



**Research**

**PANCREATIC CANCER ACTION NETWORK**

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## PANCREATIC CANCER NEWS & UPDATES – JANUARY 2013

### PANCREATIC CANCER ACTION NETWORK AND COMMUNITY NEWS

We praise President Obama for signing the *Recalcitrant Cancer Research Act* into law

[http://www.pancan.org/section\\_about/news\\_press\\_center/2013\\_press\\_releases/01\\_03\\_13\\_pr.php](http://www.pancan.org/section_about/news_press_center/2013_press_releases/01_03_13_pr.php)

President Barack Obama made history in the fight against pancreatic cancer by signing the *Recalcitrant Cancer Research Act* into law. The legislation, formerly known as the *Pancreatic Cancer Research and Education Act*, passed the U.S. Congress on December 21 after it was attached to the *National Defense Authorization Act*.

**Increased clinical trial participation needed to improve survival of pancreatic cancer**

[http://pancan.org/section\\_about/news\\_press\\_center/2013\\_press\\_releases/01\\_08\\_13\\_pr.php](http://pancan.org/section_about/news_press_center/2013_press_releases/01_08_13_pr.php)

January was National Pancreatic Cancer Clinical Trials Awareness Month and as part of this initiative, the Pancreatic Cancer Action Network called attention to the need for increased clinical trial participation to help improve patient outcomes for pancreatic cancer.

**Two-time research grant recipient helps define earliest stages of pancreatic cancer development**

[http://pancan.org/section\\_research/strategic\\_research\\_program/news/topic\\_hebrok\\_define\\_early\\_pancreatic\\_cancer\\_development.php](http://pancan.org/section_research/strategic_research_program/news/topic_hebrok_define_early_pancreatic_cancer_development.php)

*Write-up describing:* <http://www.ncbi.nlm.nih.gov/pubmed/23201164>

Since this story was continuing to pick up media attention, we prepared the above summary for the website, highlighting the involvement of Matthias Hebrok, PhD, in this study.

**Society-funded researchers take aim at pancreatic cancer**

<http://www.cancer.org/cancer/news/society-funded-researchers-take-aim-at-pancreatic-cancer>

Scientists funded by the American Cancer Society are finding ways to put a chink in pancreatic cancer's armor. Researchers are exploiting weak spots in hopes of destroying the cancer and possibly preventing it altogether. Pancreatic Cancer Action Network grant recipients William Hawkins, MD (2005 Skip Viragh – Career Development Award) and Jonathan Brody, PhD (2010 Skip Viragh – Career Development Award) are among the ACS-funded researchers featured in this article.

**Trying to raise the profile of pancreatic cancer, deadly yet lagging in research funding**

[http://articles.philly.com/2013-01-29/news/36598414\\_1\\_pancreatic-cancer-survival-rates-cancer-deaths#.UQsav7MeJp0.email](http://articles.philly.com/2013-01-29/news/36598414_1_pancreatic-cancer-survival-rates-cancer-deaths#.UQsav7MeJp0.email)

Dr. Charles Yeo, chief of surgery at Thomas Jefferson University School of Medicine, was interviewed for this article about pancreatic cancer awareness.

### **MSKCC establishes new pancreatic cancer research center**

<http://www.news-medical.net/news/20121210/MSKCC-establishes-new-pancreatic-cancer-research-center.aspx>

A new pancreatic cancer research center has been created at Memorial Sloan-Kettering Cancer Center. The ambitious initiative was established with an initial commitment of \$10 million from MSKCC Board member David M. Rubenstein. The new program, called the David M. Rubenstein Center for Pancreatic Cancer Research, will bring together Memorial Sloan-Kettering's outstanding physicians and an expanding group of scientists in an intensive program designed to spearhead crucial progress in understanding and treating one of the deadliest forms of cancer.

### **Incremental successes lead to improved patient care**

<http://gicasym.asco.org/incremental-successes-lead-improved-patient-care>

Scientific Advisory Board member Margaret Tempero, PhD reflects on progress achieved in treating GI cancers in honor of the 10-year anniversary of the Gastrointestinal Cancers Symposium.

### **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**

<http://provocativequestions.nci.nih.gov/rfa>

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**

<http://jobs.virginiamason.org/job/Seattle-Pancreas-Cancer-Research-Fellowship-Job-WA-98101/1913701/>

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>.

### **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."

## **BIOLOGY OF CANCER**

### **Pancreatic Cancer: Methods and Protocols**

<http://www.springerprotocols.com/BookToc/doi/10.1007/978-1-62703-287-2>

Edited by Gloria Su, PhD (2007 Pilot Grant and 2010 Innovative Grant), this book covers a variety of topics and includes contributions written by many Pancreatic Cancer Action Network grant recipients and Scientific and Medical Advisory Board members.

### **Downregulation of TRAF2 mediates NIK-induced pancreatic cancer cell proliferation, tumorigenicity**

<http://www.ncbi.nlm.nih.gov/pubmed/23301098>

- Journal: *PLoS One*
- 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: The authors' data indicate that the TRAF2/NIK/NF- $\kappa$ B2 pathway regulates pancreatic ductal adenocarcinoma cell tumorigenicity and could be a valuable target for therapy of this cancer.

### **Deciphering the mechanisms of tumorigenesis in human pancreatic ductal epithelial cells**

<http://www.ncbi.nlm.nih.gov/pubmed/23340292>

- Journal: *Clinical Cancer Research*
- Institution(s): The University of Texas MD Anderson Cancer Center, Houston, TX and others
- Corresponding author(s): Paul Chiao
- PanCAN affiliated authors:
  - Huamin Wang, MD, PhD: 2007 Skip Viragh – Career Development Award
  - Jason Fleming, MD: Medical Advisory Board
  - Paul Chiao, PhD: 2012 Innovative Grant
- Major finding: The combination of activated K-ras and Her2 with inactivated p16/p14 and Smad4 was sufficient and essential to transform human pancreatic ductal epithelial cells, thus revealing the potential tumorigenic mechanism.

### **The use of novel MUC1 antibody to identify cancer stem cells & circulating MUC1 in mice & patients**

<http://www.ncbi.nlm.nih.gov/pubmed/23335066>

- Journal: *Journal of Surgical Oncology*
- Institution(s): University of North Carolina, Charlotte, NC
- Corresponding author(s): Pinku Mukherjee
- PanCAN affiliated author: Pinku Mukherjee, PhD: 2007 Pilot Grant

- Major finding: The anti-MUC1 (TAB 004) antibody may be explored as a therapeutic targeting agent for cancer stem cells in pancreatic cancer. The TAB 004 enzyme immunoassay detected circulating MUC1 in a stage-dependent manner in patients with PC and thus may be explored as a PC stage diagnostic biomarker.

#### **KDM2B promotes pancreatic cancer via Polycomb-dependent, -independent transcriptional programs**

<http://www.ncbi.nlm.nih.gov/pubmed/23321669>

- Journal: *The Journal of Clinical Investigation*
- Institution(s): Massachusetts General Hospital Cancer Center, Boston, MA and others
- Corresponding author(s): Alexandros Tzatsos or Nabeel Bardeesy
- PanCAN affiliated author: Nabeel Bardeesy, PhD: 2008 Randy Pausch, PhD – Pilot Grant
- Major finding: The authors found that KDM2B (also known as Ndy1, FBXL10, and JHDM1B), an H3K36 histone demethylase implicated in bypass of cellular senescence and somatic cell reprogramming, is markedly overexpressed in human pancreatic cancer, with levels increasing with disease grade and stage, and highest expression in metastases. The results of this study defined epigenetic programs through which KDM2B subverts cellular differentiation and drives the pathogenesis of an aggressive subset of PDAC.

#### **Hypomethylating therapy in an aggressive stroma-rich model of pancreatic carcinoma**

<http://www.ncbi.nlm.nih.gov/pubmed/23204224>

- Journal: *Cancer Research*
- Institution(s): Columbia University Medical Center, New York, NY
- Corresponding author(s): Benjamin Tycko
- PanCAN affiliated author: Ken Olive, PhD: 2011 Tempur-Pedic Retailers – Career Development Award
- Major finding: These data show that the DNA demethylating drug 5-aza-2'-deoxycytidine (DAC) is effective against an aggressive mouse model of stromal rich pancreatic ductal adenocarcinoma, and provide a rationale for future studies combining hypomethylating agents with cytokines and immunotherapy.

#### **Hemoglobin-based oxygen carrier mitigates transfusion-mediated pancreas cancer progression**

<http://www.ncbi.nlm.nih.gov/pubmed/23328973>

- Journal: *Annals of Surgical Oncology*
- Institution(s): University of Colorado, Denver, CO and others
- Corresponding author(s): Carlton Barnett, Jr.
- PanCAN affiliated author: David Boothman, PhD: 2012 George & June Block Family Foundation – Innovative Grant
- Major finding: Intravenous receipt of the acellular plasma fraction of stored packed red blood cells promotes pancreatic cancer progression in an immunocompetent mouse model. These untoward events are mitigated by use of an hemoglobin-based oxygen carrier.

#### **Efficacy of dimethylaminoparthenolide and sulindac in combination with gemcitabine**

<http://www.ncbi.nlm.nih.gov/pubmed/22699205>

- Journal: *Pancreas*

- Institution(s): Indiana University School of Medicine, Indianapolis, IN and others
- Corresponding author(s): C. Max Schmidt
- PanCAN affiliated authors:
  - Ralph Hruban, MD: Emeritus Scientific Advisory Board
  - Max Schmidt, MD, PhD: 2003 Career Development Award
- Major finding: Intervention with dimethylaminoparthenolide (DMAPT) and sulindac in combination with gemcitabine may delay or prevent progression of premalignant pancreatic lesions in the LSL-Kras(G12D);Pdx-1-Cre mouse model of pancreatic cancer.

### **Mechanistic insights into self-reinforcing processes driving abnormal histogenesis**

<http://www.ncbi.nlm.nih.gov/pubmed/23375449>

- Journal: *American Journal of Pathology*
- Institution(s): Aix-Marseille University, Marseille, France and others
- Corresponding author(s): Raul Urrutia
- PanCAN affiliated author: Martin Fernandez-Zapico, MD: 2007 Carole & Bob Daly – Career Development Award
- Major finding: Mechanistic studies of genetic, epigenetic, and cell-to-cell signaling events are providing clues to molecular pathways that can be targeted in an attempt to cure pancreatic cancer. The current review article seeks to draw inferences from available mechanistic knowledge to build a theoretical framework that can facilitate these approaches.

### **Phosphorylation of ribosomal protein S6 attenuates DNA damage and tumor suppression**

<http://www.ncbi.nlm.nih.gov/pubmed/23361300>

- Journal: *Cancer Research*
- Institution(s): Hebrew University Medical School, Jerusalem, Israel and others
- Corresponding author(s): Yuval Dor
- PanCAN affiliated author: Anirban Maitra, MBBS: Chair, Scientific Advisory Board
- Major finding: These results reveal that ribosomal protein S6 phosphorylation is important for the initiation of pancreatic cancer.

### **Hyaluronan, fluid pressure, and stromal resistance in pancreas cancer**

<http://www.ncbi.nlm.nih.gov/pubmed/23299539>

- Journal: *British Journal of Cancer*
- Institution(s): Fred Hutchinson Cancer Research Center, Seattle, WA
- Corresponding author(s): Sunil Hingorani
- PanCAN affiliated author: Sunil Hingorani, MD, PhD: 2005 Dr. Laurence A. Mack and Roselle Mack – Career Development Award and 2007 Pilot Grant
- Major finding: In this review, the authors focus on altered physicomechanics as one mechanism of what they term as “stromal resistance” in pancreatic ductal adenocarcinoma. Extremely high interstitial fluid pressures and a dense extracellular matrix combine to limit the delivery and distribution of therapeutic agents. They discuss the genesis and consequences of altered fluid dynamics in PDA and strategies to restore them.

**Prrx1 homeodomain transcription factor plays central role in pancreatic regeneration, carcinogenesis**

<http://www.ncbi.nlm.nih.gov/pubmed/23355395>

- Journal: *Genes & Development*
- Institution(s): University of Pennsylvania, Philadelphia, PA and others
- Corresponding author(s): Anil Rustgi
- PanCAN affiliated authors:
  - Ben Stanger, MD, PhD: 2007 Ralph H. Hruban, MD – Career Development Award
  - Anil Rustgi, MD: Scientific Advisory Board
- Major finding: The authors' findings suggest a new hierarchical scheme whereby a Prrx1-Sox9 axis may influence the emergence of acinar-ductal metaplasia and regeneration. Furthermore, their data provide a possible explanation of why pancreatic cancer is skewed toward a ductal fate.

**Imbalance of desmoplastic stromal cell numbers drives aggressive cancer processes**

<http://www.ncbi.nlm.nih.gov/pubmed/23359139>

- Journal: *Journal of Pathology*
- Institution(s): Queen Mary University of London, London, UK and others
- Corresponding author(s): Hemant Kocher
- PanCAN affiliated author: Anil Rustgi, MD: Scientific Advisory Board
- Major finding: These studies demonstrate that context-specific cancer-stroma cross-talk 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.

**MDM2, MDMX and p53 in oncogenesis and cancer therapy**

<http://www.ncbi.nlm.nih.gov/pubmed/23303139>

- Journal: *Nature Reviews Cancer*
- Institution(s): Fondazione Istituto Italiano di Tecnologia, Milan, Italy and others
- Corresponding author(s): Geoffrey Wahl
- PanCAN affiliated author: Geoff Wahl, PhD: Scientific Advisory Board
- Major finding: This review highlights the progress made and pitfalls encountered as the field continues to search for MDM-targeted antitumour agents.

**Methylation-mediated silencing of the miR-124 genes facilitates progression and metastasis**

<http://www.ncbi.nlm.nih.gov/pubmed/23334332>

- Journal: *Oncogene*
- Institution(s): Fudan University Shanghai Cancer Center, Shanghai, China
- Corresponding author(s): L. Liu
- Major finding: This study demonstrates that miR-124 is a tumor suppressor miRNA that is epigenetically silenced in pancreatic cancer. The authors' findings suggest a previously unidentified molecular mechanism involved in the progression and metastasis of pancreatic cancer.

**Targeted degradation of KRAS by engineered ubiquitin ligase suppresses pancreatic cancer cell growth**

<http://www.ncbi.nlm.nih.gov/pubmed/23288781>

- Journal: *Molecular Cancer Therapeutics*
- Institution(s): Peking Union Medical College Hospital, Beijing, China
- Corresponding author(s): Jie Chen
- Major finding: In this study, an engineered E3 ubiquitin ligase (RC-U) was generated to target the KRAS oncprotein for ubiquitination and degradation. RC-U inhibited pancreatic cancer cell growth in vitro and in vivo.

**Tspan8, CD44v6 and alpha6beta4 are biomarkers of migrating pancreatic cancer initiating cells**

<http://www.ncbi.nlm.nih.gov/pubmed/23338841>

- Journal: *International Journal of Oncology*
- Institution(s): University Hospital of Surgery, Heidelberg, Germany
- Corresponding author(s): Margot Zöller
- Major finding: This is the first report showing that CD44v6, alpha6beta4, Tspan8 and CXCR4 are biomarkers in pancreatic cancer initiating cells (PaCIC) allowing for long-term survival, expansion and migration in immunocompromised mice. The stability of the percentage of PaCIC in long-term and freshly-established lines after a roughly 8-fold enrichment by cloning indicates PaCIC, though required for long-term survival, concomitantly depending on support by non-CIC.

**ABCB2 (TAP1) as the downstream target of SHH signaling enhances pancreatic cancer drug resistance**

<http://www.ncbi.nlm.nih.gov/pubmed/23340176>

- Journal: *Cancer Letters*
- Institution(s): Affiliated Hospital of Jiangsu University, Zhenjiang, Jiangsu, China and others
- Corresponding author(s): Youli Zhang
- Major finding: The authors' study suggests that inhibiting SHH signaling or targeting ABCB2 gene improves the efficacy of chemotherapy in patients with pancreatic ductal adenocarcinoma.

**Tumor-stromal interactions in pancreatic cancer**

<http://www.ncbi.nlm.nih.gov/pubmed/23395563>

- Journal: *Pancreatology*
- Institution(s): University of Southampton School of Medicine, Southampton, UK
- Corresponding author(s): Jo Tod
- Major finding: The tumor microenvironment of pancreatic cancer harbors a wide spectrum of cell types and a complex network of mechanisms which all serve to promote tumor progression. It is now increasingly evident that research targeted towards the interactions between these cell types, ideally at an early stage of tumor development, is imperative in order to propel the way forward to more effective treatments.

**Tumor budding cells, cancer stem cells and epithelial-mesenchymal transition-type cells**

<http://www.ncbi.nlm.nih.gov/pubmed/23316479>

- Journal: *Frontiers in Gastrointestinal Cancers*
- Institution(s): University of Bern, Bern, Switzerland

- Corresponding author(s): Eva Karamitopoulou
- Major finding: The aim of this review is to present a short overview on the morphological and molecular aspects that underline the relationship between tumor budding cells, cancer stem cells, and epithelial-mesenchymal transition-type cells in pancreatic ductal adenocarcinoma.

## ETIOLOGY

### **A prospective study of plasma adiponectin and pancreatic cancer risk in five US cohorts**

<http://www.ncbi.nlm.nih.gov/pubmed/23243202>

- Journal: *Journal of the National Cancer Institute*
- Institution(s): Brigham and Women's Hospital and Harvard Medical School, Boston, MA and others
- Corresponding author(s): Ying Bao
- Major finding: In this pooled analysis, low prediagnostic levels of circulating adiponectin were associated with an elevated risk of pancreatic cancer.

### **Flavonoid intake and risk of pancreatic cancer in the NIH-AARP Diet and Health Study Cohort**

<http://www.ncbi.nlm.nih.gov/pubmed/23299536>

- Journal: *British Journal of Cancer*
- Institution(s): Yale School of Public Health, New Haven, CT and others
- Corresponding author(s): Rachael Stolzenberg-Solomon
- Major finding: The authors examined the association between intake of flavonoids and pancreatic cancer risk in the large, prospective National Institutes of Health-AARP Diet and Health Study Cohort. Their results do not support the hypothesis that flavonoids have a protective role in pancreatic cancer carcinogenesis.

### **Identification of common variants in BRCA2 & MAP2K4 for susceptibility to sporadic pancreatic cancer**

<http://www.ncbi.nlm.nih.gov/pubmed/23299404>

- Journal: *Carcinogenesis*
- Institution(s): Cancer Institute and Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China and others
- Corresponding author(s): Dongxin Lin
- Major finding: The authors' results demonstrate for the first time that common variants in BRCA2 and MAP2K4 are susceptibility to sporadic pancreatic cancer.

### **A genome wide association study of genetic loci that influence tumour biomarkers**

<http://www.ncbi.nlm.nih.gov/pubmed/23300138>

- Journal: *Gut*
- Institution(s): Huazhong University of Science and Technology, Wuhan, Hubei, China and others
- Corresponding author(s): Tangchun Wu
- Major finding: This study identified several loci associated with cancer antigen 19-9, carcinoembryonic antigen, and α fetoprotein (CA19-9, CEA, and AFP) concentrations. The ABO variants were associated with risk of oesophageal squamous cell and pancreatic cancers and AFP variants with risk of hepatocellular cancer.

### **Identifying people at a high risk of developing pancreatic cancer**

<http://www.ncbi.nlm.nih.gov/pubmed/23222481>

- Journal: *Nature Reviews Cancer*
- Institution(s): Johns Hopkins School of Medicine, Baltimore, MD
- Corresponding author(s): Alison Klein
- Major finding: Using data from the Hopkins familial pancreatic cancer registry and other registries, this review discusses the usefulness of family registries in the study of pancreatic and other cancers, and also how such registries provide a unique opportunity for laboratory, population and clinical research.

### **HBV infection increases the risk of pancreatic cancer: a meta-analysis**

<http://www.ncbi.nlm.nih.gov/pubmed/23306552>

- Journal: *Cancer Causes & Control*
- Institution(s): XinQiao Hospital or Biomedical Analysis Center Third Military Medical University, Chongqing, People's Republic of China
- Corresponding author(s): Yao Zhang and Shi-Ming Yang
- Major finding: Findings from this meta-analysis strongly support that hepatitis B virus infection is associated with an increased risk of pancreatic cancer.

### **PREVENTION**

#### **Prolonged survival, delayed progression in LSL-KrasG12D/+;Pdx-1-Cre mice by vitamin E, δ-tocotrienol**

<http://www.ncbi.nlm.nih.gov/pubmed/23302291>

- Journal: *Carcinogenesis*
- Institution(s): H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL and others
- Corresponding author(s): Mokengen Malafa
- PanCAN affiliated authors:
  - Sunil Hingorani, MD, PhD: 2005 Dr. Laurence A. Mack and Roselle Mack – Career Development Award and 2007 Pilot Grant
  - Mo Malafa, MD: Medical Advisory Board
- Major finding: The chemopreventative potential of the bioactive vitamin E derivative δ-tocotrienol is highlighted by its ability to interfere with oncogenic Kras pathways coupled with the observed increase in median survival and significant delay in PanIN progression, and warrants further investigation of this micronutrient in individuals at high risk for pancreatic cancer.

### **Types of fish consumed and fish preparation methods in relation to pancreatic cancer incidence**

<http://www.ncbi.nlm.nih.gov/pubmed/23221729>

- Journal: *American Journal of Epidemiology*
- Institution(s): Indiana University, Bloomington, IN
- Corresponding author(s): Ka He
- Major finding: The potential health impact of fish consumption may depend on the types of fish consumed and fish preparation methods. Long-chain polyunsaturated fatty acids, particularly docosahexaenoic acid, and nonfried fish, but not shellfish or fried fish, may be beneficial in the primary prevention of pancreatic cancer.

## **EARLY DETECTION, DIAGNOSIS, AND PROGNOSIS**

**Changing the way we do business: Recommendations to accelerate biomarker development**

<http://www.ncbi.nlm.nih.gov/pubmed/23344262>

- Journal: *Clinical Cancer Research*
- Institution(s): University of California San Francisco Helen Diller Family Comprehensive Cancer Center, San Francisco, CA and others
- Corresponding author(s): Margaret Tempero
- PanCAN affiliated authors:
  - Margaret Tempero, PhD: Scientific Advisory Board
  - Jordan Berlin, MD: Chair, Medical Advisory Board
  - Tony Hollingsworth, PhD: Scientific Advisory Board
- Major finding: Many large clinical trials in pancreatic cancer in the United States are conducted within the NCI cooperative group system. These groups are strategically positioned to serve as an important infrastructure for the collection of clinically annotated biospecimens. For this reason, the Intergroup Pancreatic Cancer Task Force appointed a Tissue Acquisition Working Group to make strategic recommendations to address this problem.

## **Pancreatic cyst cytology: Optimization of cancer risk profiling**

<http://www.ncbi.nlm.nih.gov/pubmed/23319469>

- Journal: *Cancer Cytopathology*
- Institution(s): Indiana University Health Pancreatic Cyst and Cancer Early Detection Center, Indianapolis, IN
- Corresponding author(s): C. Max Schmidt
- PanCAN affiliated author: Max Schmidt, MD, PhD: 2003 Career Development Award
- Major finding: Until a cure for pancreatic cancer is found, Dr. Schmidt asserts that considerable effort needs to be invested in screening and risk stratification for patients who are at risk of pancreatic cancer. The cornerstone of screening and risk stratification must be a detailed characterization of the cytopathologic atypia at regular screening intervals.

## **Molecular analysis of precursor lesions in familial pancreatic cancer**

<http://www.ncbi.nlm.nih.gov/pubmed/23372777>

- Journal: *PLoS One*
- Institution(s): Queen Mary University of London, London, UK and others
- Corresponding author(s): Tatjana Crnogorac-Jurcevic
- PanCAN affiliated author: Teri Brentnall, MD: Emeritus Scientific Advisory Board
- Major finding: The authors' comprehensive analysis of precursor lesions without the invasive component provides the definitive molecular proof that PanIN lesions beget cancer from a molecular standpoint. We demonstrate the need for accumulation of transcriptomic changes during the progression of PanIN to PDAC, both in the epithelium and in the surrounding stroma. An identified 76-gene signature of PDAC progression presents a rich candidate pool for the development of early diagnostic and/or surveillance markers as well as potential novel preventive/therapeutic targets for both familial and sporadic pancreatic adenocarcinoma.

**The role of cytology in the preoperative assessment and management of pancreaticobiliary neoplasms**

<http://www.ncbi.nlm.nih.gov/pubmed/23297029>

- Journal: *Journal of Gastrointestinal Surgery*
- Institution(s): University of Michigan Health System, Ann Arbor, MI
- Corresponding author(s): Judy Pang
- PanCAN affiliated author: Diane Simeone, MD: 2010 The Randy Pausch Family – Innovative Grant and Scientific Advisory Board
- Major finding: The authors report that cytology adds to the assessment of solid masses, but its utility in cystic lesions is less clear. Consideration of a suspicious cytologic interpretation as a positive diagnosis for triaging patients to surgery is supported by this study.

**MicroRNA expression signatures in intraductal papillary mucinous neoplasm of the pancreas**

<http://www.ncbi.nlm.nih.gov/pubmed/23305591>

- Journal: *Surgery*
- Institution(s): Tel-Aviv Sourasky Medical Center, Tel Aviv, Israel and others
- Corresponding author(s): Nir Lubezky
- Major finding: This study demonstrates that miRNAs are involved in the development and progression of IPMN. The authors identified potential targets for diagnosis, prognostication, and treatment of IPMN.

**The prognostic influence of resection margin clearance following pancreaticoduodenectomy**

<http://www.ncbi.nlm.nih.gov/pubmed/23297028>

- Journal: *Journal of Gastrointestinal Surgery*
- Institution(s): University of Glasgow, Glasgow, UK
- Corresponding author(s): Nigel Jamieson
- Major finding: These data demonstrate that margin clearance by at least 1.5 mm identifies a subgroup of patients which may potentially achieve long-term survival. This study further confirms the need to achieve standardization across pancreatic specimen reporting. Stratification of patients into future clinical trials based upon the degree of margin clearance may identify those patients likely to benefit from adjuvant therapy.

**Complexity of molecular alterations impacts pancreatic cancer prognosis**

<http://www.ncbi.nlm.nih.gov/pubmed/23355925>

- Journal: *World Journal of Gastrointestinal Oncology*
- Institution(s): Technische Universität München, München, Germany
- Corresponding author(s): Jörg Kleeff
- Major finding: A large number of studies have demonstrated the importance of biomarkers not only in predicting prognosis but more importantly in predicting the response towards therapies. However, no biomarkers with a similar clinical impact have been identified in pancreatic ductal adenocarcinoma.

**Molecular markers in pancreatic cancer diagnosis**

<http://www.ncbi.nlm.nih.gov/pubmed/23305796>

- Journal: *Clinica Chimica Acta*

- Institution(s): Universidad del País Vasco, San Sebastián, Spain and others
- Corresponding author(s): Luis Bujanda
- Major finding: The authors review several new potential serum, plasma and stool markers that are currently under evaluation. Although these have not been sufficiently validated for routine clinical use, these markers could prove valuable with further investigations. The authors hope that a combination of some of these novel biomarkers can be a useful tool for early pancreatic ductal adenocarcinoma diagnosis before image techniques and/or patient's symptoms reveal disease in an incurable state.

## **TREATMENT**

*Data presented at the 2013 Gastrointestinal Cancers Symposium:*

**ABRAXANE® plus gemcitabine demonstrates significant survival advantage in Phase III study**

Celgene press release: <http://ir.celgene.com/phoenix.zhtml?c=111960&p=irol-newsArticle&ID=1776848&highlight=>

Pancreatic Cancer Action Network write-up:

[http://pancan.org/section\\_research/strategic\\_research\\_program/news/topic\\_abraxane\\_improves\\_survival.php](http://pancan.org/section_research/strategic_research_program/news/topic_abraxane_improves_survival.php)

- Institution(s): Virginia G. Piper Cancer Center at Scottsdale Healthcare/TGen, Scottsdale, AZ and others
- Lead author: Daniel Von Hoff
- Abstract: <http://gicasym.asco.org/content/106143-133>
- Major finding: In this multinational, multiinstitutional study, nab-paclitaxel plus gemcitabine was well tolerated and superior to gemcitabine with statistically significant and clinically meaningful results in all endpoints and across subgroups.

**Randomized phase III trial of adjuvant chemotherapy with gemcitabine versus S-1**

<http://gicasym.asco.org/s-1-considered-new-standard-care-japan-resected-pancreatic-cancer>

- Institution(s): Shizuoka Cancer Center, Shizuoka, Japan and others
- Lead author: Katsuhiko Uesaka
- Abstract: <http://gicasym.asco.org/content/105691-133>
- Major finding: The oral fluoropyrimidine S-1 adjuvant chemotherapy is shown non-inferior, and furthermore, even superior to gemcitabine in patients with resected pancreatic cancer.

**Gene profiling of circulating tumor cells may predict treatment response in pancreatic cancer**

<http://www.onclive.com/conference-coverage/gcs-2013/Gene-Profiling-of-Circulating-Tumor-Cells-May-Predict-Treatment-Response-in-Pancreatic-Cancer>

- Institution(s): Institute for Systems Biology, Seattle, WA and others
- Lead author: Kenneth Yu
- Abstract: <http://gicasym.asco.org/content/106051-133>
- Major finding: Isolation and gene expression profiling of tumor progenitor cells can be performed reliably in unresectable pancreatic cancer. Preliminary analysis suggests that cytotoxics profiling can predict response. Repeat pharmacogenomic profiling identifies key pathways associated with treatment resistance.

### **A phase I study of ASG-5ME, a novel antibody-drug conjugate, in pancreatic ductal adenocarcinoma**

<http://investor.seattlegenetics.com/phoenix.zhtml?c=124860&p=irol-newsArticle&ID=1778040&highlight>

- Institution(s): University of Washington, Seattle, WA and others
- Lead author: Andrew Coveler
- PanCAN affiliated author: Andrew Ko, MD: 2003 Career Development Award
- Abstract: <http://gicasym.asco.org/content/105489-133>
- Major finding: ASG-5ME is an antibody-drug conjugate (ADC) targeting SLC44A4, an ion transporter expressed on >90% of pancreatic ductal adenocarcinoma (PDA). ASG-5ME treatment was generally well tolerated in metastatic PDA patients, with preliminary evidence of antitumor activity. Further study of ASG-5ME in SLC44A4-expressing malignancies is warranted.

### **Capecitabine has edge in chemoradiotherapy for pancreatic cancer**

<http://www.medpagetoday.com/MeetingCoverage/MGICS/37040>

- Institution(s): University of Oxford, Oxford, UK and others
- Lead author: Somnath Mukherjee
- Abstract: <http://gicasym.asco.org/content/105226-133>
- Major finding: SCALOP is the largest randomized clinical trial comparing radio-sensitizers in pancreatic cancer and demonstrates that both gemcitabine-CRT and capecitabine-CRT can be delivered safely and effectively. Both regimens met the pre-specified progression-free survival criteria. Compared to G-CRT, Cap-CRT demonstrated significantly better survival and toxicity and should form the template regimen for future trials investigating radiotherapy dose escalation and combination with novel radio-sensitizers.

### **2013 Gastrointestinal Cancers Symposium Virtual Meeting**

[http://store2.asco.org/Gastrointestinal-Cancers-Symposium-Virtual-Meeting/dp/B0096DPL88?cmpid=kh\\_giprod\\_vm\\_etoc - all\\_01-20-13\\_net](http://store2.asco.org/Gastrointestinal-Cancers-Symposium-Virtual-Meeting/dp/B0096DPL88?cmpid=kh_giprod_vm_etoc - all_01-20-13_net)

The 2013 Gastrointestinal Cancers Symposium Virtual Meeting includes three different ways to view all captured presentations (including slides) from the meeting. Access on your computer, download your selected presentations, or view using your mobile device (free application).

#### **Other treatment news:**

### **Personalized chemotherapy profiling using cancer cell lines from selectable mice**

<http://www.ncbi.nlm.nih.gov/pubmed/23340293>

- Journal: *Clinical Cancer Research*
- Institution(s): Johns Hopkins School of Medicine, Baltimore, MD and others
- Corresponding author(s): James Eshleman
- PanCAN affiliated authors:
  - Liz Jaffee, MD: Emeritus Scientific Advisory Board
  - Ralph Hruban, MD: Emeritus Scientific Advisory Board
  - Anirban Maitra, MBBS: 2004 Career Development Award and Chair, Scientific Advisory Board
  - Jim Eshleman, MD, PhD: 2011 Innovative Grant

- Major finding: The authors produced a series of hypoxanthine phosphoribosyl transferase (hprt)-null immunodeficient mice. Pancreatic and ovarian cancers explanted from these mice were grown in selection media to produce pure human cancer cell lines. Chemotherapy can be personalized using patient-specific cell lines derived in biochemically selectable mice.

#### **Addition of algenpantucel-L immunotherapy to standard adjuvant therapy for pancreatic cancer**

<http://www.ncbi.nlm.nih.gov/pubmed/23229886>

- Journal: *Journal of Gastrointestinal Surgery*
- Institution(s): University Hospitals Seidman Cancer Center and Case Western Reserve University, Cleveland, OH and others
- Corresponding author(s): Jeffrey Hardacre
- PanCAN affiliated authors:
  - Mary Mulcahy, MD: Emeritus Medical Advisory Board
  - Mark Talamonti, MD: Medical Advisory Board
- Major finding: The addition of algenpantucel-L to standard adjuvant therapy for resected pancreatic cancer may improve survival. A multi-institutional, phase 3 study is ongoing.

#### **Randomized Phase III multi-institutional study of TNFerade Biologic with fluorouracil &radiotherapy**

<http://www.ncbi.nlm.nih.gov/pubmed/23341531>

- Journal: *Journal of Clinical Oncology*
- Institution(s): Johns Hopkins School of Medicine, Baltimore, MD and others
- Corresponding author(s): Joseph Herman
- PanCAN affiliated authors:
  - Joseph Herman, MD: 2008 Blum-Kovler – Career Development Award and Medical Advisory Board
  - Mimi Canto, MD: Medical Advisory Board
- Major finding: Standard of care + TNFerade is safe but not effective for prolonging survival in patients with locally advanced pancreatic cancer.

#### **Designing and developing S100P inhibitor 5-methyl cromolyn (C5OH) for pancreatic cancer therapy**

<http://www.ncbi.nlm.nih.gov/pubmed/23303403>

- Journal: *Molecular Cancer Therapeutics*
- Institution(s): The University of Texas MD Anderson Cancer Center, Houston, TX
- Corresponding author(s): Craig Logsdon
- PanCAN affiliated author: Craig Logsdon, PhD: Scientific Advisory Board
- Major finding: The authors have previously shown that the anti-allergic drug cromolyn blocks S100P interaction with its receptor RAGE and improves gemcitabine effectiveness in pancreatic ductal adenocarcinoma. Here, the cromolyn analog 5-methyl cromolyn (C5OH), was found to be more efficient and potent than cromolyn as a therapeutic for PDAC.

#### **Novel aspects of preoperative chemo(radiation)therapy improving anti-tumor immunity**

<http://www.ncbi.nlm.nih.gov/pubmed/23363422>

- Journal: *Cancer Science*
- Institution(s): Hokkaido University Graduate School of Medicine, Sapporo, Japan

- Corresponding author(s): Takahiro Tsuchikawa
- Major finding: Preoperative chemo(radiation)therapy in pancreatic adenocarcinoma is useful for reducing regulatory T cell levels in combination with its direct cytotoxic effects.

#### **Lenalidomide with gemcitabine as first-line treatment for metastatic carcinoma of pancreas**

<http://www.ncbi.nlm.nih.gov/pubmed/23358470>

- Journal: *Cancer Biology & Therapy*
- Institution(s): Sarah Cannon Research Institute, Nashville, TN and others
- Corresponding author(s): Jeffrey Infante
- Major finding: The observed 6-month overall survival (37%) of the thalidomide analog lenalidomide with gemcitabine does not suggest improvement compared with historical results with gemcitabine alone. Toxicities and dose modifications likely limited dose intensity. Further development of this regimen in pancreas cancer is not recommended.

#### **Beam angle selection for IMRT treatment of unresectable pancreatic cancer**

<http://www.ncbi.nlm.nih.gov/pubmed/23359183>

- Journal: *Clinical and Translational Oncology*
- Institution(s): Indiana University School of Medicine, Indianapolis, IN
- Corresponding author(s): D. S. Chang
- Major finding: The noncoplanar (NCP) intensity-modulated radiotherapy (IMRT) was able to significantly decrease bilateral kidney dose, but did not improve other dose-volume criteria. The use of NCP beam angles is preferred only in patients with risk factors for treatment-related kidney dysfunction.

#### **CANCER CONTROL, SURVIVORSHIP, AND OUTCOMES RESEARCH**

##### **Annual report to the nation on the status of cancer, 1975-2009**

<http://www.ncbi.nlm.nih.gov/pubmed/23297039>

- Journal: *Journal of the National Cancer Institute*
- Institution(s): American Cancer Society, Atlanta, GA and others
- Corresponding author(s): Ahmedin Jemal
- Major finding: The overall trends in declining cancer death rates continue. However, increases in incidence rates for some HPV-associated cancers and low vaccination coverage among adolescents underscore the need for additional prevention efforts for HPV-associated cancers, including efforts to increase vaccination coverage.

#### **Clinical Cancer Advances 2012: ASCO's Annual Report on Progress Against Cancer**

[http://www.cancerprogress.net/latest\\_advances.html](http://www.cancerprogress.net/latest_advances.html)

*Report:* [http://www.cancerprogress.net/pdf/CCA\\_2012.pdf](http://www.cancerprogress.net/pdf/CCA_2012.pdf)

The large number of advances featured in this year's Report affirms the remarkable payoff of national investments in clinical research on cancer prevention, screening, treatment and quality of life for patients with cancer.