disrupts tumor-stromal interactions and improves survival in a mouse model of pancreatic ductal adenocarcinoma
This Nature Reviews Cancer article discusses the above-mentioned JCI paper on targeting chemokine signaling in stromal cells as a means to treat pancreatic cancer.

Role of a(5)B(1) integrin up-regulation in radiation-induced invasion by human pancreatic cancer cells
This study is out of the University of Michigan (Go Blue!). The authors used pancreatic cancer cell lines to determine that radiation rapidly induces pancreatic cancer cell invasion, and that radiation-induced invasion is caused by up-regulation of a(5)B(1) integrin fibronectin receptors. Blocking this phenomenon may enhance the effects of radiation in the treatment of pancreatic cancer.

Quiescin sulfhydryl oxidase 1 promotes invasion of pancreatic tumor cells mediated by MMPs
Katchman et al analyzed quiescin sulfhydryl oxidase 1 (QSOX1) expression in pancreatic cancer cell lines and patient specimens. QSOX1 was found to be over-expressed in pancreatic cancer, and down-regulation of its expression by shRNA led to decreased growth and invasiveness, possibly via lack of activation of MMP2 and MMP9.

STAT3 knockdown reduces pancreatic cancer cell invasiveness and matrix metalloproteinase-7
PLoS One published this article describing efforts to knockdown expression of STAT3 via shRNA in xenograft mouse models of pancreatic cancer, and then evaluate resultant cellular and gene expression
changes. Successful knockdown of STAT3 led to decreased growth and invasion, perhaps via decreased expression of MMP7.

**GDC-0980 is a novel class I PI3K/mTOR kinase inhibitor with robust activity in cancer models**
This *Molecular Cancer Therapeutics* paper describes preclinical studies out of Genentech. Their GDC-0980 compound potently inhibits Class I PI3K and mTor kinase. Experiments with cell lines showed only weak activity in pancreatic cancer cells, consistent with KRAS acting as a resistance marker.

**The efficacy of a novel, dual PI3K/mTOR inhibitor NVP-BEZ235 to enhance chemotherapy**
Investigators out of UT Southwestern looked at NVP-BEZ235, another dual PI3K/mTor inhibitor, in the treatment of experimental pancreatic ductal adenocarcinoma. They treated mouse xenografts with NVP-BEZ235 in combination with gemcitabine and endothelial monocyte activating polypeptide II. This combination treatment led to enhanced survival of the mice.

**EGFR-dependent pancreatic carcinoma cell metastasis through Rap1 activation**
Investigators at UCSD put together this *Oncogene* paper to describe a novel role for EGFR in pancreatic cancer progression. Rather than impacting cell growth, they found that EGFR promotes invasion and metastasis.

**OGX-427 inhibits tumor progression and enhances gemcitabine chemotherapy in pancreatic cancer**
This paper describes usage of the OncoGenex Pharmaceuticals compound OGX-427, a modified antisense oligonucleotide that is complementary to the heat shock protein Hsp27, in pancreatic cancer cell lines (*in vitro* and *in vivo*). OGX-427 was found to inhibit proliferation, induce apoptosis, and enhance gemcitabine chemosensitivity.

**Chemotherapeutic properties of phospho-nonsteroidal anti-inflammatory drugs**
This *Cancer Research* article evaluates the efficacy of a new class of anti-cancer compounds, phospho-NSAIDs, in human pancreatic, colon, and breast cancer cell lines and xenograft models. Phospho-aspirin and phospho-sulindac were found to be effective against cancer cells implanted into mice, without detectable toxicity.

**Evolution of tumor invasiveness: the adaptive tumor microenvironment landscape model**
Lee et al combined lab experimental results with computations modeling to understand the relationship between pancreatic cancer cells and the tumor microenvironment.
An oncolytic adenovirus defective in pRb-binding can efficiently eliminate pancreatic cancer cells
Researchers at Queen Mary University of London published this Cancer Gene Therapy article. The authors evaluated whether an oncolytic adenovirus defective binding to pRb (dl922-947), could target cells with deregulated cell cycle control. In combination with 5-FU or gemcitabine, the dl922-947 virus was found to prolong survival of pancreatic cancer xenograft mice.

Anti-tumour activity of afatinib, an irreversible ErbB family blocker, in human pancreatic tumour cells
The British Journal of Cancer published this article describing alternate approaches to block EGFR in pancreatic cancer cells. Their data suggest that the small molecule tyrosine kinase inhibitor afatinib is more effective than FDA-approved erlotinib in stopping the growth of pancreatic cancer cells in vitro and in vivo.

ZSTK474 suppresses proliferation, sensitizes human pancreatic adenocarcinoma cells to gemcitabine
Researchers at the Lombardi Cancer Center at Georgetown University studied the mechanism and effects of treating pancreatic cancer cell lines with ZSTK474, a PI3K/Akt inhibitor, in combination with gemcitabine. Their experiments demonstrated that ZSTK474 inhibited cell growth by arresting cells at the G1 phase and by inducing apoptosis, as well as blocking the phosphorylation of key signaling molecules. Adding gemcitabine to ZSTK474 led to synergistic anti-tumor effects.

Tumor-specific targeting of pancreatic cancer with shiga toxin B-subunit
Maak et al looked for the expression of glycosphingolipid globotriaosylceramide [Gb(3)] on pancreatic cancer cells. Gb(3) is a receptor for shiga toxin B-subunit (STxB), and has been shown to be expressed in other cancer types. Gb(3) was found on the surface of pancreatic cancer cells; its presence had no prognostic significance. Treatment of pancreatic cancer cells with STxB covalently coupled to SN38, an active metabolite of the topoisomerase I inhibitor irinotecan, showed much more efficacy than treating with irinotecan alone.

Combinatorial therapies improve therapeutic efficacy of nanoliposomal ceramide in pancreatic cancer
This Cancer Biology & Therapy article demonstrated that nanoliposomal ceramide can be an effective anti-pancreatic cancer therapeutic in combination with gemcitabine or an inhibitor of ceramide neutralization.

ETIOLOGY
Somatic mutations in the chromatin remodeling gene ARID1A occur in several tumor types
This paper involves a team of Johns Hopkins researchers, including grant recipients Jim Eshleman, MD, PhD, Chris Iacobuzio-Donahue, MD, PhD, and Anirban Maitra, MD, as well as Scientific Advisory Board (current and emeritus) members Ralph Hruban, MD, Chris Iacobuzio-Donahue, MD, PhD, and Anirban Maitra, MD. Because mutations in the chromatin remodeling gene ARID1A have been discovered in the
majority of ovarian clear cell carcinomas, the authors investigated other tumor types, and found mutations in 2-8% of pancreatic tumors.

**Pancreatic cancer and a novel MSH2 germline alteration**
Gloria Petersen, PhD (Scientific Advisory Board) contributed to this *Pancreas* paper. MSH2 is a DNA mismatch repair gene that has been shown to be mutated in hereditary colon cancer. Here, the authors report a family in which an MSH2 P349L missense alteration is co-segregating with pancreatic cancers in three nonsmoking relatives. Based on results in this family, it appears that this particular mutation may increase their risk of developing pancreatic cancer, but further studies will be necessary to draw firm conclusions.

**Folate intake and risk of pancreatic cancer: Pooled analysis of prospective cohort studies**
This large collaborative project published in *JNCI* analyzed primary data from 14 prospective cohort studies that included over 300,000 men and over 500,000 women to assess the association between folate intake and risk of pancreatic cancer. Folate intake was measured via a food-frequency questionnaire, and no association between folate and pancreatic cancer risk was detected.

**Acute pancreatitis: Is smoking a risk factor for acute pancreatitis?**
*Review of:* Cigarette smoking, smoking cessation and acute pancreatitis: a prospective population-based study
Drs. Lowenfels and Maisonneuve wrote this *Nature Reviews Gastroenterology and Hepatology* News & Views piece. Based on the data presented in the *Gut* article mentioned above, the authors agree that smoking, along with alcohol, should be considered as risk factors for acute pancreatitis.

**IPMN of the pancreas: associated cancers, family history, genetic predisposition?**
Research published in the journal *Surgery* examined retrospective and prospective data to discover the association of intraductal papillary mucinous neoplasms (IPMNs) with extrapancreatic malignancies (EPM), malignancies in family members, and germline BRCA1 and BRCA2 mutations. Lubezky *et al* found higher rates of EPM in IPMN patients than patients with pancreatic ductal adenocarcinoma. Further, IPMN patients had a high incidence of other cancer in their families, particularly pancreatic. These findings suggest a genetic component in the pathogenesis of IPMN, possibly including BRCA2 mutations, which are found in 25 percent of IPMN patients with a family history of pancreatic cancer.

**Ethanol differentially regulates snail family of transcription factors and invasion of pancreatic cells**
Ward *et al* examined the expression of Snail family of transcription factors in pancreatic ductal epithelial and pancreatic cancer cells following exposure to ethanol. Ethanol increased Snail expression in both types of cells, with a more dramatic increase in the immortalized human pancreatic ductal epithelial
cells. The authors also observed an unexpected result, whereby ethanol decreased invasion of the immortalized ductal cells, but had no effect on pancreatic cancer cells. Together, these results highlight some of the differential effects of ethanol on premalignant and malignant pancreatic cells, and demonstrate the pleiotropic effects of ethanol on pancreatic cancer progression.

**Contribution of germline mutations in the BRCA and PALB2 genes to pancreatic cancer in Italy**


Published in *Familial Cancer*, this article described analysis of 19 Italian pancreatic cancer patients with family history of both pancreatic and breast/ovarian cancer. The authors did not detect any mutations or deletions of PALB2, but found four instances of BRCA1 and three BRCA2 mutations.

**A pilot case-cohort study of liver and pancreatic cancers in poultry workers**


This *Annals of Epidemiology* article describes a pilot case-control study evaluating the liver and pancreatic cancer rates in highly-exposed poultry works, as compared to a control population. Preliminary evidence from this study suggests that exposure to poultry, perhaps due to oncogenic viruses, may increase the risk of developing pancreatic or liver cancer.

**EARLY DETECTION, DIAGNOSIS, AND PROGNOSIS**

Variations of oral microbiota are associated with pancreatic diseases including pancreatic cancer


David Wong, DMD, DMSc and colleagues at UCLA published this study on analyzing patients’ saliva samples. These results picked up a good deal of media attention. The *Gut* paper describes a significant difference in salivary microflora observed between pancreatic cancer patients and healthy controls. Individuals with chronic pancreatitis also displayed changes in oral bacterial levels.

**Is it worth looking? Abdominal imaging after pancreatic cancer resection: a national study**


This investigation took place in the laboratory of Jennifer Tseng, MD (2006 Samuel Stroum – Pancreatic Cancer Action Network – ASCO Young Investigator Award). Analyses of SEER-Medicare data revealed that utilization of complex imaging after pancreatic cancer resection has increased substantially among Medicare beneficiaries, driven primarily by an increasing number of CT scans. However, the authors did not observe any significant survival benefit among patients who received scans on a routine basis.

**Outcomes after preoperative EUS and biopsy in patients undergoing distal pancreatectomy**


Max Schmidt, MD, PhD (2003 Pancreatic Cancer Action Network – AACR Career Development Award) contributed to this *Surgery* article. The authors demonstrate that preoperative fine needle aspiration (FNA) biopsy guided by endoscopic ultrasonography (EUS) in patients undergoing distal pancreatectomy was not associated with adverse perioperative or long-term outcomes.
Pdx1 expression in pancreatic precursor lesions and neoplasms
Authors on this article include Anirban Maitra, MD (2004 Pancreatic Cancer Action Network – AACR Career Development Award and Scientific Advisory Board) and Ralph Hruban, MD (Emeritus Scientific Advisory Board). The researchers looked at microarrays containing tissue cores from more than 250 pancreatic specimens – including precursor lesions, invasive cancer, and nondysplastic pancreatic epithelium. They analyzed these tissues for expression of pancreatic and duodenal homeobox (Pdx1), a homeobox transcription factor required for the embryonic development of the pancreas. Pdx1 protein expression was variable, and detected in some benign samples, precursors and invasive pancreatic cancer cells, and other neoplasms of the pancreas.

Analysis of incidence & clinical outcomes in patients with thromboembolic events & pancreatic cancer
This study was conducted in the laboratory of Eileen O'Reilly, MD (Medical Advisory Board) at Memorial Sloan-Kettering Cancer Center. Dr. O'Reilly and colleagues found that invasive exocrine pancreatic cancer patients who developed a thromboembolic event (TE) had a significantly higher risk of death. Moreover, the risk of death in patients with a TE was higher among those who developed the TE early in the progression of their disease. Patients with low BMI showed a significantly longer time to thrombosis. These results suggest that early TE could be considered a stratifying factor in the design of clinical trials.

Serum monocyte chemoattractant protein-1 in pancreatic cancer
Researchers at Thomas Jefferson University explored the potential of serum monocyte chemoattractant protein-1 (MCP-1) as a biomarker indicative of pancreatic cancer. Obese patients had higher MCP-1 levels than non-obese; patients with pancreatic adenocarcinoma had higher MCP-1 levels than those with intraductal papillary mucinous neoplasms (IPMNs). Further, MCP-1 levels in IPMN patients revealed which patients were more likely to progress to invasive disease.

EUS-FNA for pancreatic neuroendocrine tumors: a tertiary cancer center experience
Atiq et al looked at the utility of endoscopic ultrasound – fine needle aspiration (EUS-FNA) in diagnosing the relatively uncommon pancreatic neuroendocrine tumors (PNETs). The authors conclude that EUS-FNA is a reliable modality for further characterization of suspected lesions and for establishing a tissue diagnosis, with minimal concern of complications from the procedure.

Association of microRNA-21 expression with its targets, PDCD4 and TIMP3, in pancreatic cancer
The microRNA miRNA-21 has been shown to be expressed in several cancer types, including pancreatic. Here, the authors show that miRNA-21 was the highest expressed microRNA in pancreatic ductal adenocarcinomas. Associated with the increased expression of miRNA-21, its tumor-suppressor target genes, programmed cell death 4 (PDCD4) and tissue inhibitor of metalloproteinase (TIMP3), were down-regulated. Further, up-regulation of microRNA-21 was significantly associated with poor survival.
Heat shock protein 27 as a prognostic and predictive biomarker in pancreatic ductal adenocarcinoma
A team of researchers out of Ludwig-Maximilians-University in Munich, Germany evaluated whether heat shock protein 27 (HSP27) could serve as a biomarker for pancreatic cancer. HSP27 expression indeed was suggested to be prognostic and predictive of treatment response.

Borderline resectable pancreatic tumors: is there a need for further refinement of this stage?
This Hepatobiliary & Pancreatic Diseases International paper out of India looks at utilizing preoperative imaging to determine which borderline resectable pancreatic tumors might be candidates for a complete surgical resection, with or without vascular resection. The authors conclude that it is possible to achieve a complete resection immediately in patients found to have borderline resectable pancreatic tumors on preoperative imaging.

Laparoscopic surgeons develop fluorescent light technique to improve pancreatic cancer detection
Research out of UCSD was presented at the 2011 Clinical Congress of the American College of Surgeons. Drs. Bouvet, Hoffman, and colleagues demonstrated an improvement in laparoscopic staging of pancreatic cancer by including a light emitting diode (LED) source. In mouse experiments, injecting the animals with fluorescent-labeled antibodies for proteins commonly expressed by pancreatic tumors, followed by laparoscopy with LED, resulted in increased sensitivity, specificity, and ability to detect smaller tumors or metastatic lesions than laparoscopy alone.

ImaginAb, Inc. awarded $2.3 million from the National Cancer Institute
ImaginAb, Inc. has been awarded a total of $2.3 million in funding from the National Cancer Institute's (NCI) Small Business Innovation Research (SBIR) program to help further develop diagnostic imaging agents for Positron Emission Tomography (PET). The company hopes to improve the technology specifically for the diagnosis and staging of pancreatic and prostate cancer.

Chromogranin A and neuron-specific enolase as prognostic markers in patients with advanced pNET
Yao et al explored the expression of chromogranin A (CgA) and neuron-specific enolase (NSE), biomarkers of pancreatic neuroendocrine tumors (pNETs), after treatment with everolimus, an inhibitor of mTor that was recently approved for advanced pNETs. Their results suggested that patients with high CgA and NSE baseline levels showed poorer progression-free and overall survival. If patients’ CgA and NSE levels went down initially after treatment with everolimus, this response was associated with extended progression free survival.
TREATMENT
Gemcitabine plus nab-paclitaxel is an active regimen in patients with advanced pancreatic cancer

Pancreatic Cancer Action Network write-up:
Results from the TGen/Scottsdale Healthcare Phase I/II trial of nab-paclitaxel in combination with gemcitabine were published in JCO. A maximum tolerated dose was established, and survival data were encouraging. Patients with complete metabolic responses early and patients with increased levels of SPARC in the stroma surrounding the tumor were indicators of good survival outcome.

Gemcitabine alone versus gemcitabine plus radiotherapy in locally advanced pancreatic cancer
JCO published this article with an accompanying editorial:
Locally advanced pancreatic cancer: Where should we go from here?
Chris Crane, MD (Medical Advisory Board) is among the investigators involved in this Eastern Cooperative Oncology Group study. Patients with locally advanced unresectable pancreatic adenocarcinoma were randomized to receive gemcitabine alone, or gemcitabine with radiotherapy.
Patients with the addition of radiotherapy displayed an improved overall survival with tolerable toxicity.

Accumulation of sub-100 nm polymeric micelles in poorly permeable tumours depends on size
Nature Nanotechnology published this paper out of the University of Tokyo, evaluating the accumulation and effectiveness of different sizes of long-circulating, drug-loaded polymeric micelles in both highly and poorly permeable tumors. The authors utilized pancreatic cancer as an example of a poorly permeable tumor, and found that 30nm micelles could penetrate the tumor and elicit an anti-tumor response.

Liver metastases of pancreatic cancer: Role of repetitive transarterial chemoembolization (TACE)
Published in Pancreas, this study analyzed whether chemoembolization might affect the survival of patients with liver metastases due to pancreatic cancer. The TACE procedure was found to be safe and relatively effective.

Thymidylate synthase (TYMS) enhancer region genotype-directed phase II trial of oral capecitabine
http://www.ncbi.nlm.nih.gov/pubmed/20306339
Weekes et al performed a study to characterize the six-month overall survival and toxicity associated with second-line capecitabine treatment of advanced pancreatic cancer patients harboring the thymidylate synthase (TYMS) *2/*2 allele. The study was closed early due to poor accrual and increased toxicity. However, the presence of the *2/*2 TYMS genotype in all of the screened patients trended toward a decreased overall survival.
Phase I trial of preoperative intratumoral injection of immature dendritic cells and OK-432
This group out of Fukushima University in Japan tested the administration of endoscopic ultrasound guided fine needle injection (EUS-FNI) of immature dendritic cells with OK-432 into a pancreatic tumor prior to surgical resection. Their small Phase I trial results suggested that the EUS-FNI procedure was safe and feasible, and further experiments will be necessary to determine effectiveness. Encouragingly, the patients who underwent EUS-FNI of dendritic cells showed accumulation of CD83+ and Foxp3+ cells in the lymph nodes.

First-in-man clinical trial of the oral pan-AKT inhibitor MK-2206 in patients with advanced solid tumors
This international collaborative team of researchers produced this JCO article, describing a phase I study of MK-2206 (a potent, oral allosteric inhibitor of all AKT isoforms) in patients with advanced solid tumors. A patient with pancreatic adenocarcinoma and two patients with pancreatic neuroendocrine tumors showed responses to the drug. The authors found that MK-2206 was well tolerated and showed evidence of anti-tumor efficacy by blocking AKT signaling.

Long-term outcomes of neoadjuvant chemotherapy before chemoradiation for pancreatic cancer
Investigators at the Harvard Radiation Oncology Program determined that locally advanced pancreatic cancer patients who underwent neoadjuvant chemotherapy before chemoradiation displayed improved overall and median-free survival rates.

Clinical trials: The silent minority-unpublished data on cancer care
Commentary on: Compendium of unpublished phase III trials in oncology: characteristics and impact on clinical practice
Dan Hayes, MD at the University of Michigan wrote this Nature Reviews Clinical Oncology News & Views piece. Dr. Hayes comments that, “Patients who participated in these trials did so out of a sense of altruism, and we betray that trust if we do not handle the precious data generated in these studies appropriately.”

Inferior survival of pancreatic patients who received chemo but didn’t participate in clinical trials
The findings of this study published in Oncology suggest that the outcome for advanced pancreatic cancer patients who did not participate in clinical trials, regardless of gemcitabine-based treatment, is still bleak.

Targeting heat shock response pathways to treat pancreatic cancer
This Drug Discovery Today review describes approaches and strategies to target heat shock proteins in pancreatic cancer.
Infinity advances pancreatic cancer drug candidate
Infinity Pharmaceuticals, Inc. announced completed enrollment of their Phase 2 study testing the hedgehog inhibitor IPI-926 in combination with Gemzar, versus Gemzar alone. IPI-926 is intended to target the dense stroma surrounding pancreatic tumors, allowing better delivery of the chemotherapeutic drug to the tumor.

Amgen leads firms in pancreatic cancer drug chase
Amgen is partnered with Japan’s Takeda on development of ganitumab, a monoclonal antibody targeting type 1 insulin-like growth factor receptor (IGF-1R). A Phase III study of ganitumab in the treatment of pancreatic cancer was initiated earlier this year, with results due in October 2013.

Aduro BioTech announces first patient treated in Phase 2 pancreatic cancer trial
Aduro BioTech, Inc. is testing their CRS-207 (attenuated Listeria monocytogenes) in combination with GVAX Pancreas Cancer Vaccine (allogeneic cancer cell lines that have been genetically-modified to secrete GM-CSF to stimulate the immune system). The first patient has begun this treatment regimen; outcomes will be overall survival, safety, and immune response.

Phase 2 clinical trial to assess safety, tolerability and efficacy of gemcitabine combined with PEGPH20
Halozyme Therapeutics, Inc. announced the commencement of patient dosing in a Phase 2 clinical trial with pegylated rHuPH20 (PEGPH20) in patients with stage IV previously untreated pancreatic cancer. The article quotes Sunil Hingorani, MD, PhD (2005 Dr. Laurence A. Mack and Roselle Mack Memorial – Pancreatic Cancer Action Network – AACR Career Development Award and 2007 Pancreatic Cancer Action Network Pilot Grant), principal investigator of this trial. PEGPH20 was designed for the systemic treatment of tumors rich in hyaluronan, or HA. HA is a component of the extracellular matrix and PEGPH20 has been shown to remove the HA coating surrounding several tumor cell lines.

Regional hyperthermia combined with chemoradiotherapy in primary or recurrent pancreatic cancer
Researchers at University Hospital in Verona, Italy evaluated the addition of hyperthermia to chemoradiotherapy in patients with locally advanced pancreatic cancer. Their preliminary data suggested that treatment with hyperthermia + chemoradiotherapy led to overall survival of 15 months, compared to 11 month in patients treated with chemoradiotherapy alone. The heat treatment was delivered using the BSD-2000 Hyperthermia System.
Biocancell pancreatic cancer drug wins FDA fast-track approval
http://www.globes.co.il/serveen/globes/docview.asp?did=1000687932&fid=1725
The Biocancell Therapeutics Ltd. Compound BC-819 is a plasmid comprised of the H19 gene regulatory sequences that drive the expression of Diphtheria Toxin A (DTA). Biocancell is readying a Phase IIb clinical trial of BC-819 to test its safety and efficacy when given in conjunction with gemcitabine. Biocancell has obtained FDA fast-track approval for this experimental treatment.

Clavis Pharma announces the completion of Study 002 Low hENT1 cut-off level
Clavis Pharma’s Study 002 is a retrospective analysis of human Equilibrative Nucleoside Transporter 1 (hENT1) levels in pancreatic cancer patients, and their relationship with gemcitabine response. Their data suggest that hENT1 cut-off level shows a highly statistically significant and clinically meaningful difference in overall survival between low and high hENT1 expression in gemcitabine-treated patients.

Biotech's 5 key attacks on pancreatic cancer
http://www.fiercebiotech.com/special-reports/biotechs-5-key-attacks-pancreatic-cancer
FierceBiotech lists what they consider to be five of the industry’s “most promising” drugs in development to fight pancreatic cancer. They include brief write-ups about: Ganitumab (Amgen, Takeda), GV1001 (KAEL-GemVax), HyperAcute Pancreas (NewLink Genetics), GI-4000 (GlobeImmune), and MM-398 (Merrimack Pharmaceuticals).

CANCER CONTROL, SURVIVORSHIP, AND OUTCOMES RESEARCH

Perioperative surgical care bundle reduces pancreaticoduodenectomy wound infections
Researchers at Thomas Jefferson University came up with a list of 12 measures which were able to reduce wound infections following Whipple surgery by nearly half.

Nutritional status of patients with locally advanced pancreatic cancer: a pilot study
Researchers at Yale University School of Nursing evaluated nutritional status of locally advanced pancreatic cancer patients as they underwent chemoradiotherapy. The patients’ results of the Anorexia/Cachexia Subscale questionnaire showed a significant increase in appetite and weight concerns after treatment, compared to baseline.

SCIENTIFIC MODEL SYSTEMS

Recruitment and activation of pancreatic stellate cells from the bone marrow in pancreatic cancer
This PLoS One article describes a novel model of tumor-host interaction. The authors generate a robust model of whole bone marrow transplantation to show that in pancreatic carcinogenesis, and in chronic pancreatitis, bone marrow derived stem cells contribute significantly to the activated pancreatic stellate cell population. This model can provide further insight into tumor-host interactions.