PANCREATIC CANCER NEWS & UPDATES – JULY 2011

PANCREATIC CANCER ACTION NETWORK AND COMMUNITY NEWS

Pancreatic Cancer Special Conference

http://www.aacr.org/home/scientists/meetings--workshops/special-conferences/pancreatic-cancer.aspx

Save the date: the AACR Pancreatic Cancer Special Conference will be June 18-21, 2012, in Lake Tahoe, NV. The Pancreatic Cancer Action Network is a proud supporter of this meeting, and looks forward to the opportunity for a diverse group of investigators in the field to convene and discuss the future of pancreatic cancer research.

New Pancreatic Cancer Action Network welcomes new Scientific Advisory Board members

http://www.pancan.org/section_about/leadership_teams/sab/index.php

New members of the Scientific Advisory Board are Drs. Christine Iacobuzio-Donahue, Anirban Maitra, Frank McCormick, Anil Rustgi, Diane Simeone, Craig Thompson, and Bob Vonderheide. Additionally, the terms of three longstanding members of the Pancreatic Cancer Action Network's Scientific Advisory Board ended in June 2011, with another two members completing their terms in October 2011. The emeritus members of the Scientific Advisory Board now include Drs. Ralph Hruban, Margaret Mandelson, and Selwyn Vickers.

Pancreatic cyst and cancer early detection center new website

http://pancyst.org

C. Max Schmidt, MD, PhD (2003 Pancreatic Cancer Action Network – AACR Career Development Award) has launched a new website devoted to information and resources about pancreatic cysts. The Indiana University Pancreatic Cyst and Cancer Early Detection Clinic seeks to accurately identify, screen and risk stratify patients at increased risk for pancreatic cancer to promote early detection and prevention of pancreatic cancer. Dr. Schmidt's initiative and website have also picked up some media attention, such as articles in the *Baltimore Sun* and *LA Times*.

Pathway to Leadership Grant recipient promoted to assistant professor

http://www.hopkinsmedicine.org/kimmel_cancer_center/research_clinical_trials/research/research_labs/matsui_lab/members.html

Zeshaan Rasheed, MD, PhD was awarded the inaugural Pathway to Leadership Grant last year: 2010 Tempur-Pedic Retailers® – Pancreatic Cancer Action Network – AACR Pathway to Leadership Grant. This grant mechanism is designed to support early-career researchers as they transition from a postdoctoral, mentored position into independent faculty. We are pleased to announce that Dr. Rasheed was recently promoted to Assistant Professor of Oncology at Johns Hopkins University School of Medicine Sidney Kimmel Comprehensive Cancer Center. Congratulations!

2011 Gigi Shaw Arledge Conference on Pancreatic Disease

http://pancreasmd.org/event_20111020.html

This conference will take place on October 20, 2011, at NewYork-Presbyterian Hospital/ Columbia University Medical Center. Speakers include several grant recipients and Scientific Advisors of the Pancreatic Cancer Action Network, such as Drs. Tuveson, Bar-Sagi, Kimmelman, Petersen, and Vonderheide.

BIOLOGY OF CANCER

Oncogene-induced Nrf2 transcription promotes ROS detoxification and tumorigenesis

http://www.ncbi.nlm.nih.gov/pubmed/21734707

Pancreatic Cancer Action Network write-up:

http://www.pancan.org/section_research/strategic_research_program/news/topic_complex_role_of_antioxidants.php

This exciting *Nature* article was published out of the laboratory of Dave Tuveson, MD, PhD (Chair, Scientific Advisory Board and 2003 Pancreatic Cancer Action Network – AACR Career Development Award), and also features Christine Iacobuzio-Donahue, MD, PhD (2007 Panceatic Cancer Action Network Pilot Grant, Scientific Advisory Board member) and Ralph Hruban, MD (Scientific Advisory Board emeritus member). There is also a summary of this article in the same issue of *Nature* (see below). Dr. Tuveson and colleagues discover a finding that K-Ras activation in pancreatic tumors in a mouse model lead to the expression and activation of a transcription factor called Nrf2. Among other functions, Nrf2 leads to an inducible antioxidant program in the cells. Furthermore, genetic targeting of the Nrf2 pathway impairs oncogenic K-Ras-induced proliferation and tumorigenesis *in vivo*.

Cancer: When antioxidants are bad

http://www.ncbi.nlm.nih.gov/pubmed/21734699

This article comments on the publication listed above, and was co-written by Rushika Perera, PhD and Nabeel Bardeesy, PhD (2008 Randy Pausch, PhD – Pancreatic Cancer Action Network – AACR Pilot Grant). Drs. Perera and Bardeesy present a nice schematic to explain the seemingly contradictory roles of reactive oxygen species and antioxidants in cancer. They conclude that Dr. Tuveson's paper should not preclude individuals from taking antioxidants as a dietary supplement to prevent or treat cancer, but further work will be necessary before conclusions may be drawn.

Genome-wide analysis of promoter methylation associated with gene expression profile

http://www.ncbi.nlm.nih.gov/pubmed/21610144

Jim Eshleman, PhD (2011 Pancreatic Cancer Action Network – AACR Innovative Grant) is an author on this *Clinical Cancer Research* manuscript. The study conducted by the authors revealed 1,658 known loci that were commonly differentially methylated in pancreatic cancer compared with normal pancreas. These aberrantly hypermethylated and silenced genes may have diagnostic, prognostic, and therapeutic applications.

GATA6 activates Wnt signaling by negatively regulating the Wnt antagonist Dickkopf-1
http://www.ncbi.nlm.nih.gov/pubmed/21811562
This *PLoS One* paper is out of the laboratory of Christine Iacobuzio-Donahue, MD, PhD (2007 Panceatic Cancer Action Network Pilot Grant, Scientific Advisory Board member). The authors found that GATA6 is amplified in pancreatic intraepithelial neoplasms and pancreatic ductal adenocarcinoma. Forced over-expression of GATA6 led to increased proliferation and growth in soft agar, whereas siRNA knockdown of GATA6 had the reverse effect. Their data suggested that GATA6 activity was partly mediated by down-regulating the expression of Dickkopf-1, an antagonist of Wnt signaling.

Tumor engraftment and enrichment in stroma-related gene pathways predicts poor survival
http://www.ncbi.nlm.nih.gov/pubmed/21742805
Ralph Hruban, MD (Scientific Advisory Board emeritus member) and Anirban Maitra, MD (2004 Pancreatic Cancer Action Network – AACR Career Development Award, Scientific Advisory Board member) contributed to this *Clinical Cancer Research* publication. Samples from surgical resections were implanted into pancreata of nude mice. The investigators reached an engraftment rate of 61 percent. Tumors from patients resistant to gemcitabine were enriched in stroma-related gene pathways, whereas tumors sensitive to gemcitabine were enriched in cell cycle and pyrimidine gene pathways. Tumors that successfully engrafted represented a poor prognostic factor.

Restitution of tumor suppressor microRNAs using a systemic nanovector inhibits pancreatic cancer
http://www.ncbi.nlm.nih.gov/pubmed/21622730
Anirban Maitra, MD (2004 Pancreatic Cancer Action Network – AACR Career Development Award, Scientific Advisory Board member) is the senior author on this *Molecular Cancer Therapeutics* manuscript. MicroRNAs (miRNAs) can have either tumor promoting (oncogenic) or tumor inhibiting (tumor suppressive) properties. Here, Dr. Maitra and colleagues explore the use of nanovectors to deliver tumor suppressive miRNAs to pancreatic cancer cells. This technique proved effective in orthotopic mouse xenograft model of the disease.

Increased expression of DNA repair genes in invasive human pancreatic cancer cells
http://www.ncbi.nlm.nih.gov/pubmed/21633318
An author on this *Pancreas* article is Liz Jaffee, MD (Scientific Advisory Board member). Gene expression microarrays of pancreatic cancer cell lines revealed that genes involved in DNA repair were significantly increased. Overall, the authors' data suggest that the cells that were most invasive and carried the potential to be tumor-initiating cells had the highest level of genomic stability.

Trefoil factor 1 stimulates both pancreatic cancer and stellate cells and increases metastasis
http://www.ncbi.nlm.nih.gov/pubmed/21747314
The senior author on this *Pancreas* paper is Craig Logsdon, PhD (Scientific Advisory Board member). Trefoil factor 1 (TFF1) expression was analyzed in pancreatic ductal adenocarcinoma tissue, cell lines, and immortalized pancreatic stellate cells, the cell type that makes up the majority of the stroma surrounding pancreatic tumors. TFF1 expression was increased in preneoplastic lesions. Forced expression of TFF1 led to increased invasion of pancreatic cancer and stellate cells. In an orthotopic xenograft model, over expression of TFF1 did not impact growth of the primary tumor, but metastasis was significantly increased.

Advancing a clinically relevant perspective of the clonal nature of cancer
http://www.ncbi.nlm.nih.gov/pubmed/21730190
Tony Hollingsworth, PhD (Scientific Advisory Board member) contributed to this *PNAS* publication. The authors applied DNA content-based flow sorting to identify and isolate the nuclei of clonal populations from tumor biopsies, which was coupled with array CGH and targeted resequencing. They generated high-definition genetic profiles of 40 pancreatic adenocarcinoma samples. Overall, their results offered that high-definition analyses of the genomes of distinct clonal populations of cancer cells in patients *in vivo* can help guide diagnoses and tailor approaches to personalized treatment.

Targeting ErbB3-mediated stromal-epithelial interactions in pancreatic ductal adenocarcinoma
http://www.ncbi.nlm.nih.gov/pubmed/21792199
Liles and colleagues explore the role of ErbB3 in the cross-communication between pancreatic cancer epithelium and stroma. Cancer-associated fibroblasts (stroma) were found to secrete the ligand neuregulin-1 (NRG-1), which activated ErbB3 on the surface of the pancreatic cancer epithelial cells. MM-121, a monoclonal antibody against ErbB3, blocked signaling generated by ErbB3 and inhibited tumorigenesis *in vivo*, especially when combined with the EGFR inhibitor erlotinib.

The {alpha} subunit of the G protein G13 regulates the activity of one or more Gli transcription factors
http://www.ncbi.nlm.nih.gov/pubmed/21757753
This *JBC* paper is co-authored by Martin Fernandez-Zapico, MD (2007 Carole and Bob Daly – Pancreatic Cancer Action Network – AACR Career Development Award). In some cells evaluated, including pancreatic cancer cells, components of the Hedgehog signaling pathway interacted directly with G proteins, leading to activation of the transcription factor Gli. Also, Gli could be activated independently of Hedgehog pathway proteins.

Notch signaling activated by replication stress-induced expression of midkine drives EMT
http://www.ncbi.nlm.nih.gov/pubmed/21632553
This *Cancer Research* publication addresses the interrelationship between pancreatic cancer's chemo-resistance and over-expression of the Notch-2 receptor. Notch-2 receptor gets activated by midkine, which is also over-expressed in chemo-resistant pancreatic tumors. The Notch-2-midkine interaction leads to increased chemo-resistance, as well as epithelial-to-mesenchymal transition.

VEGF and c-Met blockade amplify angiogenesis inhibition in pancreatic islet cancer
http://www.ncbi.nlm.nih.gov/pubmed/21613405
Unlike pancreatic ductal adenocarcinoma, pancreatic islet tumors are highly vascularized. In order to determine if multi-kinase inhibitors might be more effective than blocking VEGF alone, a team at UCSF looked at treating pancreatic islet tumors with combination VEGF/c-Met inhibitors, compared to VEGF inhibitors that don't affect c-Met. Their findings suggested that dual inhibition was more effective and led to rapid, robust, and progressive regression of tumor vasculature, increased intratumoral hypoxia and apoptosis, and reduced tumor invasiveness and metastasis.

KL1 internal repeat mediates klotho tumor suppressor activities and inhibits bFGF and IGF-I signaling
http://www.ncbi.nlm.nih.gov/pubmed/21571866
This *Clinical Cancer Research* paper out of Tel Aviv University looks at the transmembrane protein klotho and its expression and activity in pancreatic cancer cells. It was known previously that klotho behaves as a tumor suppressor in breast cancer. Here, the authors demonstrated that klotho is down-regulated in pancreatic cancer, and re-administration of the protein, specifically the KL1 subdomain, could have growth inhibitory effects.

Comprehensive genomic analysis of a BRCA2 deficient human pancreatic cancer
http://www.ncbi.nlm.nih.gov/pubmed/21750719
A cell line derived from a pancreatic cancer liver metastasis, Capan-1, underwent a genome-wide assessment. These cells are BRCA-deficient, and were found to have one of the most rearranged genomes sequenced to date.

Galectin-1 secreted by activated stellate cells in stroma promotes proliferation and invasion
http://www.ncbi.nlm.nih.gov/pubmed/21747316
Published in *Pancreas*, this study investigates the origin of galectin-1 that is found at high levels in the stroma surrounding pancreatic tumors. The researchers identified activated pancreatic stellate cells as the primary source of the highly expressed galectin-1 in pancreatic cancer stroma. Galectin-1 secreted by the stellate cells increased the proliferation and invasive capacity of a pancreatic cancer cell line.

Modulation of pancreatic cancer chemoresistance by inhibition of TAK1
http://www.ncbi.nlm.nih.gov/pubmed/21743023
Melisi, *et al* explored modulation of TGFb-activated kinase-1 (TAK1) in pancreatic cancer cell lines, a MAPKKK known to activate NFkB. Blocking TAK1 expression by small hairpin RNA led to decreased NFkB activity. Inhibition of TAK1 with small molecule inhibitor LYTAK1 resulted in decreased growth of pancreatic cancer cells *in vitro* and *in vivo* in an orthotopic mouse model. Further, LYTAK1 treatment potentiated the effects of treatment with various chemotherapeutics.

Anti-VEGF treatment resistant pancreatic cancers secrete proinflammatory factors
http://www.ncbi.nlm.nih.gov/pubmed/21737511
This research team sought to identify markers to predict for which patients may be sensitive or resistant to anti-angiogenic therapies. Mouse models of human pancreatic cancer tissue samples were evaluated for sensitivity to the anti-vascular endothelial growth factor (VEGF) antibody bevacizumab. Samples that were resistant expressed high levels of pro-inflammatory factors, rather than pro-angiogenic. These cells demonstrated increased epithelial-to-mesenchymal transition, contributing to malignancy.

Genetic evolution of pancreatic cancer: Lessons learnt from the pancreatic cancer sequencing project
http://www.ncbi.nlm.nih.gov/pubmed/21749982
This review was written by Christine Iacobuzio-Donahue, MD, PhD (2007 Panceatic Cancer Action Network Pilot Grant, Scientific Advisory Board member). Dr. Iacobuzio-Donahue discusses mutational analyses of pancreatic cancer, and how these findings can elucidate potential targets for personalized diagnostic and therapeutic intervention as well as the optimal timing for intervention.

***Journal of the Pancreas* – Highlight articles from ASCO meeting**

http://www.joplink.net/ – Vol. 12, No. 4, July 2011

The *Journal of the Pancreas*, the first electronic journal of pancreatology, featured an edition focused on pancreas- related highlights from the 2011 ASCO Annual Meeting.

ETIOLOGY

Influence of obesity & other risk factors on survival in patients undergoing pancreaticoduodenectomy

http://www.ncbi.nlm.nih.gov/pubmed/21747317

Authors on this *Pancreas* paper include William Hawkins, MD (2005 Skip Viragh – Pancreatic Cancer Action Network – AACR Career Development Award). These Wash U, St. Louis researchers conducted a retrospective analysis of patients with pancreatic adenocarcinoma who underwent pancreaticoduodenectomy between 1995 and 2009, categorizing patients by body mass index (BMI) as normal , overweight, or obese. Based on their findings, the authors concluded that BMI did not have an impact on patient survival following pancreaticoduodenectomy for pancreatic cancer.

Dietary insulin load, dietary insulin index, and risk of pancreatic cancer

http://www.ncbi.nlm.nih.gov/pubmed/21775564

Bao and colleagues prospectively followed patients via the Nurses' Health Study and the Health Professionals Follow-Up Study. Their data suggested that level of insulin intake is unrelated to pancreatic cancer risk. However, in patients with preexisting conditions of insulin resistance, consuming too much insulin may affect their risk of pancreatic cancer.

A meta-analysis of coffee consumption and pancreatic cancer

http://www.ncbi.nlm.nih.gov/pubmed/21746805

Epidemiologists in Milan, Italy looked at the literature to find observational studies providing quantitative estimates for pancreatic cancer risk in relation to coffee consumption. They found that even high intake of coffee was not appreciably related to pancreatic cancer risk.

Does intentional weight loss reduce cancer risk?

http://www.ncbi.nlm.nih.gov/pubmed/21733057

Researchers out of the Colorado School of Public Health explored the medical literature to see if intentional weight loss impacted the incidence of several cancer types affected by obesity, including cancer of the pancreas. Their findings suggested that cancer risk and levels of circulating cancer biomarkers were reduced following intentional weight loss.

PREVENTION

Aspirin, nonsteroidal anti-inflammatory drugs (NSAID), acetaminophen, and pancreatic cancer risk

http://www.ncbi.nlm.nih.gov/pubmed/21803981

This *Cancer Prevention Research* paper is out of the laboratory of Gloria Petersen, PhD (Scientific Advisory Board member). Their clinic-based case-control study revealed that there is no association between non-aspirin NSAID use and risk of pancreatic cancer. However, individuals who took at least one aspirin dose per month were at significantly lower risk of developing pancreatic cancer, consistent with other recent studies. Moreover, people on low-dose aspirin regimens for heart health were also at a lower risk.

EARLY DETECTION, DIAGNOSIS, AND PROGNOSIS

Recurrent GNAS mutations define an unexpected pathway for pancreatic cyst development
http://www.ncbi.nlm.nih.gov/pubmed/21775669
This *Science Translational Medicine* paper features an all-star, collaborative lineup of authors, including Anirban Maitra, MD (2004 Pancreatic Cancer Action Network – AACR Career Development Award, Scientific Advisory Board member), Jim Eshleman, PhD (2011 Pancreatic Cancer Action Network – AACR Innovative Grant), C. Max Schmidt, MD, PhD (2003 Pancreatic Cancer Action Network – AACR Career Development Award), and Ralph Hruban, PhD (Scientific Advisory Board emeritus member). The investigators purified DNA from fluid from intraductal papillary mucinous neoplasm (IPMN) cysts, and analyzed for mutations. Recurrent mutations in KRAS and PNAS were identified, and GNAS mutations were not found in other types of pancreatic cysts or tumors not associated with IPMN, suggesting that GNAS mutations can inform the diagnosis and management of patients with cystic pancreatic lesions.

Elevated microRNA miR-21 levels in pancreatic cyst fluid are predictive of mucinous precursor lesions
http://www.ncbi.nlm.nih.gov/pubmed/21757972
The senior author on this paper is Anirban Maitra, MD (2004 Pancreatic Cancer Action Network – AACR Career Development Award, Scientific Advisory Board member), with contributions from Ralph Hruban, MD (Scientific Advisory Board emeritus member). Like the study described above, the researchers utilized pancreatic cyst fluid to evaluate for biomarkers for classification. Specifically, small RNAs were extracted to check for deregulated microRNAs. Expression of several microRNAs was found to be statistically significantly higher in mucinous versus nonmucinous cysts, suggesting that profiling microRNAs in pancreatic cyst fluid samples is feasible and can yield potential biomarkers for the classification of cystic lesions of the pancreas.

A multiplexed bead assay for profiling glycosylation patterns on serum protein biomarkers
http://www.ncbi.nlm.nih.gov/pubmed/21732554
This team of University of Michigan researchers includes Diane Simeone, MD (2010 The Randy Pausch Family – Pancreatic Cancer Action Network – AACR Innovative Grant, Scientific Advisory Board member). High-throughput bead-based screenings of glycosylation patterns of pancreatic cancer samples were differentiable from pancreatitis samples, normal control, and renal cell carcinoma samples, showing usefulness as potential pancreatic cancer biomarkers.

A functional proteomic method for biomarker discovery
http://www.ncbi.nlm.nih.gov/pubmed/21811618
Published in *PLoS One*, this paper is out of the laboratory of Kimberly Kelly, PhD (2007 Laurie and Paul MacCaskill – Pancreatic Cancer Action Network – AACR Career Development Award). Dr. Kelly and colleagues assert that genomic information alone is not sufficient to understand the progression of human disease. Therefore, the authors convert known ligands into phage particles to identify protein targets in pancreatic cancer cells.

Screening for pancreatic cancer in a high-risk population with serum CA 19-9 and targeted EUS
http://www.ncbi.nlm.nih.gov/pubmed/21704809
This paper by Zubarik and colleagues garnered some media attention, such as this *Science Daily* write-up. The authors performed a prospective cohort study in two institutions, addressing the feasibility of detecting pancreatic cancer in a high-risk population (those with at least one first-degree relative diagnosed with pancreatic adenocarcinoma) by screening with CA 19-9 followed by targeted endoscopic ultrasound (EUS). Overall, their findings revealed that potentially curative pancreatic cancer can be identified with this screening protocol. Specifically, stage one pancreatic cancer was more likely to be detected by using this screening protocol than by using standard means of detection.

Post-therapy pathologic stage and survival in patients treated with neoadjuvant chemoradiation
http://www.ncbi.nlm.nih.gov/pubmed/21735446
Jason Fleming, MD (Medical Advisory Board) contributed to this paper, along with colleagues at MD Anderson. Pancreatic ductal adenocarcinoma patients who received neoadjuvant chemoradiation treatment before pancreaticoduodenectomy (surgery) were assessed for disease-free and overall survival. In pancreatic cancer patients who received neoadjuvant chemoradiation and subsequent pancreaticoduodenectomy, post-therapy pathologic stage (by American Joint Committee on Cancer) and number of positive lymph nodes were found to be independent prognostic factors.

Intraductal papillary mucinous neoplasm
http://www.ncbi.nlm.nih.gov/pubmed/21777948
Chanjuan Shi MD, PhD and Ralph Hruban, PhD (Scientific Advisory Board emeritus member) worked on this overview of intraductal papillary mucinous neoplasm (IPMN). The most important prognostic feature of IPMNs is whether or not they are associated with invasive carcinoma. The authors assert that a better understanding of the molecular genetics of IPMN could help identify molecular markers of high-risk lesions.

IKB kinase e (IKKe) expression in pancreatic ductal adenocarcinoma
http://www.ncbi.nlm.nih.gov/pubmed/21685032
Authors of the *American Journal of Clinical Pathology* paper include Mokenge Malafa, MD (Medical Advisory Board member). As seen in other cancer types, IKKe expression was seen up-regulated in pancreatic ductal adenocarcinoma samples, whereas no IKKe expression was detectable in normal pancreas tissue. In patients, higher IKKe expression correlated with worsened survival, compared to patients with lower immunohistochemical levels of IKKe.

Leaders in Dentistry: Dr. David T.W. Wong (Salivary diagnostics for pancreatic cancer)
http://www.drbicuspid.com/index.aspx?Sec=sup&Sub=orc&pag=dis&ItemID=308050&wf=47
David Wong, DMD, DMSc is the associate dean of research and a professor of oral biology at UCLA. Dr. Wong was chosen as a leader in dentistry by the *Oral Cancer and Diagnostics Community*. Dr. Wong states: “Every oral and systemic disease that we have developed biomarkers for has produced disease signatures and fingerprints based on saliva biomarkers. These diseases include oral cancer, Sjögren's syndrome, pancreatic cancer, breast cancer, lung cancer, gastric cancer, and diabetes.”

TREATMENT

Pancreatic cancer – We have a lot of work to do: Interview with Dr. Jordan Berlin
http://www.oncologystat.com/viewpoints/when-the-smoke-clears/Pancreatic_Cancer_We_Have_a_Lot_of_Work_to_Do_Interview_With_Dr_Jordan_Berlin.html
Jordan Berlin, MD (Medical Advisory Board chair) discusses important trials currently underway in metastatic pancreatic cancer, the FOLFIRINOX regimen, molecular targets, and concludes with a take-home message for community oncologists.

Pulmonary resection for isolated pancreatic adenocarcinoma metastasis: outcomes and survival
http://www.ncbi.nlm.nih.gov/pubmed/21725701
Authors on this article include Christine Iacobuzio-Donahue, MD, PhD (2007 Pancreatic Cancer Action Network Pilot Grant, Scientific Advisory Board member), Ralph Hruban, PhD (Scientific Advisory Board emeritus member), and Joe Herman, MD (2008 Blum-Kovler – Pancreatic Cancer Action Network – AACR Career Development Award). The purpose of this study was to determine if pulmonary metastasectomy for isolated pancreatic cancer metastases was safe and effective. The investigators demonstrated that pulmonary resection of isolated lung metastasis could be performed safely with low morbidity and mortality. Data suggest an increase in patient survival, but more experimentation is warranted.

A phase 2 study of oral MKC-1, an inhibitor of importin-B, tubulin, and the mTOR pathway
http://www.ncbi.nlm.nih.gov/pubmed/21800081
Aram Hezel, MD (2005 Samuel Stroum – Pancreatic Cancer Action Network – ASCO Young Investigator Award) contributed to this *Investigational New Drugs* publication. An open-label Phase II trial was conducted to investigate MKC-1, a cell cycle inhibitor, in patients with advanced pancreatic cancer. The results showed that MKC-1 is poorly tolerated and did not sufficient activity to warrant future trials of this compound in this patient population.

Pancreatic cancer treatment and research: an international expert panel discussion
http://www.ncbi.nlm.nih.gov/pubmed/21199884
Investigators from five European countries and the United States came together to discuss progress in the treatment of pancreatic cancer. Among the US representatives were Margaret Tempero, MD (Scientific Advisory Board member) and Jordan Berlin, MD (Chair, Medical Advisory Board). Consensus statements included the need for better biospecimen repositories, improved design of phase II and III clinical trials, and searching for new genetic therapeutic targets.

Advances in pancreatic cancer
http://www.ncbi.nlm.nih.gov/pubmed/21778878
Edward Kim, MD, PhD and Diane Simeone, MD (2010 The Randy Pausch Family – Pancreatic Cancer Action Network – AACR Innovative Grant, Scientific Advisory Board member) co-wrote this review focused on directing therapies to the pancreatic cancer stroma, interactions between the stroma and the tumor cells, and ways to combat chemo-resistance.

Molecular targeted approaches for treatment of pancreatic cancer
http://www.ncbi.nlm.nih.gov/pubmed/21777178
This review, co-authored by Selwyn Vickers, MD (Scientific Advisory Board emeritus member), summarizes opioid receptors and their interacting partners, and roles in cellular signal transduction. Increasing knowledge of the mechanisms by which these interactions are regulated is expected to address problems related to phenomena such as pain perception, tolerance, and dependence that occur upon chronic opiate administration and define whether disruption of such interactions may contribute to the development of novel therapeutic strategies.

Survival after resection of pancreatic adenocarcinoma: Results from a single institution over 3 decades
http://www.ncbi.nlm.nih.gov/pubmed/21761104
This sobering study out of Memorial Sloan Kettering looked at short- and long-term survival of pancreatic cancer patients undergoing surgical resection, comparing the 1980s, 1990s, and 2000s. Encouraging, over time, operative mortality has dropped over time, and one-year survivals have seen an increase. However, the long-term survival of patients operated on in the 2000s showed no significant difference from patients in the 1980s.

Impact of radiation therapy sequence among patients with resected pancreatic head ductal carcinoma
http://www.ncbi.nlm.nih.gov/pubmed/21735324
This *Annals of Surgical Oncology* publication describes an analysis of SEER data to determine overall survival of patients receiving neoadjuvant vs. adjuvant radiation therapy. The researchers found that survival of patients undergoing pancreaticoduodenectomy for pancreatic head carcinoma does not seem to be affected by sequence of perioperative radiation therapy.

Chemotherapy: Metastatic pancreatic cancer-is FOLFIRINOX the new standard?
http://www.ncbi.nlm.nih.gov/pubmed/21727930
Published in *Nature Reviews Clinical Oncology*, this review explores the potential of making FOLFIRINOX the new standard of care for pancreatic cancer patients.

Genetic effects and modifiers of radiotherapy and chemotherapy on survival in pancreatic cancer
http://www.ncbi.nlm.nih.gov/pubmed/21487324
Researchers at Yale conducted a population-based study, looking at candidate genes involved in survival or treatment response in pancreatic cancer patients. In all, their data suggested significant associations between germ-line genetic polymorphisms and overall survival in pancreatic cancer, as well as survival interactions between various genes and radiotherapy and chemotherapy.

A dose escalation study of gemcitabine plus oxaliplatin in combination with imatinib
http://www.ncbi.nlm.nih.gov/pubmed/21750117
Patients with advanced, gemcitabine-refractory pancreatic cancer were treated with gemcitabine plus oxaliplatin, in combination with imatinib, a PDGFR-b inhibitor. The trial data suggest that this regimen is tolerable and feasible.

A multicenter analysis of GTX chemotherapy in locally advanced and metastatic pancreatic cancer
http://www.ncbi.nlm.nih.gov/pubmed/21800112
De Jesus-Acosta *et al* looked at the use of the three-drug regimen of gemcitabine, docetaxel, and capecitabine (GTX) in patients with advanced pancreatic adenocarcinoma. The investigators observed a substantial survival benefit with GTX chemotherapy in their cohort of patients with advanced pancreatic cancer.

FDA grants orphan drug status to MM-398, a nanotherapeutic encapsulation of irinotecan
http://www.prnewswire.com/news-releases/fda-grants-orphan-drug-status-to-merrimack-pharmaceuticals-mm-398-a-nanotherapeutic-encapsulation-of-irinotecan-for-the-treatment-of-pancreatic-cancer-126536913.html
The Merrimack Pharmaceuticals compound MM-398 was granted orphan drug status for the treatment of pancreatic cancer. MM-398 is a novel, stable nanotherapeutic encapsulation of the marketed chemotherapy drug irinotecan.

Systemic therapy for patients with well-differentiated neuroendocrine tumors
http://www.clinicaloncology.com/download/Neuroendocrine_con0711_WM.pdf
This review discusses some of the newer therapies becoming available for patients with pancreatic neuroendocrine tumors.

SURVIVORSHIP

Sex disparities in cancer mortality and survival
http://www.ncbi.nlm.nih.gov/pubmed/21750167
This study out of the Division of Cancer Epidemiology and Genetics at the NCI looked at mortality rate ratios between males and females for various cancer types. Their results suggest that disparities whereby males have a higher rate of mortality from particular cancers are due to higher incidence, not poorer survival.

SCIENTIFIC MODEL SYSTEMS

Establishment, characterization of new cell line, A99, from primary small cell carcinoma of pancreas
http://www.ncbi.nlm.nih.gov/pubmed/21768923
Christine Iacobuzio-Donahue, MD, PhD (2007 Panceatic Cancer Action Network Pilot Grant, Scientific Advisory Board member) was the senior author and Ralph Hruban, MD (Scientific Advisory Board emeritus member) also contributed to this study. Small cell carcinoma (SCC) of the pancreas is a rare malignancy with a poor prognosis. The authors established and characterized a primary human pancreatic SCC cell line, designated A99. These cells carried the ability to grow constantly in culture, thrive in soft agar, and were tumorigenic when implanted into the skin of nude mice. As the first cell line of SCC, these cells will be useful in understanding the biology of this rare type of pancreatic tumor.