PANCREATIC CANCER ACTION NETWORK AND COMMUNITY NEWS

Share your federal funding experiences: help our advocacy efforts

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

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

Pancreas Cancer Research Fellowship at Virginia Mason Cancer Center


Virginia Mason Cancer Center in Seattle is now accepting applications for a Pancreas Cancer Research Fellowship (PCRF) program and hopes to have their first PCRF fellow start on 7/1/2013 (the beginning of the next academic year). Vincent J. Picozzi, Jr., MD (Medical Advisory Board) is the Fellowship Director for this program. More information about the Digestive Disease Institute can be found here: https://www.virginiamason.org/ddi.

Funding opportunities: FY12 Peer Reviewed Cancer Research Program (PRCRP)

http://cdmrp.army.mil/funding/prcrp.shtml

Visionary Postdoctoral Fellow Award: http://cdmrp.army.mil/funding/pa/12prcrpvfa_pa.pdf

Career Development Award: http://cdmrp.army.mil/funding/pa/12prcrpcda_pa.pdf

The Congressionally Directed Medical Research Programs at the Department of Defense announced 2012 cancer funding opportunities. Both funding mechanisms’ program announcements (linked above) include pancreatic cancer as a topic area. Pre-application deadlines are June 19 for both types of grants.

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

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

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

“Because of the poor prognosis and overall public health impact, pancreatic ductal adenocarcinoma has been selected to be studied by TCGA. However, the pancreatic cancer project might end before it even begins unless more collaborators provide tissue samples. The collapse of this research project would be a lost opportunity for the pancreatic cancer community ... If you have frozen, untreated samples in your tissue bank accompanied by blood, please help by providing them, either retrospectively or prospectively, to TCGA.”
Call for abstracts – APA/IAP Joint Annual Meeting
The 2012 Annual Meeting of the American Pancreatic Association (APA) will be held jointly with the International Association of Pancreatology (IAP), and will take place at the Eden Roc Renaissance in Miami Beach, FL, October 31 – November 3, 2012. Abstract submission is now open, and the deadline is Monday, June 25, 2012. The young investigator travel award application (http://www.american-pancreatic-association.org/index.php?option=com_content&view=article&id=28&Itemid=26) is also due on June 25.

Funding opportunity: Caring for Carcinoid Foundation-AACR Grant: Pancreatic Neuroendocrine Tumor
http://www.aacr.org/home/scientists/aacr-research-funding/current-funding-opportunities-for-independent-researchers.aspx#CFCF
The application deadline is June 16, 2012 for the Caring for Carcinoid Foundation-AACR Grant for Carcinoid Tumor and Pancreatic Neuroendocrine Tumor Research grants. Please click the above link for eligibility criteria and additional information.

Pancreatic Cancer Research & Education Act reaches 50 Senate co-sponsors, majority of Senate HELP
The Pancreatic Cancer Research & Education Act reached an exciting milestone of securing 50 co-sponsors within the Senate, and now also a majority of the Senate Health, Education, Labor, and Pensions (HELP) committee. The bill has strong bipartisan support in both the House and Senate.

Maryland high school student wins $75,000 for science fair project on pancreatic cancer diagnosis
Example of media: http://content.usatoday.com/communities/sciencefair/post/2012/05/pancreatic-cancer-test-garners-science-prize-for-teenager/1#.T7-8PtW8YfQ
Fifteen-year-old Jack Andraka of Crownsville, MD won the 2012 Intel International Science and Engineering Fair. Jack performed his experiments in the lab of Anirban Maitra, MBBS (2004 Career Development Award and incoming Chair, Scientific Advisory Board) at Johns Hopkins. Jack hypothesized that a dipstick could be coated with antibodies specific for mesothelin, and differentiate blood or urine samples of individuals with pancreatic cancer from people with pancreatitis or healthy controls. This story picked up an enormous amount of media attention. Congratulations to Jack and Dr. Maitra!

Congratulations to Dr. Danielle Pineda and her mentor, Dr. Jonathan Brody
http://pancreasclub.com/awards/
We’d like to congratulate Danielle Pineda, MD for winning the 2012 Pancreatic Cancer Action Network Award for Resident Research at the Pancreas Club meeting. Danielle works in the laboratory of Jonathan Brody, PhD (2010 Skip Viragh Career Development Award). The abstract of Danielle’s work can be found on page 56 here: http://pancreasclub.com/wp-content/uploads/2012finalprogram.pdf.
For Jai Pausch, 'New Dreams' in wake of grief
National Board of Directors member Jai Pausch wrote a new memoir, entitled *Dream New Dreams: Reimagining My Life After Loss*, describing her experiences as a caregiver and coping with her late husband Randy’s illness and death.

**BIOLOGY OF CANCER**

**KRas induces Src/PEAK1/ErbB2 kinase amplification loop, drives metastatic growth, therapy resistance**
The story about this *Cancer Research* article was picked up by several mainstream media outlets, e.g. http://abcnews.go.com/Health/early-biomarker-found-pancreatic-cancer/story?id=16346178#.T7-xv9W8YfQ. Kelber et al describe a novel tyrosine kinase, PEAK1, that they found to be up regulated in pancreatic cancer. PEAK1 acts in a signaling pathway with Src and ErbB2, induced by KRas. The authors suggest that PEAK1 could serve as a novel biomarker, signaling component, and/or therapeutic target.

**Nuclear protein 1 promotes pancreatic cancer development and protects cells from stress**
http://www.jci.org/articles/view/60144
A collaborative team of investigators worked on this *JCI* paper, describing the expression and function of nuclear protein 1 in a mouse model of pancreatic cancer. They found that nuclear protein 1 is involved in a stress-responsive pathway that contributes to the development of pancreatic cancer, and that its expression may be correlated with a poor prognosis.

**The MUC4 mucin mediates gemcitabine resistance via Concentrative Nucleoside Transporter family**
Although the mucin MUC4 had been previously associated with drug resistance in pancreatic cancer patients, the mechanism has been unknown. This *Oncogene* article explores various potential mechanisms by which MUC4 may exert this effect, and reports that expression of the Concentrative Nucleoside Transporter (hCNT1) was directly related to MUC4 expression and also to resistance of pancreatic cancer cells to gemcitabine treatment.

**Immonoassay-based proteome profiling of 24 pancreatic cancer cell lines**
This *Journal of Proteomics* paper describes results from an antibody microarray-based proteomic analysis of pancreatic cancer cell lines. The authors identified 72 novel proteins that could serve as biomarkers for pancreatic cancer, as well as specific proteins that signify whether the cells are from the primary tumor or metastases, degree of differentiation, etc.

**The iron-regulated metastasis suppressor NDRG1 targets NEDD4L, PTEN, and SMAD4**
Researchers at the University of Sydney in Australia evaluated N-myc downstream regulated gene-1 (NDRG1), a metastasis suppressor gene, and its expression and function in pancreatic cancer cell lines. The authors report that NDRG1 up-regulates the expression of tumor suppressors PTEN and SMAD4, while inhibiting signaling from PI3K and Ras.
Molecular mechanisms involved in the synergistic interaction of the EZH2 inhibitor DZNeP
This *Molecular Cancer Therapeutics* article discusses the potential for an Enhancer-of Zeste-Homolog-2 (EZH2) inhibitor, 3-deazaneplanocin A (DZNeP), to be used in combination with gemcitabine to treat pancreatic cancer cells. The two drugs appeared to work synergistically to kill pancreatic cancer cells, and also selectively attacked the cells with stem cell properties.

Re-expression of miR-200 by novel approaches regulates the expression of PTEN and MT1-MMP
The experiments for this paper took place at the Karmanos Cancer Institute in Detroit. The paper reports that the loss of miR-200 miRNA family members and loss of PTEN, in addition to increased MT1-MMP expression, contribute to the aggressiveness of pancreatic cancer cell lines.

Ursolic acid inhibits growth and induces apoptosis in gemcitabine-resistant pancreatic cancer
*Oncology Reports* published this paper out of Sun Yat-sen University in China. The authors looked at ursolic acid, a small molecule compound extracted from some Chinese herbs and vegetables, that also has anti-inflammatory properties. Ursolic acid was explored as a treatment to kill pancreatic cancer cells that are resistant to gemcitabine. The authors found that ursolic acid induces cell death in pancreatic cancer cells via the JNK and PI3K/Akt/NF-κB pathways.

A comprehensive survey of ras mutations in cancer
This *Cancer Research* paper looks at mutations in H-Ras, K-Ras, and N-Ras found in different cancer types. Even though the regions commonly mutated share full homology with the other isoforms, the authors observed surprising variation in codon mutation and amino-acid substitution bias for each ras family member.

Tumor microenvironment complexity: emerging roles in cancer therapy
Also published in *Cancer Research*, this paper describes outcomes from the November 2011 AACR special conference focused on the tumor microenvironment.

Recurrent hemizygous deletions in cancers may optimize proliferative potential
This *Science* paper defines a “Cancer Gene Island“ model, whereby chromosomal regions with high concentration of genes with tumor suppressive capabilities, and few pro-proliferative genes, tend to be hemizygosly deleted in various tumor types.
**ETIOLOGY**

Inflammation marker and risk of pancreatic cancer: a nested case-control study within the EPIC cohort


The *British Journal of Cancer* published this study, describing a nested evaluation of the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort. The authors analyzed whether levels of inflammatory proteins such as C-reactive protein, interleukin-6, and soluble receptors of tumor necrosis factor-α may predict for pancreatic cancer risk. The results suggest that the TNF receptors are possibly associated with risk for pancreatic cancer, but further studies will be necessary to confirm.

Meat and fish consumption and risk of pancreatic cancer


Researchers throughout Europe analyzed data from the European Prospective Investigation into Cancer and Nutrition (EPIC) to search for a connection between meat and fish consumption, and risk of developing pancreatic cancer. Contrary to previous findings, the authors report that there was no association between red meat or processed meat consumption and pancreatic cancer risk. Also surprisingly, they observed an increased risk among those who eat high levels of poultry. There was no association observed surrounding eating fish.

Nicotine/cigarette smoke promotes metastasis through α7nAChR-mediated MUC4 upregulation


Although cigarette smoke has long been known to promote pancreatic cancer development and progression, the mechanism(s) has remained elusive. In this *Oncogene* paper out of the University of Nebraska, the authors report that cigarette smoke increases the expression of the mucin MUC4 in pancreatic cancer cells, via the α7 subunit of nicotinic acetylcholine receptor (nAChR). This event then activates the JAK2/STAT3 pathway, leading to increased metastasis.

Interplay between smoking-induced genotoxicity and altered signaling in pancreatic carcinogenesis


This review article published in *Carcinogenesis* discusses the link between smoking and activation of signaling pathways leading to pancreatic cancer development.

**EARLY DETECTION, DIAGNOSIS, AND PROGNOSIS**

Identification of serum biomarker signatures associated with pancreatic cancer


Investigators in Sweden prepared this *Cancer Research* paper to describe results from a recombinant antibody microarray platform, targeting mainly immunoregulatory proteins, to screen individuals with pancreatic cancer, chronic or acute pancreatitis, and healthy controls. They identified a signature of 25 serum biomarkers to differentiate the serum of pancreatic cancer patients from the others.

Diverse monoclonal antibodies against the CA 19-9 antigen show variation in binding specificity


*Proteomics* published this paper about CA 19-9 as a blood-based biomarker for pancreatic cancer. The authors describe a comparison between five different CA 19-9 antibodies that recognize various
epitopes, and found that antibodies that were specific to more than one site on CA 19-9 had greater specificity, without sacrificing sensitivity, for pancreatic cancer patient samples.

Whole blood DNA aberrant methylation shows association with the course of pancreatic cancer
Researchers at the Lithuanian University of Health Sciences published these results in *PLoS One*. The authors investigated whether DNA methylation patterns detectable in blood samples could differentiate pancreatic cancer patients from healthy controls. Indeed, several tumor suppressor genes were found to display higher levels of methylation in individuals with the disease. Additionally, methylation patterns were associated with outcome of pancreatic cancer patients. Further work will be necessary before DNA methylation in blood samples could be considered as an early detection method and/or prognostic indicator.

Google goes cancer: improving outcome prediction for cancer patients by ranking of marker genes
This *PLoS Computational Biology* article out of Dresden University, Germany describes a novel method to make prognostic predictions based on gene expression. Created to utilize similar technology as Google’s PageRank, candidate marker genes are ranked according to their prognostic relevance using both expression and network information. Their pilot experiments described in the paper involve evaluation of marker genes that provide outcome predictions for pancreatic cancer.

HOTAIR is a negative prognostic factor and exhibits pro-oncogenic activity in pancreatic cancer
HOTAIR, a long intervening non-coding RNA (lincRNA), has been shown to be associated with a poor prognosis in other cancer types. Researchers at Texas A&M report in this *Oncogene* paper that HOTAIR is also a poor prognostic indicator in pancreatic cancer. Accordingly, knockdown of HOTAIR expression leads to decreased proliferation of pancreatic cancer cells, as well as cell cycle arrest and increased apoptosis, phenotypes that hadn’t been observed in other cancer types previously.

Low expression of IGFBP7 is associated with poor outcome of pancreatic ductal adenocarcinoma
An and colleagues report that the expression of insulin growth factor binding protein 7 (IGFBP7) is down regulated in pancreatic tumors, as compared to normal adjacent pancreas. Moreover, absence of IGFBP7 expression is associated with higher proliferative areas, and lower expression correlates with worse survival. These observations implicate IGFBP7 as a possible tumor suppressor.

The risk of pancreatic cancer in symptomatic patients in primary care
A team of scientists at the University of Bristol in the UK undertook a retrospective case-control study to determine whether patients who eventually develop pancreatic cancer could be identifiable by symptoms previously presented at primary care doctor’s appointments. Other than jaundice, the association between the individual symptoms and risk of pancreatic cancer was small; however, combinations of symptoms may provide a clue to facilitate earlier detection of the disease.
Molecular signaling network complexity is correlated with cancer patient survivability
PNAS published this study that seeks a correlation between complexity of molecular signaling networks and patient survivability in various cancer types. Data from the Kyoto Encyclopedia of Genes and Genomes Cancer Pathway and Surveillance Epidemiology and End Results databases revealed an association whereby cancer types with more complex molecular signatures, like pancreatic, showed poorer survival rates.

TREATMENT
Response of borderline resectable to neoadjuvant therapy is not reflected by radiographic indicators
Among the MD Anderson team of researchers who participated in this study are Huamin Wang, MD, PhD (2007 Skip Viragh Career Development Award recipient) and Medical Advisory Board members Jason Fleming, MD and Christopher Crane, MD. The authors explored whether neoadjuvant therapy could convert borderline resectable pancreatic cancer patients to surgical candidates, and whether Response Evaluation Criteria in Solid Tumors (RECIST) and standardized anatomic criteria could predict for which patients would respond best.

Multimodality therapy offers chance for cure in patients with pancreatic cancer deemed unresectable
This study is also out of MD Anderson, primarily the laboratory of Jason Fleming, MD, with collaboration from Christopher Crane, MD, both Pancreatic Cancer Action Network Medical Advisory Board members. The investigators looked at pancreatic cancer patients deemed unresectable upon initial surgical intervention. Many patients were restaged to be considered resectable or borderline resectable, and preoperative chemo/radiotherapy allowed for successful resections in a significant fraction of patients.

VEGF pathway genetic variants as biomarkers of treatment outcome with bevacizumab
This *Lancet Oncology* paper describes data from two phase 3 randomized studies: AViTA and AVOREN. For AViTA, patients with metastatic pancreatic cancer were randomly assigned to receive gemcitabine and erlotinib plus either bevacizumab or placebo. The data suggest that a SNP in VEGFR1 was predictive for patients’ response to bevacizumab treatment.

A retrospective study of neoadjuvant FOLFIRINOX in unresectable or borderline-resectable disease
Investigators at the University of Miami underwent this retrospective study to compare neoadjuvant FOLFIRINOX to gemcitabine in patients with locally advanced pancreatic cancer. The team concludes that FOLFIRINOX is a promising neoadjuvant choice in this patient population, and subsequent resection rates were even more encouraging when the chemo was combined with radiotherapy.
Fluorescence-guided surgery allows for more complete resection of pancreatic cancer
Metildi and colleagues at UCSD prepared this Journal of the American College of Surgeons manuscript to describe a randomized preclinical trial to compare bright light surgery (BLS) to fluorescence-guided surgery (FGS) in orthotopic mouse models of pancreatic cancer.  FGS led to a more complete resection, associated with longer disease-free survival.

Developing histone deacetylase inhibitors in the therapeutic armamentarium of pancreatic cancer
Zafar et al prepared this Expert Opinion on Therapeutic Targets article to discuss the usage of histone deacetylase (HDAC) inhibitors in treating pancreatic adenocarcinoma.  The authors state their opinion that, even though preliminary early phase trials seemed discouraging, there is potential to use select HDAC inhibitors in appropriate pancreatic cancer patients.

Stereotactic body radiation therapy for reirradiation of localized adenocarcinoma of the pancreas
This Radiation Oncology paper retrospectively describes patients whose pancreatic tumors were originally treated with external beam radiation therapy, and then later received hypofractionated stereotactic body radiation therapy (SBRT).  The authors deemed the regimen tolerable, but overall survival rates remained poor.

Comparison of efficacy, toxicity between gemcitabine with capecitabine & gemcitabine with erlotinib
Researchers in Seoul, South Korea underwent a retrospective analysis of unresectable pancreatic cancer patients treated with gemcitabine in combination with either capecitabine or erlotinib.  Their findings suggest that the combination of cytotoxic agents, gemcitabine and capecitabine, led to increased efficacy and clinical success than the combination including erlotinib.

Genetically engineered mouse models: closing the gap between preclinical data and trial outcomes
Cancer Research published this paper reporting analyses by a team of Genentech researchers.  The authors describe the usefulness of various genetically engineered mouse models, including K-Ras-driven pancreatic cancer, in predicting for patients’ response to treatment, discovering biomarkers, and understanding drug resistance.

Commentary on: Gemcitabine alone versus gemcitabine plus radiotherapy in patients with locally advanced pancreatic cancer: An Eastern Cooperative Oncology Group trial
http://jco.ascopubs.org/content/30/13/1564.full?cmpid=jco_etoc_1May2012
http://jco.ascopubs.org/content/30/13/1565.full?cmpid=jco_etoc_1May2012#ref-1
http://jco.ascopubs.org/content/30/13/1566.full?cmpid=jco_etoc_1May2012
Original article: http://jco.ascopubs.org/content/29/31/4105.abstract?sid=c5e3f85a-14b6-4364-adf7-4404b670e72a
Aref and Berri and Ben-Josef et al discuss Dr. Philip Philip’s commentary on the ECOG study above.  Dr. Philip also provides a response to the scientists’ concerns about his interpretation of these results.
Studies see advances in detecting, treating pancreatic cancer
http://health.usnews.com/health-news/news/articles/2012/05/22/studies-see-advances-in-detecting-treating-pancreatic-cancer

Two stories out of Digestive Diseases Week (http://www.ddw.org/program/abstracts) picked up some media attention. Lynn Matrisian, PhD, VP of Scientific and Medical Affairs at the Pancreatic Cancer Action Network, is quoted in this article. The two scientific stories featured include updates on the NewLink Algenpantucel-L vaccine, and an intestinal probe out of Mayo Clinic as an imaging tool to diagnose pancreatic cancer.

Lymphadenectomy underused in GI cancer surgery

Dr. Attila Dubecz was interviewed at Digestive Diseases Week, to talk about his and colleagues’ analyses of SEER data to look at use of lymphadenectomy in conjunction with surgery for GI cancer patients. The data suggest that US surgeons are underperforming lymphadenectomy procedures in GI cancer patients.

Targeting hypoxia brings breath of fresh air to cancer therapy
http://www.nature.com/nm/journal/v18/n5/full/nm0512-636b.html?WT.ec_id=NM-201205

Moyer wrote this Nature Medicine News piece to discuss cancer therapies aimed at taking advantage of the tumors’ hypoxia, using the Threshold compound and its promise in pancreatic cancer as an example.

Survival from pancreatic cancer: it’s not just about the surgical mortality


Dr. Robert Padbury discusses an improvement in outcome when pancreatic cancer surgeries are limited to specialized centers in Australia.

Digestive Care, Inc. announces FDA approval of PERTZYE™ (pancrelipase) delayed-release capsules

Digestive Care, Inc., based in Bethlehem, PA, received FDA approval for a New Drug Application for PERTZYE™, used to treat pancreatic exocrine insufficiency caused by cystic fibrosis or other conditions, which could include pancreatic cancer or pancreaticoduodenectomy.

Ardea Biosciences earns milestone from Bayer HealthCare

Ardea Biosciences, Inc. reached a milestone triggered by the initiation of a Phase 2 trial investigating their MEK inhibitor (BAY 86-9766 [RDEA119]) in combination with gemcitabine for patients with advanced pancreatic cancer. Reaching this milestone earned Ardea $7.5 million from Bayer HealthCare.
BSD Medical reports hyperthermia clinical study on pancreatic cancer

The randomized, multicenter, Phase III trial entitled Hyperthermia European Adjuvant Trial (HEAT) was described at the Society of Thermal Medicine’s 29th Annual Conference. Pancreatic cancer patients who underwent surgery will then be treated with hyperthermia with chemotherapy (gemcitabine plus cisplatin) or chemotherapy (gemcitabine) alone.

Celsion Corporation and Focused Ultrasound Foundation research ThermoDox(R), focused ultrasound

Two companies, Celsion Corporation and Focused Ultrasound Foundation, will work together to support preclinical research towards determining the role of ThermoDox(R), a liposomal coated doxorubicin, combined with high intensity focused ultrasound, in pancreatic cancer. The experimentation will take place at the University of Washington.

NewLink Genetics Corporation reports first quarter 2012 financial results


CytRx reports first quarter 2012 financial results

CytRx describes their finances from the first three months of 2012. Their connection to pancreatic cancer is a drug called INNO-206, a tumor-targeted doxorubicin conjugate, that is now in Phase 2 trials in patients with pancreatic cancer.

Clovis reports $19 million loss in Q1

Similar to a loss of $8.3 million in the first quarter of 2011, Clovis Oncology Inc. is reporting a loss of $19 million in the first quarter of 2012. The company is testing a compound, CO-101, in metastatic pancreatic cancer, and hopes to file for approval for the drug in mid-2013.

Characteristics of clinical trials registered in ClinicalTrials.gov, 2007-2010

This JAMA article describes an evaluation of interventional clinical trials. The authors found a great deal of heterogeneity in the size of trials, the use of randomization and blinding, and data monitoring committees overseeing the trials.
Learning from hackers: open-source clinical trials
Researchers at the University of New South Wales, Australia wrote this Science Translational Medicine commentary to compare open-source software initiatives with sharing clinical data widely.

CANCER CONTROL, SURVIVORSHIP, AND OUTCOMES RESEARCH
The association of patients' primary goals with their doctors' responses about online health research
http://www.tandfonline.com/doi/abs/10.1080/00909882.2012.679671
This Journal of Applied Communication Research study discusses conversations between patients and physicians and the patients' Internet searches about their own ailment, and the doctors' responses. Their data suggest that patients often seek the Internet to better understand their diagnosis and options, rather than to second-guess their doctor's management of their case.