PANCREATIC CANCER NEWS & UPDATES – MARCH 2013

PANCREATIC CANCER ACTION NETWORK AND COMMUNITY NEWS

PanCAN news:
More than $5 million in research grants awarded by the Pancreatic Cancer Action Network in 2013
http://www.pancan.org/section_research/research_grants_program/grants_awarded/by_year/2013/index.php
(This technically was released in April, but it’s too exciting to wait another month!) The Pancreatic Cancer Action Network awarded 14 research grants in 2013, totaling more than $5 million. This year, we introduced a new grant mechanism: the Research Acceleration Network (RAN) grant. Click above to learn about this year’s recipients and their funded projects!

Pancreatic Cancer Action Network opposes sequestration cuts to NIH & cancer research grants
The Pancreatic Cancer Action Network is calling attention to the potential effects sequestration will have on medical research, and specifically pancreatic cancer research. The onset of sequestration could lead to significant and harmful cuts to the budget of the NIH and the NCI, which will affect cancer research grants. According to some estimates, medical research supported by the NIH would be cut by an estimated $1.5 billion, including more than a $250 million reduction in cancer research funding in 2013 alone. In total, these cuts could lead to 1,380 fewer research grants being funded next year.

IU researchers receive cancer treatment grant
http://www.insideindianabusiness.com/newsitem.asp?id=58358
Mircea Ivan, MD, PhD, recipient of a 2005 Career Development Award, is part of a research team at Indiana University Simon Cancer Center who were awarded a multi-year, $3.2 million grant to develop and improve therapies for pancreatic cancer. In their laboratory research, principal investigators Drs. Kelley and Fishel plan to block a protein, redox factor 1 (Ref-1), which is crucial to regulating pancreatic tumor growth and metastasis.

Pancreatic Cancer Methods and Protocols book
This book is edited by Gloria Su, PhD (2010 Innovative Grant and 2007 Pilot Grant), and features chapters written by many other Pancreatic Cancer Action Network grant recipients and advisors. The book details a broad range of protocols for molecular, cellular, pathological, and statistical analyses for pancreatic cancer, provides step-by-step detail essential for reproducible results, and contains key notes and implementation advice from the experts.
**Funding opportunities:**

**Funding opportunity: Clinical Assay Development Program (CADP)**


The NCI Clinical Assay Development Program (CADP) is requesting project applications from investigators in academia, government and industry seeking clinical assay validation resources. These resources are designed to assist with the development of assays that may predict therapy response or prognostic behavior of a diagnosed cancer, primarily for use in clinical trials. Remaining 2013 application deadlines: June 15 and October 15.

**Share your federal funding experiences: Help our advocacy efforts**

[http://www.pancan.org/section_research/resources_for_scientists/form_funding_experiences.php](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).

**2012 RFA Links and Provocative Questions**


The provocative questions (PQ) project is intended to assemble a list of important but non-obvious questions that will stimulate the NCI’s research communities to use laboratory, clinical, and population sciences in especially effective and imaginative ways. For the current issuance of the PQ Program, the original list of PQs is now updated to a set of 24 PQs. The new/updated PQs have been divided into four groups, resulting in four R01 FOAs and four R21 FOAs, with LOI deadlines of May 20, 2013.

**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 July 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](https://www.virginiamason.org/ddi).

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


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.”
Meetings:

NIDDK-NCI Workshop on Pancreatitis-Diabetes-Pancreatic Cancer
http://www2.niddk.nih.gov/News/Calendar/PDPC2013.htm
- June 12-13, 2013, NIH Campus, Bethesda, MD
- Registration deadline: May 11, 2013
- The purpose of the workshop on Pancreatitis-Diabetes-Pancreatic Cancer is to explore the known and suspected mechanisms for the increased risk for pancreatic ductal adenocarcinoma (PDAC) associated with chronic pancreatitis and diabetes mellitus (DM), to identify the prevalence of new-onset, tumor-related DM (T3cDM) in the overall DM population and to assess strategies to discriminate T3cDM from T2DM, to review the effects of anti-diabetic therapy on the development of PDAC, and to explore possible PDAC surveillance methods for T2DM and T3cDM patients. Note: the Pancreatic Cancer Action Network has provided a travel award for this meeting.

The 2013 Gordon Conference on Pancreatic Diseases
- July 21-26, 2013, Mount Holyoke College, South Hadley, MA
- Application deadline: June 23, 2013
- The 2013 Gordon Conference on Pancreatic Diseases will present cutting-edge research on the clinical, molecular, and cellular perspective of functional and pathological aspects of pancreas biology. The broad scope of this conference is to support the development of a multi-disciplinary research community addressing medical, biological, chemical, and pharmacological topics related to the diversity and complexity of pancreatic diseases. Note: the Pancreatic Cancer Action Network has provided a travel award for this meeting.

Pancreatic Cancer: Salerno 2013
http://www.biouniversa.com/meeting.aspx
- June 20-21, 2013, Grand Hotel Salerno, Italy
- Deadlines:
  - April 30th: Hotel booking at discounted rates
  - May 15th: Posters submission
  - May 31st: Late registration
- The meeting plans to provide a forum to discuss advances in the diagnosis and treatment of pancreatic adenocarcinoma.

Journal of the Pancreas: Highlights from the “2013 ASCO Gastrointestinal Cancers Symposium”
http://www.serena.unina.it/index.php/jop/issue/view/120
The March issue of the Journal of the Pancreas includes summaries of work presented at the 2013 ASCO GI Cancer Symposium that took place in San Francisco in January.

Other community news:
Facebook, Google technology gurus to design mobile phone game to speed up cancer cure
Cancer Research UK is bringing together the charity’s world-leading scientists alongside technology gurus – such as Amazon Web Services, Facebook and Google – to design and develop a mobile game to accelerate cures for cancer. Citizen science is a new way of including the public in our scientific research outside the laboratory.

**Cancer Dream Teams: Road to a Cure?**

An article in *Time* magazine discusses the value of group science as a better model for fighting cancer over the traditional approach of a narrowly focused investigator.

**Science Special Section: Cancer Genomics**
[http://www.sciencemag.org/content/339/6127.toc](http://www.sciencemag.org/content/339/6127.toc)

Moving from the pre-genome-era identification of single gene variants associated with hereditary cancers, advances in sequencing technology have enabled the use of a whole-genome approach to examine the differences between the genomes, and epigenetic regulation, of tumor and patient DNA. This issue of *Science* examines how these advances are shaping our current understanding of cancer at the genomic level.

**BIOLOGY OF CANCER**

**Glutamine supports pancreatic cancer growth through a KRAS-regulated metabolic pathway**

*Pancreatic Cancer Action Network write-up:*

- **Journal:** *Nature*
- **Institution(s):** Dana-Farber Cancer Institute, Boston, MA and others
- **Corresponding author(s):** Lewis Cantley and Alec Kimmelman
- **PanCAN affiliated authors:**
  - Costas Lyssiotis, PhD: 2013 Pathway to Leadership Grant
  - Jason Fleming, MD: Medical Advisory Board
  - Nabeel Bardeesy, PhD: 2008 Randy Pausch, PhD – Career Development Award
  - Alec Kimmelman, MD, PhD: 2010 Career Development Award
- **Major finding:** The authors establish that the reprogramming of glutamine metabolism is mediated by oncogenic KRAS, the signature genetic alteration in pancreatic ductal adenocarcinoma (PDAC), through the transcriptional up-regulation and repression of key metabolic enzymes in this pathway. The essentiality of this pathway in PDAC and the fact that it is dispensable in normal cells may provide novel therapeutic approaches to treat these refractory tumors.

**Hijacking the neuronal NMDAR signaling circuit to promote tumor growth and invasion**

- **Journal:** *Cell*
- **Institution(s):** Swiss Federal Institute of Technology Lausanne (EPFL), Lausanne, Switzerland
- **Corresponding author(s):** Douglas Hanahan
Pancreatic Cancer Action Network

• **PanCAN affiliated author**: Douglas Hanahan, PhD: 2007 Pilot Grant
• **Major finding**: Glutamate and its receptor N-methyl-D-aspartate receptor (NMDAR) have been associated with cancer. Using a mouse model of pancreatic neuroendocrine tumorigenesis, the authors found that, beyond its traditional role in neurons, NMDAR may be activated in human tumors by fluid flow consequent to higher interstitial pressure, inducing an autocrine glutamate signaling circuit with resultant stimulation of malignancy.

**Dormant cancer cells contribute to residual disease in a model of reversible pancreatic cancer**


• **Journal**: Cancer Research
• **Institution(s)**: University of Nebraska Medical Center, Omaha, NE and others
• **Corresponding author(s)**: Kay-Uwe Wagner
• **PanCAN affiliated authors**:
  o Tony Hollingsworth, PhD: Scientific Advisory Board
  o Matthias Hebrok, PhD: 2011 Abby Sobrato – Innovative Grant and 2008 Michael C. Sandler – Pilot Grant
  o Jonathan Brody, PhD: 2010 Skip Viragh – Career Development Award
• **Major finding**: Collectively, the results of this study suggest that c-Myc plays a significant role in the progression and maintenance of pancreatic cancer, but besides targeting this oncogene or its downstream effectors, additional therapeutic strategies are necessary to eradicate residual cancer cells to prevent disease recurrence.

**Loss of GLI1 identifies signaling in tumor microenvironment mediating KRAS-induced transformation**


• **Journal**: The Journal of Biological Chemistry
• **Institution(s)**: Mayo Clinic, Rochester, MN and others
• **Corresponding author(s)**: Martin Fernandez-Zapico
• **PanCAN affiliated authors**:
  o Marina Pasca di Magliano, PhD: 2009 Paul Mitchell – Career Development Award
  o Martin Fernandez-Zapico, MD: 2007 Carole and Bob Daly – Career Development Award
• **Major finding**: Collectively, the authors’ results define a novel role for the transcription factor GLI1 in carcinogenesis acting as a downstream effector of oncogenic KRAS in the tumor microenvironment.

**Novel role of VMP1 as modifier of the pancreatic tumor cell response to chemotherapeutic drugs**


• **Journal**: Journal of Cellular Physiology
• **Institution(s)**: Cancer Research Center of Marseille, Inserm, Marseilles, France and others
• **Corresponding author(s)**: Raul Urrutia and Juan Iovanna
• **PanCAN affiliated author**: Martin Fernandez-Zapico, MD: 2007 Carole and Bob Daly – Career Development Award
• **Major finding**: The authors investigated how VMP1, a stress-induced autophagy-associated protein, modulate stress responses triggered by chemotherapeutic agents in pancreatic cancer. Their results underscore a novel role for VMP1 as a potential therapeutic target for
combinatorial therapies aimed at sensitizing pancreatic cancer cells to chemotherapeutic agents as well as provide novel molecular mechanisms to better understand this phenomenon.

**Combining hedgehog signaling inhibition with focal irradiation on reduction of metastasis**


- **Journal:** *Molecular Cancer Therapeutics*
- **Institution(s):** IU School of Medicine, Indianapolis, IN and others
- **Corresponding author(s):** Jingwu Xie
- **PanCAN affiliated author:** Gloria Su, PhD: 2010 Innovative Grant and 2007 Pilot Grant
- **Major finding:** Taken together, the authors’ data provide a rationale for combined use of hedgehog inhibition with irradiation for clinical treatment of pancreatic cancer patients.

**Aiming for the outliers: Cancer precision medicine through targeting kinases with extreme expression**


- **Journal:** *Cancer Discovery*
- **Institution(s):** Johns Hopkins University, Baltimore, MD
- **Corresponding author(s):** Srinivasan Yegnasubramanian
- **PanCAN affiliated author:** Anirban Maitra, MBBS: 2004 Career Development Award and Chair, Scientific Advisory Board
- **Major finding:** This article references a recent study by Kothari and colleagues ([http://www.ncbi.nlm.nih.gov/pubmed/23384775](http://www.ncbi.nlm.nih.gov/pubmed/23384775); featured in the February News & Updates) that reports preclinical studies that highlight the potential of targeting kinases with extreme expression for cancer precision medicine, warranting further clinical investigation of an individual-specific outlier kinase targeting approach.

**The role of protein synthesis and digestive enzymes in acinar cell injury**


- **Journal:** *Nature Reviews Gastroenterology & Hepatology*
- **Institution(s):** The University of Texas MD Anderson Cancer Center, Houston, TX
- **Corresponding author(s):** Craig Logsdon and Baoan Ji
- **PanCAN affiliated author:** Craig Logsdon, PhD: Scientific Advisory Board
- **Major finding:** This review focuses on protein synthesis and active digestive enzymes – two key stressors faced by the acinar cell that are likely to be the major drivers of pathology encountered in the pancreas.

**Bitter melon juice activates cellular energy sensor AMPK causing apoptotic death**


- **Journal:** *Carcinogenesis*
- **Institution(s):** University of Colorado, Aurora, CO
- **Corresponding author(s):** Rajesh Agarwal
- **Major finding:** Overall, the researchers found that bitter melon juice exerts strong anticancer efficacy against human pancreatic carcinoma cells, both in vitro and in vivo, suggesting its
clinical usefulness. This publication picked up quite a bit of media attention, for example: http://www.huffingtonpost.com/2013/03/17/bitter-melon-pancreatic-cancer_n_2869131.html.

Notch signaling in pancreatic cancer: oncogene or tumor suppressor?
- **Journal:** *Trends in Molecular Medicine*
- **Institution(s):** The Wistar Institute, Philadelphia, PA and others
- **Corresponding author(s):** Joseph Kissil
- **Major finding:** Initial studies revealed that Notch signaling is reactivated during pancreatic ductal adenocarcinoma (PDAC) initiation and development, suggesting that Notch promotes PDAC and may therefore represent a target for drug development. However, more recent work reveals a tumor suppressive role for Notch receptors in the context of pancreatic intraepithelial neoplasia (PanIN) development. Here, the authors summarize the current literature describing Notch signaling in the development of PDAC, and discuss the potential of the Notch pathway as a therapeutic target.

Palladin promotes invasion of by enhancing invadopodia formation in cancer-associated fibroblasts
- **Journal:** *Oncogene*
- **Institution(s):** UNC, Chapel Hill, NC
- **Corresponding author(s):** Carol Otey
- **Major finding:** The authors’ results indicate that high levels of palladin expression in cancer-associated fibroblasts (CAFs) enhance their ability to remodel the extracellular matrix by regulating the activity of the small GTPase Cdc42, which in turn promotes the assembly of matrix-degrading invadopodia in CAFs and tumor cell invasion. Together, these results identify a novel molecular signaling pathway that may provide new molecular targets for the inhibition of pancreatic cancer metastasis.

Overexpression of AIB1 correlates inversely with E-cadherin, may promote lymph node metastasis
- **Journal:** *International Journal of Clinical Oncology*
- **Institution(s):** Henan Provincial People’s Hospital, Zhengzhou, China and others
- **Corresponding author(s):** HaiBo Yu
- **Major finding:** Overexpression of the nuclear receptor coactivator amplified in breast cancer1 (AIB1) might promote invasion and metastasis of cancer cells and is associated with down-regulation of E-cadherin in pancreatic adenocarcinomas.

Targeting miR-21 for the therapy of pancreatic cancer
- **Journal:** *Molecular Therapy*
- **Institution(s):** Cancer Research Center of Toulouse, Toulouse, France and others
- **Corresponding author(s):** Pierre Cordelier
- **Major finding:** The authors demonstrate for the first time that targeting oncogenic miRNA strongly inhibit pancreatic cancer tumor growth both in vitro and in vivo. Because miR-21 is
overexpressed in most human tumors, therapeutic delivery of miR-21 antagonists may still be beneficial for a large number of cancers for which no cure is available.

**Growth inhibition of pancreatic cancer cells by histone deacetylase inhibitor belinostat**

- **Journal:** Molecular Carcinogenesis
- **Institution(s):** National University of Singapore, Singapore and others
- **Corresponding author(s):** Wenwen Chien
- **Major finding:** Taken together, the authors found that pan-histone deacetylase inhibitor (HDACi) decreases growth, increases apoptosis, and is associated with blocking the AKT/mTOR pathway. Surprisingly, it blocked hypoxic growth related signals. Their studies of belinostat suggest it may be an effective drug for the treatment of pancreatic cancers when used in combination with other drugs such as gemcitabine.

**Chidamide, a novel histone deacetylase inhibitor, synergistically enhances gemcitabine cytotoxicity**

- **Journal:** Biochemical and Biophysical Research Communications
- **Institution(s):** Beijing Institute of Transfusion Medicine, Beijing, PR China and others
- **Corresponding author(s):** Yuezhong He, Yubin Ge, and Qun Yu
- **Major finding:** The authors’ results suggest that chidamide has a therapeutic potential for treating pancreatic cancer, especially in combination with gemcitabine.

**Role of Insulin and Igf signaling in pancreatic cancer**

- **Journal:** Journal of Molecular Endocrinology
- **Institution(s):** Technische Universität München, Munich, Germany
- **Corresponding author(s):** Marija Trajkovic-Arsic
- **Major finding:** The authors give a short summary on the complexity of insulin and the insulin-like growth factor (IGF) system in the pancreas and their potential roles in pancreatic cancer, especially pancreatic ductal adenocarcinoma. Finally, the authors discuss drug targeting options of this system and the rationale of simultaneous targeting of both the insulin and IGF systems.

**Bcl-2/Bcl-xL inhibition increases the efficacy of Mek inhibition and in combination with PI3K inhibition**

- **Journal:** Molecular Cancer Therapeutics
- **Institution(s):** Genentech, Inc., South San Francisco, CA
- **Corresponding author(s):** Lisa Belmont
- **Major finding:** Taken together, the authors’ data suggest the efficacy of agents that target the MAPK and PI3K pathways can be improved by combination with a Bcl-2 family inhibitor.

**Pancreatic cancer associated stellate cells promote differentiation of myeloid-derived suppressor cells**

- **Journal:** Cancer Research
- **Institution(s):** Ohio State University, Columbus, OH
• **Corresponding author(s):** Gregory Lesinski
• **Major finding:** The authors’ results identify a novel role for pancreatic stellate cells in driving immune escape in pancreatic cancer and extend the evidence that STAT3 acts as a driver of stromal immunosuppression to enhance its interest as a therapeutic target.

**Enhancing sorafenib-mediated sensitization to gemcitabine through EMAP II**
• **Journal:** *Journal of Experimental & Clinical Cancer Research*
• **Institution(s):** University of Texas Southwestern Medical Center, Dallas, TX and others
• **Corresponding author(s):** Roderich Schwarz
• **Major finding:** These findings demonstrate that the addition of a polymechanistic antiangiogenic agent such as endothelial monocyte activating polypeptide II (EMAP) can enhance the combination treatment effects of sorafenib and cytotoxic pancreatic ductal adenocarcinoma therapy.

**ISL1 expression is not restricted to pancreatic well-differentiated neuroendocrine neoplasms**
• **Journal:** *Modern Pathology*
• **Institution(s):** University Hospital, Erlangen, Germany
• **Corresponding author(s):** Günter Klöppel
• **Major finding:** These findings modify the role of the human insulin gene enhancer-binding protein islet-1 (ISL1) as a marker for pancreatic neuroendocrine neoplasms and suggest that ISL1 has a broader involvement in differentiation and growth of neuroendocrine neoplasms than has so far been assumed.

**Structure-based design and evaluation of naphthalene diimide G-quadruplex ligands**
• **Journal:** *Journal of Medicinal Chemistry*
• **Institution(s):** University College London, London, UK
• **Corresponding author(s):** Stephen Neidle
• **Major finding:** The present study reports the enhancement of the pharmacological properties of earlier naphthalene diimide compounds using structure-based design. The new compounds retain high affinity to human telomeric quadruplex DNA but are 10-fold more potent against the MIA PaCa-2 pancreatic cancer cell line.

**Autophagy induced by p53-reactivating molecules protects pancreatic cancer cells from apoptosis**
• **Journal:** *Apoptosis*
• **Institution(s):** University of Verona, Verona, Italy
• **Corresponding author(s):** Massimo Donadelli
• **Major finding:** The authors’ results demonstrate for the first time a survival role for autophagy induced by p53-reactivating molecules, supporting the development of an anti-cancer therapy based on autophagy inhibition associated to p53 activation.
Differential ezrin expression profiles between PanIN, IPMN, and invasive ductal carcinoma
- **Journal**: Human Pathology
- **Institution(s)**: Kyushu University, Fukuoka, Japan
- **Corresponding author(s)**: Yoshinao Oda
- **Major finding**: Ezrin phosphorylation sites differ between the developments of intraductal papillary mucinous neoplasms (IPMNs) and pancreatic intraepithelial neoplasia (PanINs). Although p-ezrin (tyr354) expression in IPMNs is associated with tumor invasion, p-ezrin (tyr353) expression in invasive ductal carcinoma plays an important role not in tumor invasion and metastasis but in the early development of PanINs.

**ETIOLOGY**

Marked expansion of exocrine and endocrine pancreas with incretin therapy
- **Journal**: Diabetes
- **Institution(s)**: UCLA, David Geffen School of Medicine, Los Angeles, CA and others
- **Corresponding author(s)**: Alexandra Butler
- **PanCAN affiliated author**: Dave Dawson, MD, PhD: Seena Magowitz – Career Development Award
- **Major finding**: (See FDA release below.) In humans, incretin therapy resulted in a marked expansion of the exocrine and endocrine pancreatic compartments, the former being accompanied by increased proliferation and dysplasia, the latter by α cell hyperplasia with the potential for evolution into neuroendocrine tumors.

FDA investigating risk of pancreatitis, pre-cancerous findings of pancreas from incretin mimetic drugs
http://www.fda.gov/Drugs/DrugSafety/ucm343187.htm
The U.S. Food and Drug Administration (FDA) is evaluating unpublished new findings by a group of academic researchers (see above) that suggest an increased risk of pancreatitis, or inflammation of the pancreas, and pre-cancerous cellular changes called pancreatic duct metaplasia in patients with type 2 diabetes treated with a class of drugs called incretin mimetics.

Risk factors for intraductal papillary mucinous neoplasm (IPMN) of the pancreas
- **Journal**: The American Journal of Gastroenterology
- **Institution(s)**: Sapienza University of Rome at S. Andrea Hospital, Rome, Italy
- **Corresponding author(s)**: Alberto Larghi
- **Major finding**: A previous history of diabetes, especially with insulin use, chronic pancreatitis, and family history of pancreatic ductal adenocarcinoma (PDAC) are all relevant risk factors for the development of intraductal papillary mucinous neoplasm (IPMN). These results suggest an overlap between certain risk factors for PDAC and IPMN.

Risk of pancreatic cancer in breast cancer families from the Breast Cancer Family Registry
- **Journal**: Cancer Epidemiology, Biomarkers & Prevention
- **Institution(s)**: Spanish National Cancer Research Centre (CNIO), Madrid, Spain and others
Corresponding author(s): David Goldgar

Major finding: Germline mutations in BRCA1 and BRCA2 are associated with an increased risk of pancreatic cancer (PC). Members of BRCAX families are also at increased risk of PC, pointing to the existence of other genetic factors that increase the risk of both PC and breast cancer. This study clarifies the relationship between familial breast cancer and pancreatic cancer. Given its high mortality, PC should be included in risk assessment in familial breast cancer counseling.

Inflammatory plasma markers and pancreatic cancer risk: a prospective study of 5 U.S. cohorts

Journal: Cancer Epidemiology, Biomarkers & Prevention
Institution(s): Brigham and Women’s Hospital, Boston, MA and others
Corresponding author(s): Ying Bao

Major finding: Pre-diagnostic levels of circulating C-reactive protein (CRP), interleukin-6 (IL-6), and TNF-α receptor II (TNF-αR2) were not associated with the risk of pancreatic cancer, suggesting that systemic inflammation as measured by circulating inflammatory factors is unlikely to play a major role in the development of pancreatic cancer.

Pancreatic cancer clusters and arsenic-contaminated drinking water wells in Florida

Journal: BMC Cancer
Institution(s): University of Miami Miller School of Medicine, Miami, FL and others
Corresponding author(s): Wen Liu-Mares

Major finding: Exposure to arsenic-contaminated drinking water wells may be associated with an increased risk of pancreatic cancer. However, case–control studies are needed in order to confirm the findings of this ecological analysis. These cluster areas may be appropriate to evaluate pancreatic cancer risk factors, and to perform targeted screening and prevention studies.

EARLY DETECTION, DIAGNOSIS, AND PROGNOSIS
Use of EUS-FNA in diagnosing pancreatic neoplasm without a definitive mass on CT

Journal: Gastrointestinal Endoscopy
Institution(s): MD Anderson Cancer Center, Houston, TX
Corresponding author(s): Jeffrey Lee
PanCAN affiliated author: Jason Fleming, MD: Medical Advisory Board

Major finding: The objective of this study was to determine the diagnostic accuracy and to identify predictors of pancreatic neoplasm by endoscopic ultrasound (EUS) with fine needle aspiration (FNA) in patients with inconclusive findings on pancreatic multidetector row CT (MDCT). The authors concluded that, when MDCT is indeterminate, EUS is a highly sensitive and accurate modality for the detection of pancreatic neoplasm, especially when the tumor is smaller than 2.0 cm.

Pancreatic cancer: FDG-PET is not useful in early pancreatic cancer diagnosis
Staging chest computed tomography and positron emission tomography: utility or futility?


- **Journal:** HPB
- **Institution(s):** Loyola University Medical Center, Maywood, IL and others
- **Corresponding author(s):** Sam Pappas
- **Major finding:** The authors found that the addition of chest CT and PET to high-quality abdominal CT is of little clinical utility; additional sites of metastasis are rarely found. As the quality of abdominal imaging declines, the yield from other imaging modalities will increase. Dedicated pancreas-specific abdominal CT remains the cornerstone of initial staging in suspected or biopsy-proven pancreatic cancer.

Role of SUVmax obtained by 18F-FDG PET/CT in patients with a solitary pancreatic lesion


- **Journal:** Nuclear Medicine Communications
- **Institution(s):** Fudan University, Shanghai, China
- **Corresponding author(s):** Ying-Jian Zhang
- **Major finding:** The maximum standardized uptake value (SUVmax) of F-FDG PET/CT can be used in the differential diagnosis of solitary pancreatic lesions and can also aid in the prediction of proliferative activity of pancreatic cancer.

Limited efficacy of 18F-FDG PET/CT for differentiation between pancreatic cancer and pancreatitis


- **Journal:** Clinical Nuclear Medicine
- **Institution(s):** Nagoya University Graduate School of Medicine, Nagoya, Japan
- **Corresponding author(s):** Katsuhiko Kato
- **Major finding:** Differentiation between metastasis-free pancreatic cancer and mass-forming pancreatitis is difficult by FDG-PET/CT due to considerable overlapping between the SUVmax values of the two diseases, although the differential diagnosis may be possible either at the higher range of SUVmax for pancreatic cancer or at the lower range of SUVmax for mass-forming pancreatitis.

Hypermetabolic lesions of the pancreas on FDG PET/CT


- **Journal:** Clinical Nuclear Medicine
- **Institution(s):** Changjiang Zuo
• **Major finding:** Knowledge of a wide spectrum of hypermetabolic pancreatic lesions on FDG PET/CT is essential in accurate reading of FDG PET/CT.

**Current status on the diagnosis, evaluation of pancreatic tumour in Asia with endoscopic ultrasound**


- **Journal:** *Journal of Gastroenterology and Hepatology*
- **Institution(s):** Chulalongkorn University, Bangkok, Thailand and others
- **Corresponding author(s):** Khek-Yu Ho

**Major finding:** Endoscopic ultrasonography (EUS) offers a higher sensitivity for the detection of small potentially curable pancreatic masses than other existing imaging modalities. It is anticipated that in the near future, molecular technologies may make it possible to detect microscopic amounts of cancer in tissue or blood, predict relapse and survival after therapy, as well as determine optimal therapy.

**CA19-9 and CA242 as tumor markers for the diagnosis of pancreatic cancer: a meta-analysis**


- **Journal:** *Clinical and Experimental Medicine*
- **Institution(s):** Fudan University, Shanghai, China and others
- **Corresponding author(s):** Xing-Dang Liu

**Major finding:** The authors’ meta-analysis showed that CA242 and CA19-9 could play different roles in the diagnosis of pancreatic cancer. Although the sensitivity of CA242 is lower than that of CA19-9, its specificity is greater.

**Alkaline phosphatase ALPPL-2 is a novel pancreatic carcinoma-associated protein**


- **Journal:** *Cancer Research*
- **Institution(s):** Dongguk University, Seoul, Korea and others
- **Corresponding author(s):** Dong-ki Lee and Soyoun Kim

**Major finding:** To identify novel pancreatic cancer biomarkers that can facilitate early diagnosis and also help in the development of effective therapeutics, the authors developed RNA aptamers targeting pancreatic cancer. The authors identified alkaline phosphatase placental-like 2 (ALPPL-2), an oncofetal protein, as ectopically expressed in many pancreatic cancer cell lines at both mRNA and protein levels.

**A novel serum metabolomics-based diagnostic approach to pancreatic cancer**


- **Journal:** *Cancer Epidemiology, Biomarkers & Prevention*
- **Institution(s):** Kobe University Graduate School of Medicine, Kobe, Japan
- **Corresponding author(s):** Masaru Yoshida

**Major finding:** The authors’ serum metabolomics model possessed higher accuracy than conventional tumor markers at detecting the resectable patients with pancreatic cancer in cohort including patients with chronic pancreatitis. It is a promising method for improving the prognosis of pancreatic cancer via its early detection and accurate discrimination from chronic pancreatitis.
Cancer detection by ubiquitin carboxyl-terminal esterase L1 methylation in pancreatobiliary fluids
- **Journal**: *World Journal of Gastroenterology*
- **Institution(s)**: Sapporo Medical University School of Medicine, Sapporo, Japan and others
- **Corresponding author(s)**: Hiroyuki Yamamoto
- **Major finding**: The authors’ results suggest that hypermethylation of ubiquitin carboxyl-terminal esterase L1 (UCHL1) and runt-related transcription factor 3 (RUNX3) in pancreatobiliary fluid might be useful for the diagnosis of pancreatobiliary cancers.

Immunohistochemically detected expression of 3 major genes strongly predicts survival
- **Journal**: *Annals of Surgery*
- **Institution(s)**: Kagawa University, Kagawa, Japan and others
- **Corresponding author(s)**: Shinichi Yachida
- **Major finding**: Genetic alterations of CDKN2A/p16, TP53, and SMAD4/DPC4 and their accumulation are strongly associated with malignant behavior of pancreatic ductal adenocarcinoma. Their immunohistochemical assessment at the time of diagnosis may provide a new prognostic tool, assisting in deciding optimal therapeutic strategies for patients.

Pathohistological subtype predicts survival in patients with intraductal papillary mucinous neoplasm
- **Journal**: *Annals of Surgery*
- **Institution(s)**: Technical University Dresden, Dresden, Germany and others
- **Corresponding author(s)**: Robert Grützmann
- **Major finding**: Evaluation of IPMN subtypes supports postoperative patient prognosis prediction. Therefore, subtype differentiation could lead to improvements in clinical management. Potentially identifying subgroups with the need for adjuvant therapy may be possible.

Pancreatic cancer and predictors of survival: comparing the CA 19-9/bilirubin ratio with the MBBS
- **Journal**: *HPB*
- **Institution(s)**: McGill University Health Center, Montreal, Canada and others
- **Corresponding author(s)**: Jeffrey Barkun
- **Major finding**: CA19-9 levels and the CA19-9-to-bilirubin ratio are poor predictors of survival for pancreatic cancer, whereas the McGill Brisbane Symptom Score (MBSS) is a far better predictor, confirming its clinical value. By adding the CA19-9-to-bilirubin ratio to the MBSS the predictive characteristics improved.

Comparison of prognosis between patients of pancreatic head cancer with and without jaundice
- **Journal**: *International Journal of Surgery*
- **Institution(s)**: Osaka City University Graduate School of Medicine, Osaka, Japan
- **Corresponding author(s)**: Bunzo Nakata
• **Major finding:** The presence of obstructive jaundice at diagnosis in patients with pancreatic head cancer may predict an unfavorable survival compared to such patients without obstructive jaundice.

**Follow-up after curative surgery:** Asymptomatic recurrence is associated with improved survival


• **Journal:** European Journal of Surgical Oncology

• **Institution(s):** Oslo University Hospital, Oslo, Norway

• **Corresponding author(s):** Knut Joergen Labori

• **Major finding:** Patients with asymptomatic pancreatic cancer recurrence have improved recurrence-free, post-recurrence and overall survival. Symptoms when recurrence is diagnosed are a good surrogate marker of biological aggressiveness. Detection of asymptomatic recurrence may facilitate patient eligibility for investigational studies or other forms of treatment.

**TREATMENT**

**Agonistic CD40 antibodies and cancer therapy**


• **Journal:** Clinical Cancer Research

• **Institution(s):** University of Pennsylvania, Philadelphia, PA and others

• **Corresponding author(s):** Robert Vonderheide and Martin Glennie

• **PanCAN affiliated author:** Bob Vonderheide, MD, DPhil: 2013 Tempur-Pedic – Inaugural RAN Grant in Memory of Tim Miller and member, Scientific Advisory Board

• **Major finding:** Recent success in cancer immunotherapy has reinvigorated the hypothesis that the immune system can control many if not most cancers, in some cases producing durable responses in a way not seen with many small-molecule drugs. Here, the authors review the preclinical and clinical data and discuss the major issues facing the field.

**SBRT planning with duodenal sparing using VMAT vs IMRT in locally advanced pancreatic cancer**


• **Journal:** Medical Dosimetry

• **Institution(s):** Johns Hopkins University School of Medicine, Baltimore, MD and others

• **Corresponding author(s):** Joseph Herman

• **PanCAN affiliated author:** Joe Herman, MD: 2008 Blum-Kovler – Career Development Award and member, Medical Advisory Board

• **Major finding:** This study dosimetrically evaluates the feasibility of implementing duodenal constraints for stereotactic body radiation therapy (SBRT) using volumetric-modulated arc therapy (VMAT) vs intensity-modulated radiation therapy (IMRT). The authors’ findings suggest clinical situations where each technique may be most useful if duodenal-sparing constraints are to be employed.

**Neoadjuvant interferon chemoradiation for borderline resectable, locally advanced pancreas cancer**


• **Journal:** HPB

• **Institution(s):** University of Minnesota Medical Center, Minneapolis, MN and others
Corresponding author(s): Eric Jensen
PanCAN affiliated author: Selwyn Vickers, MD: Emeritus Scientific Advisory Board
Major finding: Interferon-based neoadjuvant chemoradiotherapy may allow for resection of locally advanced pancreatic cancer, but with significant toxicity. In the absence of surgical resection, survival remains dismal.

2564 resected periampullary adenocarcinomas at a single institution: trends over three decades
Journal: HPB
Institution(s): Johns Hopkins University School of Medicine, Baltimore, MD
Corresponding author(s): Christopher Wolfgang
PanCAN affiliated author: Ralph Hruban, MD: Emeritus Scientific Advisory Board
Major finding: There are significant differences among periampullary adenocarcinomas in long-term survival following pancreaticoduodenectomy. Although the numbers of patients undergoing safe resection have increased, overall long-term outcomes have not improved significantly.

Sunitinib malate for the treatment of pancreas malignancies - where does it fit?
Journal: Expert Opinion on Pharmacotherapy
Institution(s): Columbia University College of Physicians and Surgeons, New York, NY and others
Corresponding author(s): Eileen O’Reilly
PanCAN affiliated author: Eileen O’Reilly, MD: Medical Advisory Board
Major finding: The experts’ opinion is that sunitinib malate has become integrated into routine clinical management for pancreatic neuroendocrine tumors; however, its role in pancreas adenocarcinoma is not.

Gemcitabine-based or capecitabine-based chemoradiotherapy for locally advanced pancreatic cancer
Journal: The Lancet Oncology
Institution(s): NIHR Oxford Biomedical Research Centre, Oxford, UK and others
Corresponding author(s): Somnath Mukherjee
Major finding: The authors’ results suggest that a capecitabine-based regimen might be preferable to a gemcitabine-based regimen in the context of consolidation chemoradiotherapy after a course of induction chemotherapy for locally advanced pancreatic cancer. However, these findings should be interpreted with caution because the difference in the primary endpoint was non-significant and the number of patients in the trial was small.

Chemoradiotherapy for locally advanced pancreatic cancer
Journal: The Lancet Oncology
Institution(s): University of Heidelberg, Heidelberg, Germany
Corresponding author(s): Markus Büchler
Major finding: The authors feel that the study presented above could change medical practice if the concomitant improvement in progression-free survival and overall survival with decreased toxicity of the capecitabine regimen can be reproduced in a larger number of patients. The SCALOP investigators acknowledge the fairly small sample size of their trial and the non-significant difference in primary endpoint, which impairs the interpretative power of the results. The authors therefore agree with their conclusion that these findings have to be interpreted with caution, especially with respect to the efficacy endpoints such as survival.

Toxicity study of gemcitabine, oxaliplatin, bevacizumab; 5-FU, oxaliplatin, bevacizumab, radiotherapy
- Journal: Cancer Chemotherapy and Pharmacology
- Institution(s): Cleveland Clinic, Taussig Cancer Institute, Cleveland, OH and others
- Corresponding author(s): Davendra Sohal
- Major finding: The authors piloted a combination of gemcitabine/oxaliplatin/bevacizumab, followed by oxaliplatin and bevacizumab added to infusional 5-FU and radiotherapy, in patients with locally advanced pancreatic cancer. This combination, associated with higher response rates in metastatic disease, had a lower than expected response rate in primary tumors. Although tolerable, our approach failed to affect clinical outcomes meaningfully.

Aggressive surgery for borderline resectable pancreatic cancer: Evaluation of NCCN guidelines
- Journal: Pancreas
- Institution(s): Nagoya University Graduate School of Medicine, Nagoya, Japan
- Corresponding author(s): Akimasa Nakao
- Major finding: The objective of this study was to evaluate the relevance of defining borderline resectable (BR) pancreatic cancer as a distinct entity in the treatment scheme of pancreatic cancer as proposed by the National Comprehensive Cancer Network. The authors conclude that the optimal treatment strategy may differ among various subgroups within the BR category.

Phase II trial of nab-paclitaxel as second-line therapy in patients with advanced pancreatic cancer
- Journal: American Journal of Clinical Oncology
- Institution(s): University of Miami, Miami, FL and others
- Corresponding author(s): Caio Rocha Lima
- Major finding: This study suggested that nab-Paclitaxel was well tolerated, and it demonstrated preliminary evidence of activity in a subset of patients who progressed on gemcitabine-based therapy.

Stereotactic body radiation therapy with concurrent full-dose gemcitabine
- Journal: Radiation Oncology
- Institution(s): Georgetown University Hospital, Washington, DC and others
- Corresponding author(s): Michael Pishvaian
Major finding: Stereotactic body radiation therapy with concurrent full dose gemcitabine is safe when administered to patients with locally advanced pancreatic cancer. There is no delay in administration of radiation or chemotherapy, and radiation is completed with minimal toxicity.

Gemcitabine plus erlotinib for advanced pancreatic cancer: a systematic review with meta-analysis
- Journal: *PLoS One*
- Institution(s): The Chinese University of Hong Kong, Hong Kong, China and others
- Corresponding author(s): Chen Mao and Jin-Ling Tang
- Major finding: Gemcitabine plus erlotinib represent a new option for the treatment of advanced pancreatic cancer, with mild but clinically meaningful additive efficacy compared with gemcitabine alone. Its safety profile is generally acceptable, although careful management is needed for some specific adverse events.

Transferrin receptor targeting nanomedicine delivering wild-type p53 gene sensitizes to gemcitabine
- Journal: *Cancer Gene Therapy*
- Institution(s): Medical University of South Carolina, Charleston, SC
- Corresponding author(s): Dennis Watson
- Major finding: To overcome gene therapy barriers such as low transfection efficiency and nonspecific delivery, liposomal nanoparticles targeted by a single-chain antibody fragment to the transferrin receptor (TfRscFv) delivering wild-type human p53 (SGT-53) were developed for tumor-specific targeting. The tumor targeting liposomal-based SGT-53 nanoparticle was found to be capable of sensitizing pancreatic cancer to conventional chemotherapy in pancreatic cancer models. Further optimization is ongoing, moving towards a Phase 1B/2 clinical trial.

Synergistic interactions between sorafenib and everolimus in pancreatic cancer xenografts in mice
- Journal: *Cancer Chemotherapy and Pharmacology*
- Institution(s): State University of New York at Buffalo, Buffalo, NY
- Corresponding author(s): William Jusko
- Major finding: The results indicate that combinations of mTOR and multi-kinase inhibitors may offer greater efficacy in pancreatic cancer than either drug alone. Drug effects upon tumor stromal elements may contribute to the enhanced anti-tumor efficacy.

Human equilibrative nucleoside transporter 1 and Notch3 can predict gemcitabine effects
- Journal: *British Journal of Cancer*
- Institution(s): Hokkaido University Graduate School of Medicine, Sapporo, Japan
- Corresponding author(s): Naoya Sakamoto
- Major finding: Human equilibrative nucleoside transporter 1 (hENT1) and Notch3 mRNA expressions in endoscopic ultrasound-guided fine-needle aspiration specimens were the key predictive biomarkers of gemcitabine effect and gemcitabine sensitivity in patients with unresectable pancreatic ductal carcinoma.
Treatment of malignant pancreatic neuroendocrine neoplasms: middle-term (2-year) outcomes


- **Journal:** HPB
- **Institution(s):** Humanitas Clinical and Research Center, Milan, Italy and others
- **Corresponding author(s):** Alessandro Zerbi
- **Major finding:** A radical resection is the cornerstone treatment of malignant pancreatic neuroendocrine neoplasms and represents, together with Ki67 assessment, the most powerful prognostic factor for 2-year outcomes.

FOLFRINOX useful in locally advanced pancreatic cancer


The chemotherapy regimen known as FOLFRINOX produces an "impressive clinical response" in locally advanced pancreatic ductal adenocarcinoma, according to the authors of a new small, retrospective, cohort study, presented at the Society of Surgical Oncology (SSO) 66th Annual Cancer Symposium.

General surgeons perform most cancer operations in US


General surgeons appear to perform the majority of cancer procedures in the United States, according to a study discussed at the Society of Surgical Oncology (SSO) 66th Annual Cancer Symposium. However, with regard to even more technical and less common procedures, surgical oncologists performed the majority of cases, including about one-third of all pancreatic cancer procedures.

Ushering in a new era of open science through data sharing: the wall must come down


- **Journal:** JAMA
- **Institution(s):** Yale University, New Haven, CT
- **Corresponding author(s):** Joseph Ross, and Harlan Krumholz
- **Major finding:** Nearly 30,000 trials globally are recruiting patients, and results from 75 trials are published daily in biomedical journals. However, there is a crisis, with an attendant opportunity, that requires change. A wall surrounds much of these clinical research data, sequestering knowledge, impeding the free flow of information, and obscuring a clear view of the totality of evidence relevant to many research questions and clinical decisions.

CANCER CONTROL, SURVIVORSHIP, AND OUTCOMES RESEARCH

Supportive care of the patient with advanced pancreatic cancer

http://www.cancernetwork.com/pancreatic-cancer/content/article/10165/2132138

This Cancer Network article describes how providing meaningful supportive care for patients with advanced pancreatic cancer is complex and requires ongoing close monitoring of the physical and emotional aspects of the patient’s experience of illness. Prompt management of the many symptoms and problems associated with pancreatic cancer is essential to minimize distress and optimize quality of life for patients with this devastating disease. Recognizing end-of-life concerns and patient preferences during the dying process helps clinicians find ways to alleviate suffering for patients and families. Early conversations about death will allay concerns and guide an oncologist to recommend antineoplastic therapy based on individual patient preferences and plans.
Perioperative and long-term outcomes after pancreaticoduodenectomy in elderly patients
- **Journal:** Langenbeck’s Archives of Surgery
- **Institution(s):** National Cancer Center Hospital, Tokyo, Japan and others
- **Corresponding author(s):** Kazuki Shimada
- **Major finding:** Pancreaticoduodenectomy for pancreatic cancer in patients aged 80 and older should be carefully selected, because it is associated with a higher incidence of severe postoperative complications and a small change of long-term survival.

Regional variation in spending and survival for older adults with advanced cancer
- **Journal:** Journal of National Cancer Institute
- **Institution(s):** Dana-Farber Cancer Institute, Boston, MA and others
- **Corresponding author(s):** Gabriel Brooks
- **Major finding:** There is substantial regional variation in Medicare spending for advanced cancer, yet no consistent association between mean regional spending and survival.

Public perception of cancer survival rankings
- **Journal:** Health Education & Behavior
- **Institution(s):** University of Utah, Salt Lake City, UT and others
- **Corresponding author(s):** Jakob Jensen
- **Major finding:** A sample of 400 Indiana adults completed a survey with questions regarding perceived cancer survival rates. Distortions observed mirror past content analytic work demonstrating that breast, stomach, and pancreatic cancers are misrepresented in the news.

Education and referral criteria: Impact on oncology referrals to palliative care
- **Journal:** Journal of Palliative Medicine
- **Institution(s):** University of Pennsylvania, Philadelphia, PA
- **Corresponding author(s):** Barbara Reville
- **Major finding:** A quality improvement project supported the use of education and referral criteria to influence both the frequency and reasons for palliative care referral by oncology providers.

Health care-associated infections after major cancer surgery
- **Journal:** Cancer
- **Institution(s):** Henry Ford Health system, Detroit, MI and others
- **Corresponding author(s):** Jesse Sammon
- **Major finding:** Between 1999 and 2009, the incidence of major cancer surgery (MCS)-associated healthcare-associated infections (HAI) events increased; however, HAI-associated mortality decreased. That said, significant disparities exist in the hospital and demographic attributes.
associated with MCS-associated HAI, with attendant health policy implications. Moreover, HAI remains detrimentally linked to mortality during hospitalization.

**Does DoD have secret to ending racial disparities in cancer?**


Black and white patients with pancreatic cancer in the Department of Defense (DoD) healthcare system received similar treatments and have a similar median overall survival, according to a retrospective study presented at the Society of Surgical Oncology (SSO) 66th Annual Cancer Symposium.