# PANCREATIC CANCER NEWS & UPDATES – MAY 2013

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Pancreatic Cancer Action Network and Community News

PanCAN news:

Big news! Evaluation of research grants program: Private funding creates exponential progress
http://pancan.org/section_research stratégic_research_program/evaluation_of_research_grants_program_2013.php#.UZxH-rVlk2c

Press release:
http://pancan.org/section_about/news_press_center/2013_press_releases/05_15_13_pr.php#.UZxISLVlk2c

Pancreatic Cancer Action Network rigorously evaluated our research grants program in early 2013, looking at grants awarded from 2003-2011. During that time, 66 grants were awarded totaling $9.15 million. We found that the scientists funded during that time were able to leverage our $9.15 million investment into $91 million in subsequent pancreatic cancer research funding. The 62 researchers who received grants from 2003-2011 authored an impressive 813 papers, many of which were published in high-tier journals, and then went on to be cited a combined 6,285 times.

Plant biologist Shruti Lal, PhD, identifies molecule that could prove key in treating pancreatic cancer
http://jdc.jefferson.edu/jss/vol8/iss1/7/

This is a nice write-up about Shruti Lal, PhD, a postdoctoral fellow in the laboratory of Jonathan Brody, PhD, recipient of a 2010 Pancreatic Cancer Action Network Career Development Award in memory of Skip Viragh.
**Funding opportunities:**

**Updated!** FY13 Peer Reviewed Cancer Research Program (PRCRP)

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

- Pre-Application (Preproposal) deadline: July 16, 2013
- Congressionally directed topic areas for FY13 Peer Reviewed Cancer Research Program (PRCRP) include pancreatic cancer. **Please note that, new for FY13, applications must also fit into a military relevance focus area.**

**New!** FY13 Peer Reviewed Medical Research Program – Discovery Award


- Pre-Application (Letter of Intent) deadline: July 23, 2013
- Also through the DOD, the PRMRF Discovery Award includes pancreatitis as one of the topic areas. Again, applications are required to include an explanation of how the proposed project has military relevance.

Clinical Assay Development Program (CADP)

http://cadp.cancer.gov/

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 deadline: October 15.

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).

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.”
Meetings:

New! Save the date: 2013 Gigi Shaw Arledge Conference on Pancreatic Disease

- Monday, September 9, 2013, 8:00am–7:00pm, NewYork-Presbyterian/Columbia University Medical Center
- This event is co-chaired by Ken Olive, PhD (2011 Tempur-Pedics Retailers – Career Development Award) and Tim Wang, MD (2013 Innovative Grant). The keynote speaker is Ralph Hruban, MD (Emeritus Scientific Advisory Board), and other speakers include many other Pancreatic Cancer Action Network research grant recipients and Scientific Advisory Board members.

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.
**Other community news:**

May is National Cancer Research Month

The American Association for Cancer Research (AACR) acknowledges May as National Cancer Research Month, declared by the United States Congress in 2007 and 2011, in recognition of high-quality, innovative cancer research.

Florida Hospital Tampa offers fully robotic Whipple surgery

Florida Hospital Tampa is among an elite group of hospitals across the United States offering fully robotic Whipple surgery. The robotic approach enhances the operation with its three-dimensional portrayal of the abdominal cavity, assisting the surgeons in making precise dissections. Since the operation employs minimally invasive techniques, patients do not have large scars. This also allows patients who have cancerous masses to start chemotherapy sooner.
BIOLOGY OF CANCER
Macropinocytosis of protein is an amino acid supply route in Ras-transformed cells
Pancreatic Cancer Action Network write-up:
http://pancan.org/section_research/strategic_research_program/news/topic_energy-source-for-pancreatic-tumors.php#.UZrrWbVlk2c

- **Journal**: Nature
- **Institution(s)**: New York University, New York, NY and others
- **Corresponding author(s)**: Dafna Bar-Sagi
- **PanCAN-affiliated authors**:
  - Cosimo Commissio, PhD: 2011 Samuel Stroum – Fellowship Award
  - Craig Thompson, MD: Scientific Advisory Board
  - Dafna Bar-Sagi, PhD: 2013 Tempur-Pedic – Inaugural Research Acceleration Network Grant in Memory of Tim Miller (co-PI), 2008 Pilot Grant, and Scientific Advisory Board
- **Major finding**: The authors’ results identify macropinocytosis as a mechanism by which cancer cells support their unique metabolic needs and point to the possible exploitation of this process in the design of anticancer therapies.

Small molecule inhibition of the KRAS-PDEδ interaction impairs oncogenic KRAS signalling

- **Journal**: Nature
- **Institution(s)**: Max Planck Institute of Molecular Physiology, Dortmund, Germany and others
- **Corresponding author(s)**: Herbert Waldmann, Philippe Bastiaens, and Alfred Wittinghofer
- **Major finding**: Here the authors report that interfering with binding of mammalian PDEδ to KRAS by means of small molecules provides a novel opportunity to suppress oncogenic RAS signaling by altering its localization to endomembranes. Biochemical screening and subsequent structure-based hit optimization yielded inhibitors of the KRAS–PDEδ interaction that selectively bind to the prenyl-binding pocket of PDEδ with nanomolar affinity, inhibit oncogenic RAS signaling and suppress *in vitro* and *in vivo* proliferation of human pancreatic ductal adenocarcinoma cells that are dependent on oncogenic KRAS. (See accompanying editorial below.)

Cancer: Drug for an 'undruggable' protein

- **Journal**: Nature
- **Institution(s)**: University of North Carolina at Chapel Hill, Chapel Hill, NC
- **Corresponding author(s)**: Channing Der
- **PanCAN-affiliated author**: Channing Der, PhD: 2012 Tempur-Pedic® Retailers – Innovative Grant
- **Major finding**: This News & Views piece accompanies the above article, and describes the authors’ approach to target KRAS’s cellular localization as “reigniting lost enthusiasm.”
Nr5a2 maintains acinar cell differentiation, constrains oncogenic Kras-mediated pancreatic initiation
- **Journal**: Gut
- **Institution(s)**: University of California-San Francisco, San Francisco, CA and others
- **Corresponding author(s)**: Matthias Hebrok
- **PanCAN-affiliated author**: Matthias Hebrok, PhD: 2011 Abby Sobrato – Innovative Grant and 2008 Michael C. Sandler – Pilot Grant
- **Major finding**: Nr5a2 is a key regulator of acinar plasticity. It is required for maintenance of acinar identity and re-establishing acinar fate during regeneration. Nr5a2 also constrains pancreatic neoplasia driven by oncogenic Kras, providing functional evidence supporting a potential role as a susceptibility gene for human pancreatic ductal adenocarcinoma.

Imbalance of desmoplastic stromal cell numbers drives aggressive cancer processes
- **Journal**: The Journal of Pathology
- **Institution(s)**: Queen Mary University of London, UK and others
- **Corresponding author(s)**: Hemant Kocher
- **PanCAN-affiliated author**: Anil Rustgi, MD: 2013 Skip Viragh – Inaugural Research Acceleration Network Grant (co-PI) and Scientific Advisory Board
- **Major finding**: These studies demonstrate that context-specific cancer-stroma crosstalk requires to be precisely defined for effective therapeutic targeting. These data may be relevant to non-malignant processes where epithelial cells interact with stromal cells, such as chronic inflammatory and fibrotic conditions. (See accompanying invited commentary below.)

Understanding stroma: Coevolution of microenvironment with epithelial carcinogenesis
- **Journal**: The Journal of Pathology
- **Institution(s)**: Technische Universität München, Munich, Germany
- **Corresponding author(s)**: Mert Erkan
- **Major finding**: This invited commentary on the above article describes that the authors’ work may be instrumental for better understanding the types of stoma in pancreatic ductal adenocarcinoma before eliminating it non-selectively.

FAM190A deficiency creates a cell division defect
- **Journal**: The American Journal of Pathology
- **Institution(s)**: Johns Hopkins Medical Institutions, Baltimore, MD
- **Corresponding author(s)**: Scott Kern
- **PanCAN-affiliated author**: Christine Iacobuzio-Donahue, MD, PhD: 2007 Pilot Grant and Scientific Advisory Board
- **Major finding**: Like the p16, SMAD4, and RB1 genes, FAM190A (alias CCSER1) lies at a consensus site of homogeneous genomic deletions in human cancer. The authors propose that FAM190A is a regulator or structural component required for normal mitosis and that both the rare
truncating mutations and common in-frame deletion alteration of FAM190A may contribute to the chromosomal instability of cancer.

**Triptolide induces the expression of miR-142-3p: a negative regulator of heat shock protein 70**


- **Journal:** *Molecular Cancer Therapeutics*
- **Institution(s):** University of Minnesota, Minneapolis, MN
- **Corresponding author(s):** Ashok Saluja
- **PanCAN-affiliated author:** Selwyn Vickers, MD: Emeritus Scientific Advisory Board
- **Major finding:** The authors found that miR-142-3p regulates heat shock protein 70 (HSP70) independently of heat shock factor 1. Furthermore, Minnelide, a water soluble prodrug of triptolide, induced the expression of miR-142-3p in vivo. This is the first description of an miRNA-mediated mechanism of HSP70 regulation in cancer, making miR-142-3p an attractive target for pancreatic ductal adenocarcinoma therapeutic intervention.

**Special issue of Gastroenterology: The Pancreas: Biology, Diseases, and Therapy**


Many Pancreatic Cancer Action Network grant recipients and members of our Scientific and Medical Advisory Boards are featured in this special issue of *Gastroenterology* which reviews the significant advances in understanding disease mechanisms and the manner in which they can be applied to develop treatments for pancreatic disorders.

**Mesothelin binding to CA125/MUC16 promotes pancreatic cancer cell motility, invasion via MMP-7**


- **Journal:** *Scientific Reports*
- **Institution(s):** Johns Hopkins University, Baltimore, MD and others
- **Corresponding author(s):** Konstantinos Konstantopoulos
- **Major finding:** The authors’ findings provide a novel perspective on the enhanced invasive potential associated with mesothelin and cancer antigen125/mucin 16 (CA125/MUC16) co-over-expression, and the mechanism underlying matrix metalloproteinase (MMP)-7 activation in pancreatic cancer invasion and metastasis.

**Neuropilin-2 promotes extravasation and metastasis by interacting with endothelial α5 integrin**


- **Journal:** *Cancer Research*
- **Institution(s):** Mayo Clinic, Rochester, MN and others
- **Corresponding author(s):** Debabrata Mukhopadhyay
- **Major finding:** Taken together, the authors’ studies reveal a clinically significant role of neuropilin-2 in cancer cell extravasation and promotion of metastasis, determined using several cancer models, including pancreatic.
Extracellular DNA in pancreatic cancer promotes cell invasion and metastasis


- Journal: *Cancer Research*
- Institution(s): University of Arizona, Tucson, AZ and others
- Corresponding author(s): Jiaqi Shi and Fushi Wen
- Major finding: Extracellular DNA (exDNA) is a recently discovered component of inflammatory tissue states. Taken together, the authors’ results strongly suggest that exDNA contributes to the highly invasive and metastatic character of pancreatic cancer.

Three-dimensional collagen I promotes gemcitabine resistance in vitro through HMGA2-dependent


- Journal: *PLoS One*
- Institution(s): Northwestern University, Chicago, IL
- Corresponding author(s): Surabhi Dangi-Garimella and Hidayatullah Munshi
- Major finding: Overall, the authors’ results increase our understanding of how the collagen microenvironment contributes to chemo-resistance in vitro and identify histone acetyltransferases as potential therapeutic targets against pancreatic cancer.

GSK-3α promotes oncogenic KRAS via TAK1-TAB stabilization and regulation of noncanonical NF-κB


- Journal: *Cancer Discovery*
- Institution(s): University of North Carolina at Chapel Hill, Chapel Hill, NC
- Corresponding author(s): Albert Baldwin
- Major finding: These data identify glycogen synthase kinase 3α (GSK-3α) as a key downstream effector of oncogenic KRAS via its ability to coordinately regulate distinct NF-κB signaling pathways.

4-hydroxy tamoxifen induces autophagic death through K-Ras degradation


- Journal: *Cancer Research*
- Institution(s): University of Alabama at Birmingham, Birmingham, AL
- Corresponding author(s): Kevin Roth
- Major finding: The authors’ findings describe a novel mechanism of autophagic death triggered by tamoxifen and its derivative 4-dehydroxy-tamoxifen (OHT) in tumor cells that may be more broadly useful clinically in cancer treatment.

Depletion of RAD17 sensitizes pancreatic cancer cells to gemcitabine


- Journal: *Journal of Cell Science*
- Institution(s): Deutsches Krebsforschungszentrum, Heidelberg, Germany
- Corresponding author(s): Jörg Hoheisel
- Major finding: The authors’ data suggest RAD17 as a novel target for gemcitabine combination therapy supplementing or complementing inhibition of checkpoint kinase 1. As opposed to
checkpoint kinase 1 (CHK1), RAD17 knockdown by itself does not lead to abnormal DNA segregation, suggesting a more specific action.

**Hypoxia induces the overexpression of microRNA-21 in pancreatic cancer cells**


- **Journal:** Journal of Surgical Research
- **Institution(s):** Ohio State University, Columbus, OH
- **Corresponding author(s):** Mark Bloomston
- **Major finding:** MicroRNA miR-21 is induced by hypoxia in pancreatic cancer cells via hypoxia-inducible factor (HIF)-1α upregulation. MiR-21 overexpression allows cells to avoid apoptosis in a hypoxic microenvironment. Inhibition of miR-21 expression may increase cellular susceptibility to hypoxia in pancreatic cancer.

**ARID1B, member of SWI/SNF complex, exhibits tumour-suppressor activities in pancreatic cancer**


- **Journal:** British Journal of Cancer
- **Institution(s):** Centre for DNA Fingerprinting and Diagnostics, Hyderabad, India
- **Corresponding author(s):** Murali Bashyam
- **Major finding:** The results therefore suggest a possible tumor-suppressor function for AT-rich interaction domain 1B (ARID1B) in pancreatic cancer, thus adding to the growing list of human ATP-dependent SWItch/sucrose nonfermentable (SWI/SNF) components with a similar function.

**Heparanase promotes lymphangiogenesis and tumor invasion in pancreatic neuroendocrine tumors**


- **Journal:** Oncogene
- **Institution(s):** Memorial Sloan-Kettering Cancer Center, New York, NY
- **Corresponding author(s):** Johanna Joyce
- **Major finding:** Together, these data identify important roles for heparanase in regulating several critical aspects of tumorigenesis, demonstrating that heparanase represents a potential therapeutic target for pancreatic neuroendocrine tumors (PanNET) patients.
ETIOLOGY
A critical analysis of the clinical use of incretin-based therapies: Are the GLP-1 therapies safe?
- Journal: Diabetes Care
- Institution(s): University of California Los Angeles, David Geffen School of Medicine, Los Angeles, CA and others
- Corresponding author(s): Edwin Gale
- Major finding: Diabetes Care published a point-counterpoint sequence of articles (see below) discussing the recent findings that incretin-based diabetes drugs may increase the risk of pancreatitis and, in the long run, pancreatic cancer. Dr. Butler and colleagues conclude that the case presented here does not prove that these agents are unsafe, but it does suggest that the burden of proof now rests with those who wish to convince us of their safety.

A critical analysis of the clinical use of incretin-based therapies: The benefits outweigh potential risks
- Journal: Diabetes Care
- Institution(s): Diabetes Center, Bad Lauterberg, Bad Lauterberg im Harz, Germany
- Corresponding author(s): Michael Nauck
- Major finding: Diabetes Care published a point-counterpoint sequence of articles (see above) discussing the recent findings that incretin-based diabetes drugs may increase the risk of pancreatitis and, in the long run, pancreatic cancer. Dr. Nauck concludes that, based on today’s available knowledge, incretin-based medications can be considered effective and safe. Such considerations should not currently influence our treatment decisions regarding the potential prescription of GLP-1 receptor agonists or DPP-4 inhibitors within a treatment regimen for type 2 diabetes.

Duration of diabetes and pancreatic cancer in a case-control study
- Journal: Journal of the Pancreas
- Institution(s): University of Minnesota Masonic Cancer Center, Minneapolis, MN
- Corresponding author(s): Kristin Anderson
- Major finding: Diabetes and diabetes duration were examined in relation to pancreatic cancer in a population-based case-control study in the Midwest and the Iowa Women’s Health Study (IWHS) Cohort. The authors found that diabetes is associated with pancreatic cancer risk and this is similar across different duration categories.

Cancer detection rates following enrollment in a disease management programme for type 2 diabetes
- Journal: Diabetologia
- Institution(s): Westfälische Wilhelms-Universität Münster, Münster, Germany
- Corresponding author(s): A. Geier
- Major finding: Enrollment in a disease management program for type 2 diabetes mellitus (DMP-DM2) did not appear to induce ascertainment bias for most cancers. Cancer risks were initially
increased, especially for pancreatic cancer, potentially as a result of reverse causality. Ascertainment bias and time-dependent incidence of cancer appear to be less of a problem in settings using DMP-like structures for the study of the association between diabetes duration, glucose-lowering medication and cancer incidence.

**High prevalence of BRCA1, BRCA2 germline mutations with LOH in pancreatic adenocarcinoma**
- **Journal:** Clinical Cancer Research
- **Institution(s):** Icahn School of Medicine at Mount Sinai, New York, NY
- **Corresponding author(s):** Aimee Lucas
- **Major finding:** The authors show a high prevalence of BRCA1/2 mutations with loss of heterozygosity (LOH) in an Ashkenazi Jewish cohort of surgically resected pancreatic ductal adenocarcinoma and neoplastic lesions, suggesting that these germline mutations are causal in selected individuals.

**A prospective analysis of telomere length and pancreatic cancer**
- **Journal:** International Journal of Cancer
- **Institution(s):** Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD and others
- **Corresponding author(s):** Shannon Lynch
- **Major finding:** To test whether telomere length is associated with pancreatic cancer risk, the authors conducted a nested case-control study in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Study cohort of male smokers. This is the first prospective study to suggest an association between longer blood leukocyte telomere length and increased pancreatic cancer risk.

**Active and passive smoking and risk of death from pancreatic cancer**
- **Journal:** Pancreatology
- **Institution(s):** Aichi Medical University School of Medicine, Aichi, Japan and others
- **Corresponding author(s):** Shogo Kikuchi
- **Major finding:** Using data from the Japan Collaborative Cohort Study, the authors found that cigarette smoking is associated with an approximately 70% increase in the risk of death from pancreatic cancer. Further studies with improved exposure assessment are needed to better quantify the association between passive smoking and pancreatic cancer.

**Blood group determinates incidence for pancreatic cancer in Germany**
- **Journal:** Frontiers in Physiology
- **Institution(s):** Charité - Universitätsmedizin Berlin Berlin, Germany
- **Corresponding author(s):** Uwe Pelzer
Major finding: The incidence of pancreatic cancer (PC) in the German cohort is highly associated with the AB0-system as well. More patients with blood group A suffer from PC (p < 0.001) whereas blood group 0 was less frequent in patients with PC (p < 0.001). Thus, the authors' findings support the results from other non-German surveys. The causal trigger points of this carcinogenesis correlation are still not known.

ABO blood group and risk of pancreatic cancer: A study in Shanghai and meta-analysis

- **Journal:** American Journal of Epidemiology
- **Institution(s):** Yale School of Public Health, New Haven, CT
- **Corresponding author(s):** Harvey Risch
- **Major finding:** Studies over 5 decades have examined ABO blood groups and risk of pancreatic cancer in Western, Asian, and other populations, though no systematic review has been published. The authors studied data from 908 pancreatic cancer cases and 1,067 population controls collected during December 2006-January 2011 in urban Shanghai, China, and reviewed the literature for all studies of this association.
PREVENTION

Receptivity, preferences of pancreatic cancer family members for participating in lifestyle programs


- **Journal:** *Hereditary Cancer in Clinical Practice*
- **Institution(s):** Mayo Clinic Rochester, Rochester, MN
- **Corresponding author(s):** Christi Patten
- **PanCAN-affiliated author:** Gloria Petersen, PhD: Scientific Advisory Board
- **Major finding:** Family members of those with pancreatic cancer are receptive to cancer risk reduction programs focusing on nutrition and weight management delivered via the internet. Further research is indicated to determine how to best incorporate a family-based approach when designing lifestyle intervention programs.
**EARLY DETECTION, DIAGNOSIS, AND PROGNOSIS**

**Pronecrotic mixed lineage kinase domain-like protein expression is a prognostic biomarker**


- **Journal:** Cancer
- **Institution(s):** Emory University, Atlanta, GA
- **Corresponding author(s):** David Sung-wen Yu
- **PanCAN-affiliated author:** David Sung-wen Yu, MD, PhD: 2012 Career Development Award
- **Major finding:** Low expression of mixed lineage kinase domain-like protein (MLKL) is associated with decreased overall survival (OS) in patients with resected pancreatic adenocarcinoma (PAC) and decreased recurrence-free survival and OS in the subset of patients with resected PAC who receive adjuvant chemotherapy. The use of this biomarker in patients with PAC may provide important prognostic information.

**MicroRNA array finds elevated serum miR-1290 distinguishes low-stage pancreatic cancer**


- **Journal:** Clinical Cancer Research
- **Institution(s):** The Johns Hopkins Medical Institutions, Baltimore, MD
- **Corresponding author(s):** Michael Goggins
- **PanCAN-affiliated authors:**
  - Mimi Canto, MD: 2013 Skip Viragh – Inaugural Research Acceleration Network Grant (co-PI) and Medical Advisory Board
  - Ralph Hruban, MD: Emeritus Scientific Advisory Board
  - Michael Goggins, MD: 2013 Skip Viragh – Inaugural Research Acceleration Network Grant (PI)
- **Major finding:** The detection of elevated circulating miR-1290 has the potential to improve the early detection of pancreatic cancer.

**Should we do EUS/FNA on pancreatic cysts? The incremental diagnostic yield of EUS over CT/MRI**


- **Journal:** Pancreas
- **Institution(s):** The Johns Hopkins Medical Institutions, Baltimore, MD
- **Corresponding author(s):** Marcia Canto
- **PanCAN-affiliated authors:**
  - Ralph Hruban, MD: Emeritus Scientific Advisory Board
  - Mimi Canto, MD: 2013 Skip Viragh – Inaugural Research Acceleration Network Grant (co-PI) and Medical Advisory Board
- **Major finding:** The incremental increase in diagnostic yield of endoscopic ultrasound (EUS) and fluid analysis over computed tomography (CT) and magnetic resonance imaging (MRI) for prediction of a neoplastic cyst is 36% and 54%, respectively. The addition of EUS-FNA (EUS with fine needle aspiration) to abdominal imaging significantly increases overall accuracy for diagnosis of neoplastic pancreatic cysts.
Unnecessary tests and procedures in patients presenting with solid tumors of the pancreas
- **Journal:** *Journal of Gastrointestinal Surgery*
- **Institution(s):** Johns Hopkins Hospital, Baltimore, MD
- **Corresponding author(s):** Michol Cooper
- **PanCAN-affiliated author:** Joe Herman, MD: 2008 Blum-Kovler – Career Development Award and Medical Advisory Board
- **Major finding:** Wide variation exists for evaluation of newly discovered resectable solid pancreas masses, which is associated with delays to surgical intervention and added costs.

The association between chemoradiation-related lymphopenia and clinical outcomes in LAPC
- **Journal:** *American Journal of Clinical Oncology*
- **Institution(s):** Johns Hopkins University School of Medicine, Baltimore, MD
- **Corresponding author(s):** Joseph Herman
- **PanCAN-affiliated author:** Joe Herman, MD: 2008 Blum-Kovler – Career Development Award and Medical Advisory Board
- **Major finding:** Severe treatment-related lymphopenia occurs frequently after chemoradiation for locally advanced pancreatic cancer (LAPC) and is an independent predictor of inferior survival.

Autoantibodies to MUC1 glycopeptides cannot be used as a screening assay for early detection
- **Journal:** *British Journal of Cancer*
- **Institution(s):** King’s College London, London, UK and others
- **Corresponding author(s):** Joy Burchell
- **PanCAN-affiliated author:** Tony Hollingsworth, PhD: Scientific Advisory Board
- **Major finding:** This robust, validated study shows autoantibodies to MUC1 peptide or glycopeptides cannot be used for breast, ovarian, lung or pancreatic cancer screening. This has significant implications for research on the use of MUC1 in cancer detection.

Comparison of WHO classifications, Hochwald grading system, and AJCC and ENETS staging systems
- **Journal:** *The American Journal of Surgical Pathology*
- **Institution(s):** Washington University School of Medicine, St Louis, MO and others
- **Corresponding author(s):** Dengfeng Cao
- **PanCAN-affiliated author:** William Hawkins, MD: 2005 Skip Viragh – Career Development Award
- **Major finding:** The authors aimed to examine commonly used stratification systems [World Health organization (WHO) 2004 and 2010 classifications, American Joint Committee on Cancer (AJCC) and European Neuroendocrine Tumor Society (ENETS) staging, and the Hochwald grading system] for their power in predicting recurrence-free survival (RFS) in patients with locoregional well-differentiated pancreatic neuroendocrine tumors (PanNET). The authors found that Hochwald grading system achieves the highest predictive ability, and further predictive power can be achieved by combining the Hochwald grading system and Ki-67 proliferation index.
Identification and characterization of poorly differentiated invasive carcinomas in a mouse model
• Journal: *PLoS One*
• Institution(s): Memorial Sloan-Kettering Cancer Center, New York, NY and others
• Corresponding author(s): Johanna Joyce
• PanCAN-affiliated author: Doug Hanahan, PhD: 2007 Pilot Grant
• Major finding: The identification of poorly differentiated invasive carcinomas in this mouse model provides a unique opportunity to study the pathology and molecular characteristics of poorly differentiated pancreatic neuroendocrine tumors.

A single institution’s 26-year experience with nonfunctional pancreatic neuroendocrine tumors
• Journal: *Annals of Surgery*
• Institution(s): Johns Hopkins University School of Medicine, Baltimore, MD and others
• Corresponding author(s): Barish Edil
• PanCAN-affiliated author: Ralph Hruban, MD: Emeritus Scientific Advisory Board
• Major finding: Both the 2010 American Joint Committee on Cancer (AJCC) and 2006 European Neuroendocrine Tumor Society (ENETS) tumor staging systems for pancreatic neuroendocrine tumors are valid and indistinguishable in their survival prognostication. A new, simpler prognostic tool can be used to predict survival and decrease inter-institutional mistakes and uncertainties regarding these neoplasms.

False-negative rate of EUS-FNA for pancreatic solid and cystic lesions with matched surgical resections
• Journal: *Cancer Cytopathology*
• Institution(s): University of Rochester Medical Center, Rochester, NY
• Corresponding author(s): Zhongren Zhou
• Major finding: The results of the current study confirm that pancreatic endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) diagnosis has a very low false-positive rate but a relatively high false-negative rate using matched surgical resections as the gold standard. The major cause of a false-negative cytology diagnosis is sampling error and the rate of sampling error in cystic lesions is significantly higher than that in solid lesions.

Differentiation of pancreatic cancer and chronic pancreatitis using computer-aided diagnosis of EUS
• Journal: *PLoS One*
• Institution(s): Shanghai Jiao Tong University, Shanghai, China and others
• Corresponding author(s): Zhendong Jin and Zhaoshen Li
• Major finding: Digital image processing and computer-aided endoscopic ultrasound (EUS) image differentiation technologies are highly accurate and non-invasive. This technology provides a kind of new and valuable diagnostic tool for the clinical determination of pancreatic cancer.
Application of contrast-enhanced ultrasound in the diagnosis of solid pancreatic lesions

- **Journal:** European Journal of Radiology
- **Institution(s):** Peking University Cancer Hospital & Institute, Beijing, China
- **Corresponding author(s):** Kun Yan and Xiaopeng Zhang
- **Major finding:** Contrast-enhanced ultrasound (CEUS) has obvious superiority over conventional US in the general diagnostic accuracy of solid pancreatic lesions and in the diagnostic consistency among doctors. The performances of CEUS are similar to that of CECT in the diagnosis of pancreatic carcinoma and focal pancreatitis.

Imaging features to distinguish malignant and benign branch-duct type IPMNs of the pancreas

- **Journal:** Annals of Surgery
- **Institution(s):** University of Ulsan College of Medicine, Seoul, Korea and others
- **Corresponding author(s):** Nikhil Ramaiya
- **Major finding:** The authors systematically determined the imaging findings for distinguishing malignant and benign branch-duct type intraductal papillary mucinous neoplasms (BD-IPMNs), including mixed type, and their diagnostic value through meta-analysis of published studies. They found that presence of mural nodules should be regarded highly suspicious for malignancy warranting a surgical excision whereas cyst size, main pancreatic duct dilatation, or thick septum/wall may better be managed by careful observation and/or further evaluation.

Circulating tumor cells in locally advanced pancreatic adenocarcinoma

- **Journal:** Annals of Oncology
- **Institution(s):** Institut Curie, Paris, France and others
- **Corresponding author(s):** François-Clément Bidard
- **Major finding:** The evaluation of micrometastatic disease using circulating tumor cell detection appears as a promising prognostic tool in locally advanced pancreatic carcinoma patients.

S100A2 is a predictive biomarker of adjuvant therapy benefit in pancreatic adenocarcinoma

- **Journal:** European Journal of Cancer
- **Institution(s):** Medical University Pierre et Marie Curie, Paris, France and others
- **Corresponding author(s):** Jean-Baptiste Bachet
- **Major finding:** S100A2 expression predicts longer disease-free survival and overall survival in patients with resected pancreatic adenocarcinoma treated with adjuvant therapy and should be evaluated as a predictive biomarker.

Mass profiling serum to distinguish mice with pancreatic cancer induced by transgenic kras mutation

- **Journal:** International Journal of Cancer
- **Institution(s):** University of Oklahoma Health Sciences Center, Oklahoma City, OK
• **Corresponding author(s):** Jay Hanas

• **Major finding:** These studies indicate electrospray ionization mass spectrometry (ESI-MS) serum mass profiling can detect physiological changes associated with pancreatic cancer initiation and development in a GEM (genetic engineered mouse) model that mimics pancreatic cancer development in humans. Such technology has the potential to aid in early detection of pancreatic cancer, and in developing therapeutic drug interventions.

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**Epigenetic regulation and role of metastasis suppressor genes in pancreatic ductal adenocarcinoma**


• **Journal:** BMC Cancer

• **Institution(s):** University Hospital of Muenster, Muenster, Germany

• **Corresponding author(s):** Joerg Haier

• **Major finding:** Genes with metastasis suppressing functions in other tumor entities did not show evidence of assuming the same role in pancreatic ductal adenocarcinoma (PDAC). Inactivation of metastasis suppressor genes (MSG) by promoter methylation was an infrequent event and unsuitable as a diagnostic marker of PDAC. A distinct methylation pattern was identified, that resulted in reduced mRNA expression in all cases. Thus, constant methylation patterns could predict regulatory significance of a promoter's methylation prior to expression analysis and hence present an additional tool during target gene selection.

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**Molecular marker from pancreatic 'juices' helps identify pancreatic cancer**


Researchers at Mayo Clinic have developed a promising method to distinguish between pancreatic cancer and chronic pancreatitis — two disorders that are difficult to tell apart. A molecular marker obtained from pancreatic "juices," CD1D, can identify almost all cases of pancreatic cancer, their study shows. The findings were being presented at Digestive Disease Week 2013 in Orlando, Fla.
TREATMENT
A multi-institutional phase 2 study of neoadjuvant gemcitabine and oxaliplatin with radiation therapy

- **Journal:** Cancer
- **Institution(s):** University of Michigan, Ann Arbor, MI and others
- **Corresponding author(s):** Mark Zalupski
- **PanCAN-affiliated authors:**
  - Joe Herman, MD: 2008 Blum-Kovler – Career Development Award and Medical Advisory Board
  - Diane Simeone, MD: 2010 The Randy Pausch Family – Innovative Grant and Scientific Advisory Board
- **Major finding:** Preoperative therapy with full-dose gemcitabine, oxaliplatin, and radiation therapy was feasible and resulted in a high percentage of R0 resections. The current results are particularly encouraging, because the majority of patients had borderline resectable disease.

Targeting the alternative NF-κB pathway in pancreatic cancer: a new direction for therapy?

- **Journal:** Expert Review of Anticancer Therapy
- **Institution(s):** Mayo Clinic, Jacksonville, FL
- **Corresponding author(s):** Peter Storz
- **PanCAN-affiliated author:** Peter Storz, PhD: 2008 Patty Boshell – Career Development Award
- **Major finding:** Recent demonstration of the importance of constitutive signaling of NF-κB-inducing kinase (NIK, also named MAP3K14) in maintaining the high basal activity of the alternative NF-κB pathway in pancreatic cancer suggests novel possibilities for therapeutic intervention. Strategies to target the alternative NF-κB pathway include not only the use of small molecule inhibitors for NIK and IkB kinase α (IKKα), but also broad spectrum approaches such as using proteasome inhibitors or combinatorial approaches targeting both alternative and canonical pathways.

Phase I study of U3-1287, a fully human anti-HER3 monoclonal antibody, in advanced solid tumors

- **Journal:** Clinical Cancer Research
- **Institution(s):** Cancer Institute, Wayne State University, Detroit, MI and others
- **Corresponding author(s):** Patricia LoRusso
- **PanCAN-affiliated author:** Jordan Berlin, MD: Chair, Medical Advisory Board
- **Major finding:** U3-1287 treatment was well tolerated, and some evidence of disease stabilization was observed. Pharmacokinetic data support U3-1287 dosing of 9 to 20 mg/kg every 2 to 3 weeks. Combination studies of U3-1287 are ongoing.

Understanding pancreatic cancer genomes

- **Journal:** Journal of Hepato-Biliary-Pancreatic Sciences
- **Institution(s):** The Kinghorn Cancer Centre, Darlinghurst, Australia and others
• **Corresponding author(s):** Andrew Biankin
• **Major finding:** The authors aim to develop stratified, molecular phenotype-guided therapeutic strategies using existing therapeutics that are either rescued, repurposed, in development, or are known to be effective in an undefined subgroup of pancreatic cancer patients. The authors are launching a clinical trial called IMPaCT (Individualized Molecular Pancreatic Cancer Therapy). This umbrella design trial randomizes patients with metastatic disease to either standard first-line therapy with gemcitabine, or a molecular phenotype-guided approach using next-generation sequencing strategies to screen for actionable mutations defined through the International Cancer Genome Consortium (ICGC) effort.

**From trial highlights to clinical context: putting ASCO gastrointestinal news into practice**


• **Journal:** *Future Oncology*
• **Institution(s):** University & General Hospital, Udine, Italy and others
• **Corresponding author(s):** Giuseppe Aprile
• **Major finding:** Celebrating its tenth anniversary, the Gastrointestinal Cancers Symposium is a world class, international conference focused on research and multidisciplinary management of digestive tract malignancies, co-sponsored by the American Society of Clinical Oncology, the American Society for Radiation Oncology, the American Gastroenterological Association Institute and the Society of Surgical Oncology. This short article offers a summarized opinion-based overview of the most significant studies presented at the meeting that are likely to impact on clinical practice as well as new drug development.

**EORTC intergroup trial opens for patients with resected head of pancreas adenocarcinoma**


EORTC trial 40084-22084 has two primary objectives: to determine if adding erlotinib to gemcitabine adjuvant chemotherapy will improve survival as compared to gemcitabine alone following resection of head of pancreas adenocarcinoma, then, following adjuvant chemotherapy, determine if concurrent fluoropyrimidine and radiotherapy improves survival for patients who have no evidence of progressive disease.

**A multicenter phase II trial of gemcitabine and candesartan combination therapy: GECA2**


• **Journal:** *Investigational New Drugs*
• **Institution(s):** The University of Tokyo, Tokyo, Japan and others
• **Corresponding author(s):** Hiroyuki Isayama
• **Major finding:** In this multicenter phase 2 trial, gemcitabine and candesartan (an angiotensin receptor blocker) combination therapy was tolerable but failed to demonstrate activity against advanced pancreatic cancer.
FOLFIRINOX in locally advanced pancreatic cancer: Massachusetts General Hospital Cancer Center
- **Journal**: The Oncologist
- **Institution(s)**: Massachusetts General Hospital, Boston, MA and others
- **Corresponding author(s)**: Jason Faris
- **Major finding**: The objective of this retrospective institutional experience is to report the overall response rate, R0 resection rate, progression-free survival, and safety/toxicity of neoadjuvant FOLFIRINOX (5-fluorouracil [5-FU], oxaliplatin, irinotecan, and leucovorin) and chemoradiation in patients with locally advanced pancreatic cancer (LAPC). The recurrences following R0 resections and the toxicities observed with the use of this regimen raise important questions about how to best treat patients with LAPC.

The addition of erlotinib to gemcitabine and cisplatin does not appear to improve median survival
- **Journal**: Investigational New Drugs
- **Institution(s)**: M.D. Anderson Cancer Center, Houston, TX
- **Corresponding author(s)**: David Fogelman
- **Major finding**: The authors retrospectively compared outcomes of patients treated with either the three drug regimen of gemcitabine, cisplatin, and erlotinib or the doublet of gemcitabine and cisplatin in order to assess the potential benefit of erlotinib. Though there was a trend towards improved survival with the addition of erlotinib to gemcitabine and cisplatin, this does not reach statistical significance.

Role of adjuvant surgery for patients with initially unresectable pancreatic cancer
- **Journal**: Journal of Hepato-Biliary-Pancreatic Sciences
- **Institution(s)**: Kansai Medical University, Moriguchi, Japan and others
- **Corresponding author(s)**: Hiroki Yamaue
- **Major finding**: Adjuvant surgery for initially unresectable pancreatic cancer patients can be a safe and effective treatment. The overall survival rate from the initial treatment is extremely high, especially in patients who received non-surgical anti-cancer treatment for more than 240 days.

Nanoparticle albumin bound Paclitaxel: nanodelivery reaches prime-time?
- **Journal**: Journal of Drug Delivery
- **Institution(s)**: University "Magna Graecia" of Catanzaro and "Tommaso Campanella" Cancer Center, Catanzaro, Italy and others
- **Corresponding author(s)**: Pierosandro Tagliaferri
- **Major finding**: Nab-paclitaxel has produced a paradigm change in the treatment of tumors like breast cancer, pancreatic cancer, and melanoma and a large use in these important diseases can be predicted. The authors think that nab-paclitaxel has opened a new way to human cancer treatment and indeed reached the prime-time.
Stromal expression of SPARC in pancreatic adenocarcinoma
- **Journal**: Cancer and Metastasis Reviews
- **Institution(s)**: Beaujon University Hospital, Clichy-La-Garenne, France and others
- **Corresponding author(s)**: Eric Raymond
- **Major finding**: In this review, the authors focused on key preclinical and clinical data describing the role of secreted protein acid and rich in cysteine (SPARC) in pancreatic ductal adenocarcinoma biology, the properties, and mechanisms of delivery of drugs that interact with SPARC and discuss the proof-of-concept clinical trials using nab-paclitaxel.

Second-line treatment in advanced pancreatic cancer: a comprehensive analysis of published trials
- **Journal**: Annals of Oncology
- **Institution(s)**: National Cancer Institute, Bethesda and Rockville, MD
- **Corresponding author(s)**: Tim Greten
- **Major finding**: Although not conclusive, the authors’ data showed that the advantage of second-line chemotherapy in pancreatic cancer is very limited and there is a need for more studies.

Treatment outcome of advanced pancreatic cancer patients who are ineligible for a clinical trial
- **Journal**: Onco Targets and Therapy
- **Institution(s)**: University of Toyama, Toyama, Japan
- **Corresponding author(s)**: Ayumu Hosokawa
- **Major finding**: The outcome of the patients who did not meet the eligibility criteria for a clinical trial was very poor. It is important to select the patients that could benefit from either chemotherapy or optimal supportive care.

Therapeutic perspectives on pancreatic cancer
- **Journal**: Current Cancer Drug Targets
- **Institution(s)**: University of New South Wales, Sydney, Australia
- **Corresponding author(s)**: Levon Khachigian
- **Major finding**: This article reviews current concepts in the pathogenesis and treatment of pancreatic cancer, the latter including tumor resection approaches and the current standard of care. The authors further describe recent advances in new and combination therapies, which result only in modest increases in survival, and discuss challenges in drug delivery and limiting toxicity.

Novel curcumin loaded magnetic nanoparticles for pancreatic cancer treatment
- **Journal**: Molecular Cancer Therapeutics
- **Institution(s)**: Sanford Research/University of South Dakota, Sioux Falls, SD
- **Corresponding author(s)**: Subhash Chauhan
Major finding: The authors developed a novel curcumin loaded magnetic nanoparticle (MNP-CUR) formulation. This study suggests that their novel MNP-CUR formulation can be valuable for the treatment of pancreatic cancer.

BIBF 1120 (nintedanib), triple angiokinase inhibitor, induces hypoxia but not EMT, blocks progression
- Journal: Molecular Cancer Therapeutics
- Institution(s): University of Texas Southwestern Medical Center, Dallas, TX
- Corresponding author(s): Rolf Brekken
- Major finding: The authors evaluated the antitumor and biologic effects of BIBF 1120 (nintedanib), a tyrosine kinase inhibitor that targets VEGF receptor, platelet-derived growth factor receptor, and fibroblast growth factor receptor in preclinical models of lung and pancreatic cancer, including models resistant to VEGF-targeted treatments. BIBF 1120 showed potent antitumor and antiangiogenic activity in preclinical models of lung and pancreatic cancer where it induced hypoxia but not epithelial-to-mesenchymal transition (EMT). The absence of EMT induction, which has been implicated in resistance to antiangiogenic therapies, is noteworthy.

Pancreateicojejunostomy vs. pancreaticogastrostomy reconstruction after pancreaticoduodenectomy
- Journal: The Lancet Oncology
- Institution(s): University Hospitals KU Leuven, Leuven, Belgium
- Corresponding author(s): Baki Topal
- Major finding: In patients undergoing pancreaticoduodenectomy for pancreatic head or periampullary tumours, pancreaticogastrostomy is more efficient than pancreateicojejunostomy in reducing the incidence of postoperative pancreatic fistula.

Pancreatic surgery with vascular reconstruction in locally advanced pancreatic neuroendocrine tumors
- Journal: Journal of Gastrointestinal Surgery
- Institution(s): Oslo University Hospital, Oslo, Norway
- Corresponding author(s): Sven-Petter Haugvik
- Major finding: Pancreatic surgery with vascular reconstruction in patients with locally advanced pancreatic neuroendocrine tumors (PNET) is feasible with acceptable outcome.

OncoGenex announces plans for Rainier™ clinical trial evaluating OGX-427, ABRAXANE®, gemcitabine
http://ir.oncogenex.com/releasedetail.cfm?ReleaseID=760802
- Company: OncoGenex Pharmaceuticals, Inc., Bothell, WA and Vancouver, British Columbia
- PanCAN-affiliation: Trial sponsor Andrew Ko, MD: 2003 Career Development Award
- Major finding: OncoGenex Pharmaceuticals, Inc. announced plans for the initiation of the Rainier™ trial, an investigator-sponsored, randomized, placebo-controlled Phase 2 trial evaluating OGX-427 (inhibits production of heat shock protein [Hsp27]) in combination with
ABRAXANE® (paclitaxel protein-bound particles for injectable suspension)(albumin-bound) and gemcitabine in patients with previously untreated metastatic pancreatic cancer.

**Celgene announces U.S. FDA grants Priority Review for ABRAXANE® sNDA in pancreatic cancer**


- **Company**: Celgene International Sàrl, Boudry, Switzerland
- **Major finding**: Celgene International Sàrl, a subsidiary of Celgene Corporation announced that the U.S. Food and Drug Administration (FDA) has assigned a Priority Review designation to the supplemental New Drug Application (sNDA) for the use of ABRAXANE® (paclitaxel protein-bound particles for injectable suspension) (albumin-bound) in combination with gemcitabine for the first–line treatment of patients with advanced pancreatic cancer.
CANCER CONTROL, SURVIVORSHIP, AND OUTCOMES RESEARCH

Celiac plexus block for treatment of pain associated with pancreatic cancer: A meta-analysis

- **Journal**: *Pain Practice*
- **Institution(s)**: Sun Yat-Sen University, Guangzhou, Guangdong, China
- **Corresponding author(s)**: Qi-Kui Chen
- **Major finding**: This meta-analysis identified and compared seven randomized control trials of pain relief from pancreatic cancer, by treatment with medical management alone to celiac plexus blockade (CPB) with medical management. The combined CPB groups had a significantly lower pain score at 4 weeks, but significance was not maintained at 8 weeks. The combined CPB groups required significantly less drug use compared to the combined control groups treated with pharmaceutical analgesics.

‘One also needs a bit of trust in the doctor ... ’ : a qualitative interview with pancreatic cancer patients

- **Journal**: *Annals of Oncology*
- **Institution(s)**: Ruhr-University Bochum, Bochum, Germany and others
- **Corresponding author(s)**: Jan Schildmann
- **Major finding**: The authors’ findings can serve as starting point for reflection on professional decision-making in pancreatic cancer and larger representative surveys on ethical issues in treatment decision-making in pancreatic cancer.