PANCREATIC CANCER NEWS & UPDATES – JUNE 2011

BIOLOGY OF CANCER

***Journal of Gastrointestinal Cancer* – guest edited by Martin Fernandez-Zapico**

http://www.springerlink.com/content/1941-6628/42/2/

The June 2011 edition of the *Journal of Gastrointestinal Cancer* was guest edited by Martin Fernandez-Zapico, MD (2007 Carole and Bob Daly – Pancreatic Cancer Action Network – AACR Career Development Award). Included among pancreatic cancer-specific articles in this journal is a review co-written by Dr. Fernandez-Zapico.

Stromal biology and therapy in pancreatic cancer

http://www.ncbi.nlm.nih.gov/pubmed/20966025

This *Gut* article is out of the laboratory of Dave Tuveson, MD, PhD (Chair, Scientific Advisory Board and 2003 Pancreatic Cancer Action Network – AACR Career Development Award), also includes Dr. Tuveson's former postdoctoral fellow Ken Olive, PhD (2011 Tempur-Pedic® Retailers – Pancreatic Cancer Action Network – AACR Career Development Award). The authors discuss the importance of stromal cells within the pancreatic tumor microenvironment, and consideration of this feature of the disease in designing preclinical and clinical studies.

Retinoic acid-induced pancreatic stellate cell quiescence reduces paracrine Wnt-b-catenin signaling

http://www.ncbi.nlm.nih.gov/pubmed/21704588

Barts Cancer Institute press release: http://www.bci.qmul.ac.uk/new-publication.html

This study has picked up some media attention, showing encouraging results that vitamin A might play a role in fighting pancreatic cancer. Dave Tuveson, MD, PhD (Chair, Scientific Advisory Board and 2003 Pancreatic Cancer Action Network – AACR Career Development Award) was an author on this study published in *Gastroenterology*. Since pancreatic cancer patients are frequently deficient in vitamin A, the investigators treated genetically engineered pancreatic cancer mice with all-trans retinoic acid (ATRA; a form of vitamin A). ATRA was found to induce quiescence and reduce motility of pancreatic stellate cells, leading to reduced proliferation and increased apoptosis of surrounding pancreatic cancer cells.

Counterbalancing angiogenic regulatory factors control the rate of cancer progression and survival

http://www.ncbi.nlm.nih.gov/pubmed/21622854

This *PNAS* paper was contributed and coauthored by Doug Hanahan, PhD (2007 Pancreatic Cancer Action Network Pilot Grant). The authors looked at endogenous angiogenesis inhibitors (EAIs) and their balance with pro-angiogenic factors in pancreatic neuroendocrine tumors. They found that EAIs can serve as intrinsic microenvironmental barriers to tumorigenesis.

N-terminal domain of G3BP enhances cell motility, invasion by posttranscriptional regulation of BART
http://www.ncbi.nlm.nih.gov/pubmed/21665939
This *Molecular Cancer Research* paper is out of the laboratory of Tony Hollingsworth, PhD (Scientific Advisory Board). G3BP (GTPase-activating protein SH3-binding protein) is a marker of stressed cells and regulates mRNA stability. G3BP binds and degrades the mRNA of BART (binding of Arl two), blocking its repression of invasion and metastasis in pancreatic cancer cells. Here, the authors report that the N-terminal region of G3BP is responsible for binding to BART mRNA and inducing invasion of pancreatic cancer cells.

Molecular profiling of direct xenograft tumors established after neoadjuvant therapy
http://www.ncbi.nlm.nih.gov/pubmed/21701930
Scientific Advisory Board member Craig Logsdon, PhD teamed up with Medical Advisory Board member Jason Fleming, MD for this *Annals of Surgical Oncology* publication. The researchers directly engrafted pancreatic cancer tumor samples from patients who were either untreated or treated with neoadjuvant therapy, and analyzed which genes were differentially expressed. Of note, TGFb-R2 expression was decreased and IGFBP3 was increased in samples of patients whose tumors were treated, as compared to treatment-naïve.

Altered telomeres in tumors with ATRX and DAXX mutations
http://www.ncbi.nlm.nih.gov/pubmed/21719641
Media attention: http://www.eurekalert.org/pub_releases/2011-06/jhmi-ttg063011.php
Authors on this *Science* paper include Ralph Hruban, MD (Scientific Advisory Board) and Anirban Maitra, MD (2004 Pancreatic Cancer Action Network – AACR Career Development Award). Alternative lengthening of telomeres (ALT) was found to occur in the majority of pancreatic neuroendocrine tumors (PanNETs) evaluated. All of the PanNETs exhibiting these abnormal telomeres had mutations in ATRX or DAXX, proteins known to be involved in chromatin remodeling at telomeres.

High-throughput RNAi screening identifies a role for TNK1 in growth and survival
http://www.ncbi.nlm.nih.gov/pubmed/21536687
A team of T-Gen scientists performed an RNAi screen of kinases in a pancreatic cancer cell line. Data revealed that tyrosine kinase nonreceptor 1 (TNK1) appeared to be a hit, whereby decreased expression of TNK1 led to reduced proliferation of the pancreatic cancer cells. Whereas TNK1 had previously been shown to have tumor suppressive qualities in embryonic stem cells, in pancreatic cancer cells, it appears to be positively associated with growth and survival.

Autophagy suppression promotes apoptotic cell death in response to inhibition of PI3K-mTOR
http://www.ncbi.nlm.nih.gov/pubmed/21678117
The PI3K-AKT-mTOR cascade is downstream of K-Ras and known to be active in pancreatic cancer. Here, a team of UCSF researchers sought to determine whether targeting the pathway at different intervals via dual inhibition of PI3K and mTOR may be more effective than blocking either molecule alone. Indeed, combined inhibition of PI3K and mTOR led to decreased cancer growth, but also led to an increase in autophagy as a survival mechanism. Therefore, the researchers combined a PI3K/mTOR inhibitor with chloroquine, a malaria drug known to block autophagy, and found an increase in pancreatic cancer cell death *in vitro* and *in vivo*.

Activated K-ras & INK4a/Arf deficiency cooperate by activation of Notch & NF-κB signaling pathways
http://www.ncbi.nlm.nih.gov/pubmed/21673986
Researchers at the Karmanos Cancer Institute studied the mechanism whereby K-ras activation and Ink4a/Arf deficiency cooperate to induce pancreatic ductal adenocarcinoma. Their results suggest that, in K-ras mutant, Ink4a/Arf deficient transgenic mice, the formation of pancreatic cancer is linked to activation of Notch and NF-kB together with the loss of microRNA-200 family members.

The Id3/E47 axis mediates cell-cycle control in human pancreatic ducts and adenocarcinoma
http://www.ncbi.nlm.nih.gov/pubmed/21498546
The authors hypothesized that the balance between basic helix-loop-helix (bHLH) transcription factors and a repressor of bHLH, Id3, may play a role in pancreatic cancer initiation. Indeed, this *Molecular Cancer Research* paper reports that Id3 expression was up-regulated in mouse models of pancreatitis and pancreatic intraepithelial neoplasm, as well as human pancreatic ductal adenocarcinoma. Forced over-expression of Id3 in human pancreatic duct cells induced cell cycle entry, suggesting that deregulation of bHLH and Id3 may play an important role in the initiation of pancreatic cancer.

FAP-overexpressing fibroblasts produce an extracellular matrix that enhances invasive velocity
http://www.ncbi.nlm.nih.gov/pubmed/21668992
This *BMC Cancer* publication out of Fox Chase Cancer Center looks at the role of fibroblast activation protein (FAP) in the formation of a permissive microenvironment promoting tumor invasion in pancreatic cancer. Overall, the investigators found that blocking FAP-directed organization of the microenvironment may interfere with the invasive velocity and directionality of pancreatic cancer cells.

Molecular signatures of pancreatic cancer
http://www.ncbi.nlm.nih.gov/pubmed/21631264
This review, coauthored by Ralph Hruban, MD (Scientific Advisory Board), summarizes recent research findings on the genetics and epigenetics of pancreatic cancer, and characterizes the alterations within histological subtypes of the disease.

ETIOLOGY

Pancreatic cancer and exposure to dietary nitrate and nitrite in the NIH-AARP Diet and Health Study
http://www.ncbi.nlm.nih.gov/pubmed/21685410
This story received some media attention, including this Reuters article quoting Andrew Ko, MD (2003 Pancreatic Cancer Action Network – ASCO Career Development Award). Although previously implicated in increasing the risk of pancreatic cancer, this study suggests that dietary nitrate and nitrite from cured meats only very slightly (and statistically insignificantly) affects the incidence of pancreatic cancer in men, and has no effect on women.

Pancreatitis-induced inflammation contributes to pancreatic cancer by inhibiting senescence
http://www.ncbi.nlm.nih.gov/pubmed/21665147
This *Cancer Cell* paper reports that pancreatitis contributes to tumor progression by abrogating the oncogene-induced senescence barrier characteristic of low-grade pancreatic intraepithelial neoplasms (panINs).

How to recycle cancer GWAS data
http://sciencelife.uchospitals.edu/2011/06/06/how-to-recycle-cancer-gwas-data/
The University of Chicago *Science Life* blog highlights work by assistant professor Brandon Pierce, PhD. Although the field is moving away from depending upon genome-wide association studies (GWAS), Dr. Pierce and colleagues published two papers recently in *Cancer Causes & Control* and *Cancer Research* (*see below*) that "recycle" GWAS data to answer important questions about genetic factors that contribute to the initiation of pancreatic cancer.

Genome-wide "pleiotropy scan" identifies HNF1A region as a pancreatic cancer susceptibility locus
http://www.ncbi.nlm.nih.gov/pubmed/21498636
(*See blog post above discussing this paper.*) Drs. Pierce and Ahsan restricted their genome-wide association (GWA) scan to search for small nuclear polymorphisms (SNPs) that had enhanced likelihood of variance in pancreatic cancer cells. This way, they were able to reduce the number of SNPs analyzed and allow less stringent statistical significance to indicate positive findings. Using this method, the authors determined that a SNP in the HNF1A region had the strongest association with pancreatic cancer, and serves as a susceptibility locus.

DNA mismatch repair network gene polymorphism as a susceptibility factor for pancreatic cancer
http://www.ncbi.nlm.nih.gov/pubmed/21681824
MD Anderson researchers retrospectively genotyped single nucleotide polymorphisms (SNPs) in DNA mismatch repair genes in pancreatic cancer patients and normal controls. They found 28 SNPs statistically significantly associated with pancreatic cancer risk.

Chemical found in foam cups a possible carcinogen
http://health.usnews.com/health-news/family-health/cancer/articles/2011/06/10/chemical-found-in-foam-cups-a-possible-carcinogen?PageNr=1
The Department of Health and Human Services released its 12th Report on Carcinogens, now including the chemical styrene, as "reasonably anticipated" to be associated with increased cancer risk. Exposure to styrene had been previously suggested to increase the risk of pancreatic cancer.

Tobacco consumption and pancreatic cancer mortality: what can we conclude from historical data?
http://www.ncbi.nlm.nih.gov/pubmed/21616993
A long-term population-level study was conducted in Australia to analyze the relationship between tobacco consumption and pancreatic cancer mortality. Encouragingly, the results suggested that smoking reduction correlated with statistically significantly decreased pancreatic cancer mortality in men. The authors are hopeful that a similar pattern will be evident in women as tobacco usage continues to decline.

Ethanol differentially regulates Snail family of transcription factors and invasion
http://www.ncbi.nlm.nih.gov/pubmed/21678462
Ward and colleagues at Northwestern University explored the different effects of ethanol (to mimic alcohol consumption, a major cause of pancreatitis, which is known to be a risk factor for pancreatic cancer) on precancerous and cancerous pancreatic ductal cells. Looking specifically at the Snail family of

transcription factors, which are known to play a role in epithelial to mesenchymal transition, the authors found variations between nonmalignant ductal epithelial cells and pancreatic cancer cells.

EARLY DETECTION, DIAGNOSIS, AND PROGNOSIS

MicroRNA-10b expression correlates with response to neoadjuvant therapy and survival
http://www.ncbi.nlm.nih.gov/pubmed/21652542
Co-corresponding author on this paper is Lorenzo Sempere, PhD, who cites his 2008 Laurie and Paul MacCaskill – Pancreatic Cancer Action Network – AACR Career Development Award as a funding source for this project. This *Clinical Cancer Research* paper describes an evaluation of expression of various microRNAs (miR) in pancreatic ductal adenocarcinoma cells. It was found that miR-10b was the most frequently and consistently over-expressed miRNA, compared to its expression in normal pancreatic epithelial cells. Further, miR-10b expression correlated with poor response to cancer therapy, lower likelihood of surgical resection, and shorter survival. Therefore, miR-10b may be considered a diagnostic and predictive biomarker for pancreatic cancer.

Proteomic analysis of urinary upper gastrointestinal cancer markers
http://www.ncbi.nlm.nih.gov/pubmed/21538913
This study out of the University of Edinburgh received some media attention. Husi, *et al* report that SELDI-TOF mass spectrometry is a rapid and valid screening tool in the search for urinary cancer biomarkers, and is potentially useful in defining and consolidating biomarker patterns for upper GI cancer screening.

Weight loss precedes cancer-specific symptoms in pancreatic cancer-associated diabetes mellitus
http://www.ncbi.nlm.nih.gov/pubmed/21654538
Since adult-onset diabetes mellitus has been shown to be associated with pancreatic cancer formation, researchers at the Mayo Clinic sought to determine whether changes in body weight were also relevant. Surprisingly, rather than weight gain typically seen in relation to type 2 diabetes initiation, patients with pancreatic cancer-associated diabetes exhibited weight loss preceding the onset of disease.

Neogenix Oncology & Cambridge Biomedical form partnership for blood based cancer diagnostic tests
http://www.businesswire.com/news/home/20110615006744/en/Neogenix-Oncology-Cambridge-Biomedical-Form-Partnership-Development
Neogenix Oncology, Inc brings its expertise in pancreatic and other cancer biomarkers to a partnership with Cambridge Biomedicals, Inc, experts in assay validation and use of CLIA and CAP certified lab environment. Together, the companies will develop an ELISA-based serum assay for diagnosis of pancreatic and colorectal cancer.

Review of screening for pancreatic cancer in high risk individuals
http://www.ncbi.nlm.nih.gov/pubmed/21633635
This *World Journal of Gastroenterology* article reviews high-risk groups, screening methods, and current screening programs and their results in pancreatic cancer.

Prognostic validity of a novel American Joint Committee on Cancer staging classification
http://www.ncbi.nlm.nih.gov/pubmed/21709192
This *Journal of Clinical Oncology* paper reports the first TNM staging classification for pancreatic neuroendocrine tumors (NETs). Patients treated with pancreatic NETs at the Moffitt Cancer Center were retrospectively assigned a stage based on this new American Joint Committee on Cancer (AJCC) designations. The researchers discover that the AJCC TNM classification for pancreatic NETs is prognostic for overall survival, and can therefore be adopted in clinical practice.

TREATMENT

Data from the 47th Annual Meeting of the American Society of Clinical Oncology (ASCO), June 3-7:

Blood proteins may identify vulnerability of pancreatic cancers to Avastin
http://www.dukehealth.org/health_library/news/blood-proteins-may-identify-vulnerability-of-pancreatic-cancers-to-avastin
A team of Duke researchers presented this abstract at ASCO, looking to predict which pancreatic cancer patients are most likely to respond to Avastin (bevacizumab) treatment, and explain the prior studies showing negative results for these patients. The investigators found three proteins, vascular endothelial growth factor-D, stromal cell-derived factor-1B, and angiopoietin-2, whose expression in the blood was predictive of pancreatic cancer patients' response to Avastin.

Astellas announces new study results showing increased survival rate for metastatic pancreatic cancer
http://www.prnewswire.com/news-releases/astellas-announces-new-study-results-showing-increased-survival-rate-for-metastatic-pancreatic-cancer-123220143.html
The Astellas compound AGS-1C4D4 was tested at Agensys, Inc, a member of the Astellas group of companies. Data presented at ASCO (abstract) describes AGS-1C4D4, a monoclonal antibody that targets prostate stem cell antigen (PSCA) on the surface of cancer cells, in a Phase II clinical trial for advanced pancreatic cancer, in combination with gemcitabine. This Phase II randomized trial demonstrated that the combination of AGS-1C4D4 plus gemcitabine is well tolerated and improves the six month estimated survival rate as compared to gemcitabine alone in patients with metastatic pancreas cancer.

Infinity reports results from Phase 1b clinical trial of IPI-926 in pancreatic cancer
http://www.globenewswire.com/newsroom/news.html?d=223661
Data describing a Phase 1b trial of IPI-926, an oral Smoothened antagonist, in combination with gemcitabine, were presented at a poster session at the annual ASCO meeting (see abstract). This inhibitor of the Hedgehog signaling pathway was found to be well tolerated in combination with gemcitabine, and preliminary evidence suggests that partial responses were occurring at a higher rate than retrospectively observed with gemcitabine alone.

Onconova presents positive data on ESTYBON® (rigosertib, ON 01910.Na), a novel anti-cancer agent
http://www.businesswire.com/news/home/20110606005917/en/Onconova-Presents-Positive-Data-ESTYBON%C2%AE-rigosertib-ON%C2%A001910.Na
Described here and in the abstract, Onconova Therapeutics, Inc announced a Phase II/III clinical trial following positive results in a Phase I trial. The drug being investigated is ESTYBON® (rigosertib, ON 01910.Na), a multi-targeted kinase inhibitor, blocking polo-like kinase 1 and PI-3 kinases, tested in

combination with gemcitabine. Based on the safety and efficacy results observed, the Phase II/III trial, designated ONTRAC (ON 01910.Na TRial in Patients with Advanced Pancreatic Cancer), is being launched to further test efficacy and safety of gemcitabine alone vs. gemcitabine combined with rigosertib (ON 01910.Na) in patients with previously untreated metastatic pancreatic cancer.

Clavis Pharma: expansion of the study to determine patient stratification in pivotal LEAP clinical trial
http://www.clavispharma.com/News+%26+Events/2011+Press+releases/857.cms
Clavis Pharma announces the expansion of its partner Clovis Oncology's LEAP trial, aimed to treat patients with newly diagnosed metastatic pancreatic cancer. Patients will be treated with CP-4126, a new, patented, lipid-conjugated form of the anti-cancer compound gemcitabine developed by Clavis Pharma using its lipid vector technology. Clovis Oncology has also developed a biomarker assay for hENT1 (human Equilibrative Nucleoside Transporter 1), to predict for patients' response to gemcitabine. These data were presented at ASCO; see abstract.

Addition of sorafenib to gemcitabine does not improve survival in advanced pancreatic cancer
http://www.empr.com/addition-of-sorafenib-to-gemcitabine-does-not-improve-survival-in-advanced-pancreatic-cancer/article/204642/
This multicenter randomized Phase III trial of sorafenib plus gemcitabine showed results in contrast to a previous Phase I trial. Here, addition of sorafenib to gemcitabine did not improve progression-free survival, response rate, or overall survival in patients with advanced pancreatic cancer. The ASCO abstract can be found here.

Moving the bar in clinical trials in upper GI malignancies
http://www.cancernetwork.com/conference-reports/asco2011/content/article/10165/1872979
This conference report from the 2011 ASCO Annual Meeting features Dr. Eileen O'Reilly (Medical Advisory Board) among other clinicians/researchers, discussing recent phase III trials in upper GI malignancies, with hopes of improving trial design.

Other Treatment Highlights

Aptamers: potential applications to pancreatic cancer therapy
http://www.ncbi.nlm.nih.gov/pubmed/21492073
This review was co-written by Kristy Rialon, MD and Rebekah White, MD (2007 Seena Magowitz – Pancreatic Cancer Action Network – AACR Career Development Award). Drs. Rialon and White discuss recent advances in the field of aptamers (single-stranded DNA or RNA oligonucleotide ligands) and how they relate to treatment of pancreatic cancer.

A phase II randomized study of cetuximab and bevacizumab alone or in combination with gemcitabine
http://www.ncbi.nlm.nih.gov/pubmed/21629990
Andrew Ko, MD (2003 Pancreatic Cancer Action Network – ASCO Career Development Award) is the lead author on this study out of UCSF. In this phase II trial, previously untreated advanced pancreatic cancer patients were randomized to receive either cetuximab (anti-EGFR) and bevacizumab (anti-VEGF), or both agents in combination with gemcitabine. The trial was closed early due to lack of efficacy in either arm.

Phase II trial of cetuximab, gemcitabine, and oxaliplatin followed by chemoradiation with cetuximab
http://www.ncbi.nlm.nih.gov/pubmed/21709185
Christopher Crane, MD and Jason Fleming, MD, both members of the Medical Advisory Board, contributed to this paper published in the *Journal of Clinical Oncology*. Previously untreated patients with locally advanced pancreatic cancer were given cetuximab, gemcitabine, and oxaliplatin followed by cetuximab, capecitabine, and radiation therapy. The authors saw encouraging survival results, and also observed that Smad4 (Dpc4) immunostaining correlated with the pattern of disease progression, suggesting this protein's utility as a predictive biomarker in pancreatic cancer.

Phase II trial of full-dose gemcitabine and bevacizumab in combination with radiotherapy
http://www.ncbi.nlm.nih.gov/pubmed/20598452
Medical Advisory Board members Mary Mulcahy, MD and Mark Talamonti, MD participated in this study. Patients with localized pancreatic cancer were treated with full-dose gemcitabine and bevacizumab in combination with attenuated three-dimensional conformal radiotherapy. Based on their findings, the authors concluded that the combination of full-dose gemcitabine, bevacizumab, and radiotherapy was active and was not associated with a high rate of major surgical complications.

Survival and quality of life of patients treated with adjuvant interferon-based chemoradiation
http://www.ncbi.nlm.nih.gov/pubmed/21701927
Jason Fleming, MD (Medical Advisory Board) was among the authors of this *Annals of Surgical Oncology* study. The authors conducted a phase II trial of resected pancreatic cancer patients treated with adjuvant interferon-based chemoradiation after surgery. The treatment was safe and tolerable, although patients experienced substantial reversible toxicity, and may be associated with improved overall survival.

Assessment of chk1 phosphorylation as a pharmacodynamic biomarker of chk1 inhibition
http://www.ncbi.nlm.nih.gov/pubmed/21482692
Diane Simeone, MD (2010 The Randy Pausch Family – Pancreatic Cancer Action Network – AACR Innovative Grant) was among authors on this *Clinical Cancer Research* publication. The chk1 inhibitor AZD7762 was investigated in a mouse xenograft model of pancreatic cancer, administered either during and after, or after, gemcitabine treatment. Presumably due to DNA damage induction (suggested by phosphorylation of chk1), AZD7762 sensitizes pancreatic cancer cells to gemcitabine.

Increased organ sparing using shape-based treatment plan optimization for IMRT
http://www.ncbi.nlm.nih.gov/pubmed/21680036
Joe Herman, MD (2008 Blum-Kovler – Pancreatic Cancer Action Network – AACR Career Development Award) is among the authors on this *Molecular Carcinogenesis* article. The goal of this study was to develop a model to assess the quality of intensity modulated radiation therapy (IMRT) of pancreatic adenocarcinoma. The model described leads to avoidance of organ at risk dosages, and increase in treatment planning efficiency.

Current treatment options for pancreatic carcinoma
http://www.ncbi.nlm.nih.gov/pubmed/21491194
This *Current Oncology Reports* review is coauthored by Jordan Berlin, MD (Chair, Medical Advisory Board).

Defining new paradigms for the treatment of pancreatic cancer
http://www.ncbi.nlm.nih.gov/pubmed/21461670
Researchers at the Moffitt and Karmanos cancer centers wrote this review focused on the development of novel treatments for pancreatic cancer.

Fighting pancreatic cancer: Treatments on the horizon
http://www.johnshopkinshealthalerts.com/alerts/digestive_health/pancreatic-cancer-treatments_5760-1.html
This Johns Hopkins *Health Alert* discusses promising treatments for pancreatic cancer that are currently in development.

A phase II study of oral S-1 with concurrent radiotherapy followed by chemotherapy with S-1 alone
http://www.ncbi.nlm.nih.gov/pubmed/21647560
Shinchi, *et al* report that S-1, a new oral fluoropyrimidine anticancer agent, was effective against locally advanced pancreatic cancer. Overall, combination therapy with S-1 and radiation in patients with locally advanced and unresectable pancreatic cancer is considered a promising, well-tolerated regimen that can be recommended as an effective treatment.

Treatment of advanced pancreatic carcinoma with ^{90}Y-clivatuzumab tetraxetan
http://www.ncbi.nlm.nih.gov/pubmed/21527562
(*See also data presented below.*) This phase I single-dose escalation trial evaluated a humanized antibody, hPAM4, labeled with ^{90}Y, that binds a mucin glycoprotein expressed in pancreatic cancer cells. The authors' overall conclusion is that ^{90}Y-hPAM4 was well tolerated with manageable hematologic toxicity at the maximal tolerated ^{90}Y dose, and is a potential new therapeutic for advanced pancreatic cancer.

Immunomedics reports final survival data with yttrium-90-labeled clivatuzumab tetraxetan
http://www.globenewswire.com/newsroom/news.html?d=223813
(*See also abstract presented above.*) These data, reported at the 2011 Annual Meeting of Society of Nuclear Medicine, discuss the Immunomedics proprietary humanized antibody, clivatuzumab tetraxetan, labeled with yttrium-90 (^{90}Y) and combined with low-dose gemcitabine, in patients with advanced pancreatic cancer. ^{90}Y clivatuzumab tetraxetan targets a human mucin antigen. Phase Ib/II clinical trial results suggested tolerability and evidence of anti-tumor activity of this combination.

Combination radioimmunotherapy and chemoimmunotherapy involving different or the same targets
http://www.ncbi.nlm.nih.gov/pubmed/21467164
Investigators from the Garden State Cancer Center and Immunomedics wrote this paper to discuss combining antibody-drug conjugates (ADC) with radioimmunotherapy (RAIT) for the treatment of human pancreatic cancer mouse xenograft models. The treatment included ^{90}Y clivatuzumab tetraxetan

(hPAM4; *discussed above*) and an anti-Trop-2–SN-38 conjugate. The combination controlled tumor progression and cured established xenografts significantly better than the individual treatments, without appreciable toxicity.

Phase I study of axitinib (AG-013736) in combination with gemcitabine
http://www.ncbi.nlm.nih.gov/pubmed/21670972
Advanced pancreatic cancer patients were treated with axitinib, a potent inhibitor of vascular endothelial growth factor (VEGF) receptors 1, 2, and 3. Overall, this French study showed that xxitinib and gemcitabine were well tolerated when administered together, without any pharmacokinetic interactions, and showed encouraging antitumor activity.

Trabedersen shows signs of encouraging efficacy in solid tumors
http://www.dddmag.com/Trabedersen-Shows-Signs-of-Encouraging-Efficacy-in-Solid-Tumors-060911.aspx
The Antisense Pharma drug trabedersen (AP 12009) is a gene silencing antisense compound designed to selectively down regulate the production of transforming growth factor-beta 2 (TGF-B2) at the translational level. Early clinical trials have shown excellent safety and encouraging survival rates for this compound. Advanced pancreatic cancer patients treated second-line with trabedersen reached a median overall survival of 6.9 months, which is comparable to best available chemotherapy.

Threshold Pharmaceuticals announces completion of patient recruitment for Phase 2 TH-302 study
http://www.marketwatch.com/story/threshold-pharmaceuticals-announces-completion-of-patient-recruitment-for-phase-2-th-302-pancreatic-cancer-study-2011-06-21?reflink=MW_news_stmp
Threshold Pharmaceutics, Inc announced that their completed accrual of pancreatic cancer patients was faster and included more patients than anticipated. For this Phase 2 trial, patients will be randomized to one of two arms receiving TH-302 (at different doses) plus gemcitabine, or receive gemcitabine alone. TH-302 is a novel small molecule tumor selective hypoxia-activated prodrug. The primary endpoint of this study is progression-free survival.

CureFAKtor Pharmaceuticals: novel FAK inhibitors decrease pancreatic cancer tumor blood flow
http://www.prnewswire.com/news-releases/curefaktor-pharmaceuticals-demonstrates-that-novel-focal-adhesion-kinase-fak-inhibitors-decrease-pancreatic-cancer-tumor-blood-flow-and-reduce-blood-vessel-density-124414173.html
Reported at the European Society for Medical Oncology 13th World Congress on Gastrointestinal Cancer meeting in Barcelona, Spain, CureFAKtor has seen encouraging results with its novel focal adhesion kinase (FAK) inhibitor in pancreatic cancer preclinical testing. The drug, CFAK-4, blocks the site on FAK where vascular endothelial growth factor receptor 3 (VEGFR3) binds. As a result of treatment with CFAK-4, tumor cells in a pancreatic cancer mouse model show decreased blood flow and reduced blood vessel density. CFAK-4 was granted Orphan Drug Designation by the US FDA a few months ago.

Morphotek, Inc. announces that two investigational drugs have received orphan drug designations
http://www.prnewswire.com/news-releases/morphotek-inc-announces-that-two-investigational-drugs-have-received-orphan-drug-designations-123450889.html
The Morphotek compound MORAb-066, a humanized monoclonal antibody to tissue factor, was granted orphan drug designation from the US FDA for the treatment of pancreatic cancer.

Cellceutix's Kevetrin(TM) slows pancreatic cancer tumor growth by 94%
http://www.marketwatch.com/story/cellceutixs-kevetrintm-slows-pancreatic-cancer-tumor-growth-by-94-protocol-towards-clinical-trials-nearing-end-2011-06-20?reflink=MW_news_stmp
The Cellceutix compound Kevetrin™ displayed impressive anti-pancreatic cancer efficacy in a mouse xenograft model of the disease. Kevetrin acts to activate p53, a tumor suppressor whose activity is frequently turned off in pancreatic cancer. Cellceutix will continue to treat animals with Kevetrin, and hopes to launch a Phase I clinical trial in the near future.

ERYTECH Pharma completes the enrollment of patients in its Phase I clinical trial in pancreatic cancer
http://www.businesswire.com/news/home/20110627005759/en/ERYTECH-Pharma-Completes-Enrollment-Patients-Phase-Clinical
The flagship product of ERYTECH, Graspa®, contains the enzyme L-asparaginase encapsulated in red blood cells. A Phase I clinical trial of Graspa® for the treatment of pancreatic cancer patients has announced completed accrual. ERYTECH has high expectations of the safety and efficacy of this drug.

SURVIVORSHIP

Cancer Facts & Figures 2011
http://www.cancer.org/Research/CancerFactsFigures/CancerFactsFigures/cancer-facts-figures-2011
Pancreatic Cancer Action Network write-up:
http://www.pancan.org/section_about/news_press_center/2011_press_releases/06_17_11_pr.php
The American Cancer Society has released its 2011 cancer facts and figures. While cancer incidence and death rates on the whole are continuing to decline, alarmingly, pancreatic cancer diagnoses and deaths are on the rise.

Marital status and survival in pancreatic cancer patients: a SEER based analysis
http://www.ncbi.nlm.nih.gov/pubmed/21698253
Published in *PLoS One*, this study analyzed whether there was a connection between marital status and pancreatic cancer survival. Interestingly, their data suggest that marital status is an independent prognostic factor of both perioperative and long-term survival in patients with pancreatic ductal adenocarcinoma.

Helping terminal patients make tough choices
http://www.cbsnews.com/stories/2011/06/01/eveningnews/main20068123.shtml
This CBS News article features Eileen O'Reilly, MD (Medical Advisory Board), and discusses the use of videos to explain options to patients towards end-of-life.

SCIENTIFIC MODEL SYSTEMS

Alteration of strain background & high omega-6 fat diet induces earlier onset of pancreatic neoplasia
http://www.ncbi.nlm.nih.gov/pubmed/20725998
This study is out of the laboratory of Paul Grippo, PhD (2007 Nancy Daly Riordan – Pancreatic Cancer Action Network – AACR Career Development Award). Elastase-Kras mice were developed in different mouse strains, and were fed a diet high in omega-six fatty acids (23% corn oil) and compared to mice fed with standard chow. The omega-six fatty acid diet led to increased frequency and size of pancreatic lesions.

Inactivation of Brca2 cooperates with Trp53 to induce pancreatic ductal adenocarcinomas in mice
http://www.ncbi.nlm.nih.gov/pubmed/21455033
Anirban Maitra, MD (2004 Pancreatic Cancer Action Network – AACR Career Development Award) is co-corresponding author on this *Cancer Biology & Therapy* publication. To model familial pancreatic cancer, the investigators created genetically engineered mice with both copies of BRCA2 deleted specific to the pancreas (CB mice), as well as the same mice with mutated, inactivated p53 (CBP mice). Some (~15%) of CB mice develop invasive and metastatic pancreatic ductal adenocarcinoma by about 15 months latency; CBP mice uniformly develop aggressive disease by that age. Their data suggest that BRCA2 deletion leads to rampant DNA damage, and tumor initiation is promoted by concominant inactivation of p53.

The ARF tumor suppressor inhibits tumor cell colonization independent of p53
http://www.ncbi.nlm.nih.gov/pubmed/21636682
A multi-institutional team of researchers published this *Molecular Cancer Research* article, describing a novel mouse xenograft model of pancreatic ductal adenocarcinoma metastasis. Pancreatic cancer cell lines were labeled with luciferase and introduced to the mouse via intracardial injection. Tracking the cells, MiaPaCa-2 cells exhibited the most strongly metastatic behavior, migrating to locations common for pancreatic cancer spread. Addition of the p14ARF tumor suppressor inhibited this metastasis, independent of p53, showing a proof-of-principle that this model can mimic the behavior of human pancreatic cancer.