March 2017

PANCREATIC CANCER ACTION NETWORK AND COMMUNITY NEWS

Pancreatic Cancer Action Network news:

Pancreatic Cancer Action Network’s Know Your Tumor® Program Surpasses 1,000 Enrolled Patients

The Pancreatic Cancer Action Network announced that since the 2014 inception of its Know Your Tumor personalized medicine service, more than 1,000 pancreatic cancer patients have enrolled. To date, approximately 500 of these patients and their oncologists have received a molecular profiling report to help guide treatment decisions.

Clinical Trial Finder
clinicaltrials.pancan.org/hcp

The Clinical Trial Finder saves you time and energy by helping you quickly and easily find the most current pancreatic cancer clinical trials information. By registering for an account, you will have access to the most up-to-date and comprehensive database of pancreatic cancer clinical trials in the United States. Our online tool allows you to perform a patient-specific search to locate available trials based on your patients’ needs or a general search to understand the current clinical trials landscape to inform research or trial design.

Know Your Tumor®
Powerful Knowledge. Personal Treatment.®
pancan.org/knowyourtumor/hcp

Our Know Your Tumor service is an IRB-approved protocol that provides you and your pancreatic cancer patients with a molecular profiling report of their tumor, which includes personalized treatment options – including standard treatments, off-label treatments and available clinical trials. Treatment options are determined after findings of the molecular reports are interpreted by an expert panel, providing valuable insight to support your treatment decisions.

Patient Registry
pancan.org/patientregistry

The Patient Registry is a global online database created to look for patterns in treatments, side effect management and diagnostics that will lead to improved treatment options and outcomes for patients. Whether you have been diagnosed with pancreatic cancer or have provided care for someone with pancreatic cancer, your contributions are meaningful. By joining our quickly growing community and sharing your experiences, you’re giving researchers access to crucial data that will help make discoveries. Together, we will move pancreatic cancer research forward.
**Funding opportunities:**

**New! Cancer Moonshot℠ – Funding Opportunities**
https://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative/funding?cid=eb_govdel

Following receipt of the Blue Ribbon Panel report, NCI identified funding opportunity announcements (FOAs) from within its extensive research portfolio that address the goals of the Cancer Moonshot. These opportunities mark the beginning of a growing Cancer Moonshot portfolio which will continue to expand given the authorization of the 21st Century Cures Act to fund the Beau Biden Cancer Moonshot with $1.8 billion over 7 years. While the FOAs listed below highlight research initiatives that align with the efforts of the Cancer Moonshot, they may be supported with existing funds or with the 21st Century Cures funding.

**Stand Up To Cancer – Lustgarten Foundation Pancreatic Cancer Interception Dream Team**
http://www.aacr.org/Funding/Pages/Funding-Detail.aspx?ItemID=66#.WIjz_lMrKUk

*Letter of Intent deadline: March 22, 2017*
*Application deadline: June 26, 2017*

Submissions of ideas will be invited for a translational cancer research project that addresses critical problems in pancreatic cancer and positively impacts patients in the near future, with the goal of advancing innovative approaches to prevent or intercept the disease-causing process, and making data available in a format amenable to open access analytics.

**The Pancreatic Cancer Detection Consortium (U01)**

*Deadlines: May 26, 2017; September 21, 2017; April 6, 2018*

This Funding Opportunity Announcement (FOA) invites applications from multi-disciplinary teams of researchers and clinicians to establish the Pancreatic Cancer Detection Consortium (PCDC) to conduct research to improve the detection of early stage pancreatic ductal adenocarcinoma (PDAC) and characterization of its precursor lesions.

**Job opportunities:**

**Faculty Position: Assistant Professor of Cancer Cell Biology**
https://www.ndsu.edu/biology/job_openings/

North Dakota State University is looking to hire an Assistant Professor of Cancer Cell Biology who conducts pancreatic cancer research.

**Meetings:**

**Updated! AACR Annual Meeting 2017**
http://www.aacr.org/Meetings/Pages/MeetingDetail.aspx?EventItemID=105#.WAFbpvkrlIU

*Meeting: April 1 – 5, 2017, Walter E. Washington Convention Center, Washington, D.C., USA*

**Pancreatic Cancer Action Network Grantee Discussion and Poster Session:**
http://www.abstractsonline.com/pp8/#!/4292/session/899

The AACR Annual Meeting highlights the best cancer science and medicine from institutions all over the world. Attendees are invited to stretch their boundaries, form collaborations, attend sessions outside their own areas of expertise, and learn how to apply exciting new concepts, tools, and techniques to their own research.
Pancreas Club Annual Meeting  
**Meeting:** May 5 – 6, 2017, Drake Hotel, Chicago, IL  
**Deadline for early registration:** April 7, 2017  
Registration includes access to all scientific sessions, posters viewing, exhibits, printed proceedings, Friday and Saturday continental breakfast and lunch, and Saturday Closing Reception.

ASCO Annual Meeting 2017  
[http://am.asco.org/?cmpid=nm_abst_ascoex - all_12-06-16_sub&et_cid=38688115&et_rid=977587026&linkid=ASCO+Annual+Meeting](http://am.asco.org/?cmpid=nm_abst_ascoex - all_12-06-16_sub&et_cid=38688115&et_rid=977587026&linkid=ASCO+Annual+Meeting)  
**Meeting:** June 2 – 6, 2017, McCormick Place, Chicago, IL  

2nd International Conference on Pancreatic Cancer & Liver Diseases  
**Meeting:** June 12 – 13, 2017, London, UK  
**Registration rates increase March 20 and April 30; final call is June 12**  
Pancreatic Cancer 2017 gives an extraordinary platform for changing capacity ideas into superb business. This conference will convey together a vast participation of customers came from entrepreneurs, Proposers, buyers, international monetary companies, business institutions, academia and experts within the area of pancreatic studies and treatment.

Aspen Cancer Conference  
**Meeting:** July 15 – July 18, 2017, the Gant Conference Center and Resort, Aspen, CO  
The Aspen Cancer Conference, a series of yearly meetings conceived by Drs. Benjamin F. Trump and Curtis C. Harris, was begun in 1985. The Conference has continued to emphasize the relationships between toxicity and carcinogenesis and the identification of novel strategies in cancer prevention, diagnosis, and therapy. It is evident that new paradigms are needed to explain that an increasing number of mutagenic and non-mutagenic agents result in carcinogenesis, that cell injury and death, repair, and inflammation are constant companions of cancer.

European Pancreatic Club (EPC) 2017  
**Meeting:** June 28 – July 1, 2017, Budapest, Hungary  
**Early registration deadline:** April 15, 2017  
The meeting will be an important event in European pancreatology and related areas, where basic scientists and clinicians can exchange ideas and novel research findings, and also deepen their scientific knowledge.

Other community news:

ASCO’s 12th Annual Report on Progress Against Cancer  
Cancer is one of the world’s most pressing health care challenges. On the whole, research progress from one year to the next is incremental, and true breakthroughs are exceptional. Nevertheless, every year brings new knowledge and insights that help direct further research and ultimately improve the outlook for patients with cancer. Clinical Cancer Advances 2017 highlights the most important clinical advances of the past year and previews where cancer science is headed. Advances highlighted in this report cover the full range of clinical research disciplines: prevention, treatment, patient care, and tumor biology.

PCRF Founder Joins CRUK Grand Challenge Team Investigating Causes of Pancreatic Cancer
Pancreatic Cancer Research Fund founder, Maggie Blanks, has been announced as a member of one of the first global research teams to be recipients of Cancer Research UK’s £20m Grand Challenge award. In a project of epic scale that spans five continents, including countries that have high and low levels of particular cancers, Professor Stratton’s team will study 5,000 pancreatic, kidney, oesophageal and bowel cancer samples to build a much deeper understanding of DNA damage – what causes it and how it leads to cancer.

RAS Pathway v3.0?
This RAS Dialogue blog article is written by former grantee and Emeritus Scientific & Medical Advisory Board member Frank McCormick, PhD, FRS. The article includes “v2.0” of the RAS signaling pathway, and Dr. McCormick is calling for submissions of genes/proteins to add or remove to create v3.0.

Cell Special Issue: Cancer: The Road Ahead
This reviews issue highlights the converging paths in cancer research that are enabling changes in clinical treatment and removing obstacles between patients in need and access to effective care. Empowered by these breakthroughs, it is possible to imagine major gains against cancer’s relentless advance. In thinking about the scope of cancer research today, the editors were struck by a few themes that transcend the individual topics presented in this issue.

Call for Papers: Research on Pancreatic Cancer
http://liebertopenaccess.com/News?id=31
Journal of Pancreatic Cancer is seeking high quality clinical, translational and basic science papers on malignancies of the pancreas and the peripancreatic region. Submitted papers will be peer reviewed and consider for publication in the Journal.

BIOLOGY OF CANCER

Pancreatic Cancer: Progress and Challenges in a Rapidly Moving Field
- Journal: Cancer Research
- Institution(s): University of California, San Francisco, San Francisco, CA, and others
- Corresponding author(s): Eric Collisson or Kenneth Olive
- Pancreatic Cancer Action Network-affiliated authors:
  - Eric Collisson, MD: recipient, 2012 Skip Viragh – Career Development Award, co-PI, Precision Promise Clinical Trial Consortium site and member, Scientific and Medical Advisory Board
Kenneth Olive, PhD: recipient, 2011 Tempur-Pedic Retailers – Career Development Award

- Major finding: "Pancreatic Cancer: Advances in Science and Clinical Care," a Special Conference of the American Association for Cancer Research, was held in Orlando, FL, on May 12 to 15, bringing together more than 450 basic, translational, clinical, and epidemiologic pancreatic cancer researchers as well as pancreatic cancer patients, survivors, and advocates. The authors present a summary of meeting highlights, a series of "success factors" that will benchmark the progress of the field over the next 2 years, and three challenges to the pancreatic cancer research community as it moves toward the goal of extending patient survival.

Synthetic Vulnerabilities of Mesenchymal Subpopulations in Pancreatic Cancer
- Journal: *Nature*
- Institution(s): The University of Texas MD Anderson Cancer Center, Houston, TX, and others
- Corresponding author(s): Giannicola Genovese or Giulio Draetta
- Pancreatic Cancer Action Network-affiliated authors:
  - Jason Fleming, MD: co-PI, 2015 Research Acceleration Network Grant and member, Scientific & Medical Advisory Board
  - Michael Goggins, MD: PI, 2013 Skip Viragh – Inaugural Research Acceleration Network Grant
  - Anirban Maitra, MBBS: recipient, 2014 Robert Aronson – Innovative Grant and 2004 Career Development Award and member, Scientific & Medical Advisory Board
  - Huamin Wang, MD, PhD: recipient, 2007 Skip Viragh – Career Development Award
  - Giulio Draetta, MD, PhD: PI, 2014 Skip Viragh – Research Acceleration Network Grant
- Major finding: Here the authors determine the molecular and cellular mechanisms of cancer cell plasticity in a conditional oncogenic *Kras* mouse model of pancreatic ductal adenocarcinoma (PDAC), a malignancy that displays considerable phenotypic diversity and morphological heterogeneity. In this model, stochastic extinction of oncogenic *Kras* signaling and emergence of *Kras*-independent escaper populations (cells that acquire oncogenic properties) are associated with de-differentiation and aggressive biological behavior.

Distinct Populations of Inflammatory Fibroblasts and Myofibroblasts in Pancreatic Cancer
- Journal: *The Journal of Experimental Medicine*
- Institution(s): Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, and others
- Corresponding author(s): David Tuveson
- Pancreatic Cancer Action Network-affiliated authors:
  - Mikala Egeblad, PhD: recipient, 2012 The Daniel and Janet Mordecai Foundation – Career Development Award
  - Douglas Fearon, MD: co-PI, 2015 Celgene Corporation – Research Acceleration Network Grant
  - David Tuveson, MD, PhD: recipient, 2003 Career Development Award and member, Emeritus Scientific & Medical Advisory Board
- Major finding: The authors We identified a cancer-associated fibroblast (CAF) subpopulation with elevated expression of α-smooth muscle actin (αSMA) located immediately adjacent to neoplastic cells in mouse and human pancreatic ductal adenocarcinoma (PDA) tissue. These findings were corroborated in mouse and human PDA tissue, providing direct evidence for CAF heterogeneity in PDA tumor biology with implications for disease etiology and therapeutic development.

Mutant Kras- and p16-regulated NOX4 Activation Overcomes Metabolic Checkpoints in Development of Pancreatic Ductal Adenocarcinoma
Journal: Nature Communications
Institution(s): Collaborative Innovation Center for Cancer Medicine, Guangzhou, China, and others
Corresponding author(s): Peng Huang, Rui-Hua Xu or Paul Chiao
Pancreatic Cancer Action Network-affiliated authors:
   o Huamin Wang, MD, PhD: recipient, 2007 Skip Viragh – Career Development Award
   o Paul Chiao, PhD: recipient, 2012 Innovative Grant (Grant funded in part by the Lefkofsky Foundation)
Major finding: The authors provide a biochemical explanation for the cooperation between p16 inactivation and Kras activation in pancreatic ductal adenocarcinoma (PDAC) development and suggest that NAD(P)H oxidase 4 (NOX4) is a potential therapeutic target for PDAC.

Whole-genome Landscape of Pancreatic Neuroendocrine Tumours
Journal: Nature
Institution(s): University and Hospital Trust of Verona, Verona, Italy, and others
Corresponding author(s): Aldo Scarpa, Andrew Biankin or Sean Grimmond
Pancreatic Cancer Action Network-affiliated author: William Fisher, MD: co-PI, 2016 Translational Research Grant
Major finding: The authors performed whole-genome sequencing of 102 primary pancreatic neuroendocrine tumors and defined the genomic events that characterize their pathogenesis.

ATXN1L, CIC, and ETS Transcription Factors Modulate Sensitivity to MAPK Pathway Inhibition
Journal: Cell Reports
Institution(s): Dana-Farber Cancer Institute, Boston, MA, and others
Corresponding author(s): William Hahn
Pancreatic Cancer Action Network-affiliated author: Andrew Aguirre, MD, PhD: recipient, 2013 Samuel Stroum – Fellowship
Major finding: These observations identify the ATXN1L-CIC-ETS transcription factor axis as a mediator of resistance to MEK and RAF inhibitors (MAPKi).

Genetic Analyses of Isolated High-grade Pancreatic Intraepithelial Neoplasia (HG-PanIN) Reveal Paucity of Alterations in TP53 and SMAD4
Journal: The Journal of Pathology
Institution(s): The Johns Hopkins University School of Medicine, Baltimore, MD, and others
Corresponding author(s): Laura Wood
Pancreatic Cancer Action Network-affiliated authors:
   o Michael Goggins, MD: PI, 2013 Skip Viragh – Inaugural Research Acceleration Network Grant
   o Ralph Hruban, MD: member, Emeritus Scientific & Medical Advisory Board
Major finding: These results suggest that inactivation of TP53 and SMAD4 are late genetic alterations, predominantly occurring in invasive pancreatic ductal adenocarcinoma.

Journal: Surgery
Institution(s): David Geffen School of Medicine at UCLA, Los Angeles, CA, and others
Corresponding author(s): Guido Eibl
Pancreatic Cancer Action Network-affiliated author: David Dawson, MD, PhD: recipient, 2008 Seena Magowitz – Career Development Award
Major finding: The authors’ study provides evidence that prostaglandin E₂ (PGE₂) can inhibit directly pancreatic ductal adenocarcinoma cell growth through an E-type prostaglandin-4 (EP4)-mediated mechanism. Together with their gene expression and survival analysis, this observation suggests a protective role of EP4 receptors in human pancreatic ductal adenocarcinoma that expresses E-type prostaglandin receptors.

Untangling the Genetics from the Epigenetics in Pancreatic Cancer Metastasis
http://www.nature.com/ng/journal/v49/n3/full/ng.3798.html
Journal: Nature Genetics
Institution(s): Cold Spring Harbor Laboratory, Cold Spring Harbor, NY
Corresponding author(s): Christopher Vakoc or David Tuveson
Pancreatic Cancer Action Network-affiliated authors:
- Christopher Vakoc, MD, PhD: recipient, 2016 The Daniel and Janet Mordecai – Career Development Award
- David Tuveson, MD, PhD: recipient, 2003 Career Development Award and member, Emeritus Scientific & Medical Advisory Board
Major finding: Comparative genomic analyses of primary tumors and metastases within individuals with pancreatic cancer have exposed the complex clonal dynamics that underlie the dissemination of cancer cells to distant sites. Recent studies implicate non-genetic mechanisms in this process, particularly fluctuations in chromatin states and metabolism, which can endow rare cells within a primary tumor with metastatic potential.

An Integrative Approach Unveils FOSL1 as an Oncogene Vulnerability in KRAS-Driven Lung and Pancreatic Cancer
Journal: Nature Communications
Institution(s): University of Navarra, Pamplona, Spain, and others
Corresponding author(s): Silve Vicent
Major finding: Here the authors report the identification of a common transcriptional signature across mutant KRAS cancers of distinct tissue origin that includes the transcription factor FOSL1. Their findings unveil KRAS downstream effectors that provide opportunities to treat KRAS-driven cancers.

PAK4 Interacts with p85 alpha: Implications for Pancreatic Cancer Cell Migration
Journal: Scientific Reports
Institution(s): King’s College London, UK, and others
Corresponding author(s): Claire Wells
Major finding: These results implicate a novel role for p21-activated kinase 4 (PAK4) within the PI3K pathway via interaction with p85α. Thus, PAK4 could be an essential player in pancreatic ductal adenocarcinoma progression representing an interesting therapeutic opportunity.

Mitochondrial Mutations and Metabolic Adaptation in Pancreatic Cancer
Pancreatic Cancer: Stroma and Its Current and Emerging Targeted Therapies
- **Journal:** Cancer Letters
- **Institution(s):** Indiana University School of Medicine (IUSM), Indianapolis, IN, and others
- **Corresponding author(s):** Janaiah Kota
- **Major finding:** In this review, the authors summarized the state of current and emerging anti-stromal targeted therapies, with major emphasis on the role of miRNAs in pancreatic ductal adenocarcinoma (PDAC) stroma and their potential use as novel therapeutic agents to modulate PDAC tumor-stromal interactions.

ETIOLOGY

Patients with McCune-Albright Syndrome Have a Broad Spectrum of Abnormalities in the Gastrointestinal Tract and Pancreas
- **Journal:** Virchows Archiv
- **Institution(s):** Johns Hopkins University School of Medicine, Baltimore, MD, and others
- **Corresponding author(s):** Laura Wood
- **Pancreatic Cancer Action Network-affiliated authors:**
  - Aatur Singhi, MD, PhD: recipient, 2016 Translational Research Grant
  - James Eshleman, MD, PhD: recipient, 2011 Innovative Grant
  - Michael Goggins, MD: PI, 2013 Skip Viragh – Inaugural Research Acceleration Network Grant
  - Ralph Hruban, MD: member, Emeritus Scientific & Medical Advisory Board
- **Major finding:** McCune-Albright Syndrome (MAS) is a rare sporadic syndrome caused by postzygotic mutations in the GNAS oncogene, leading to constitutional mosaicism for these alterations. These studies suggest that there is a broad spectrum of abnormalities in the gastrointestinal tract and pancreas in patients with MAS and that patients with MAS should be evaluated for gastrointestinal pathology, some of which may warrant clinical intervention due to advanced dysplasia.

Mediterranean Diet and Risk of Pancreatic Cancer in the European Prospective Investigation into Cancer and Nutrition Cohort
- **Journal:** British Journal of Cancer
- **Institution(s):** Spanish National Cancer Research Center (CNIO), Madrid, Spain, and others
- **Corresponding author(s):** María-José Sánchez
- **Major finding:** The Mediterranean diet (MD) has been proposed as a means for cancer prevention, but little evidence has been accrued regarding its potential to prevent pancreatic cancer. The authors investigated the association between the adherence to the MD and pancreatic cancer risk within the European Prospective Investigation into Cancer and Nutrition
(EPIC) cohort. A high adherence to the MD is not associated with pancreatic cancer risk in the EPIC study.

No Effect of Dietary Aspartame or Stevia on Pancreatic Acinar Carcinoma Development, Growth, or Induced Mortality in a Murine Model
- **Journal:** Frontiers in Oncology
- **Institution(s):** Translational Immunology Laboratory, VIB, Leuven, Belgium
- **Corresponding author(s):** Adrian Liston
- **Major finding:** Here, the authors used longitudinal tracking of pancreatic acinar carcinoma development, growth, and lethality in a sensitized mouse model. Despite exposure to aspartame and stevia from the *in utero* stage onward, they found no disease modification activity, in either direction. These results contribute to the data on aspartame and stevia safety, while also reducing confidence in several of the purported health benefits.

**EARLY DETECTION, DIAGNOSIS, AND PROGNOSIS**

Nanoplasmonic Quantification of Tumour-derived Extracellular Vesicles in Plasma Microsamples for Diagnosis and Treatment Monitoring
http://www.nature.com/articles/s41551-016-0021
- **Journal:** Nature Biomedical Engineering
- **Institution(s):** Houston Methodist Research Institute, Houston, TX, and others
- **Corresponding author(s):** Kai Liang, Fei Liu or Ye Hu
- **Pancreatic Cancer Action Network-affiliated author:** Eugene Koay, MD, PhD; recipient, 2014 Skip Viragh – Career Development Award
- **Major finding:** Here, the authors describe a rapid, ultrasensitive and inexpensive nanoplasmon-enhanced scattering (nPES) assay that directly quantifies tumor-derived extracellular vesicles (EVs) from as little as 1 μl of plasma. They identified a pancreatic cancer EV biomarker, ephrin type-A receptor 2 (EphA2), and demonstrate that an nPES assay for EphA2-EVs distinguishes pancreatic cancer patients from pancreatitis patients and healthy subjects.

High Prevalence of Mutant KRAS in Circulating Exosome-derived DNA from Early Stage Pancreatic Cancer Patients
- **Journal:** Annals of Oncology
- **Institution(s):** The University of Texas MD Anderson Cancer Center, Houston, TX, and others
- **Corresponding author(s):** Hector Alvarez
- **Pancreatic Cancer Action Network-affiliated author:** Anirban Maitra, MBBS; recipient, 2014 Robert Aronson – Innovative Grant and 2004 Career Development Award and member, Scientific & Medical Advisory Board
- **Major finding:** Exosomes are a distinct source of tumor DNA that may be complementary to other liquid biopsy DNA sources. A higher percentage of patients with localized pancreatic ductal adenocarcinoma exhibited detectable *KRAS* mutations in exosome-derived DNA (exoDNA) than previously reported for circulating cell-free DNA (cfDNA). A substantial minority of healthy samples demonstrated mutant *KRAS* in circulation, dictating careful consideration and application of liquid biopsy findings, which may limit its utility as a broad cancer-screening method.

Predicting the Grade of Dysplasia of Pancreatic Cystic Neoplasms Using Cyst Fluid DNA Methylation Markers
Major finding: A panel of methylated gene markers quantified by methylation-specific droplet-digital PCR (dd-QMSP) can be used to predict the grade of dysplasia of pancreatic cysts.

Major finding: In this retrospective analysis, the prognosis of surgically resectable BRCA-associated pancreatic ductal adenocarcinoma (PDAC) is no different than that of sporadic PDAC from the same institution. The role of platinum-based adjuvant therapy in this setting requires prospective investigation.

Major finding: As the diagnostic-criteria of pancreatic mucinous cystic neoplasms (MCN) have standardized over time, MCN diagnosis has decreased in males and head/neck location. Despite this, MCN-associated adenocarcinoma/high-grade dysplasia has been stable and remains high in males. Any male with suspected MCN, regardless of location, should undergo resection.
Major finding: Within this review, the authors discuss novel DNA, miRNA, protein and metabolite biomarkers, and their relevance in clinical practice. In addition, they focus on future areas of research that have the potential to change pancreatic cyst management.

Genomic Characterization of Low- and High-Grade Pancreatic Mucinous Cystic Neoplasms Reveals Recurrent KRAS Alterations in "High-Risk" Lesions


- **Journal:** Pancreas
- **Institution(s):** Massachusetts General Hospital, Boston, MA
- **Corresponding author(s):** Leona Doyle
- **Major finding:** The low frequency of KRAS alterations in cysts without a high-grade component suggests that a subset of mucinous cystic neoplasms may have a low risk for malignant progression. Novel single-nucleotide variants that occur at a lower rate may help identify this group and provide a substrate for new diagnostic, prognostic, and therapeutic targets.

Validation of the American Joint Commission on Cancer (AJCC) 8th Edition Staging System for Patients with Pancreatic Adenocarcinoma: A Surveillance, Epidemiology and End Results (SEER) Analysis


- **Journal:** Annals of Surgical Oncology
- **Institution(s):** University of Birmingham, Birmingham, UK, and others
- **Corresponding author(s):** Hari Nathan
- **Major finding:** This is the first large-scale validation of the AJCC 8th edition staging system for pancreatic cancer. The revised system provides discrimination similar to that of the 7th-edition system. However, the 8th-edition system allows for finer stratification of patients with resected tumors according to extent of nodal involvement.

Knowledge About the Presence or Absence of miRNA Isoforms (isomiRs) Can Successfully Discriminate Amongst 32 TCGA Cancer Types


- **Journal:** Nucleic Acids Research
- **Institution(s):** Thomas Jefferson University, Philadelphia, PA
- **Corresponding author(s):** Isidore Rigoutsos
- **Major finding:** Given their ability to successfully classify datasets from 32 cancers, isoforms of human miRNAs (isomiRs) and the authors’ resulting ‘Pan-cancer Atlas’ of isomiR expression could serve as a suitable framework to explore novel cancer biomarkers.

A microRNA Signature in Circulating Exosomes Is Superior to Exosomal Glypican-1 Levels for Diagnosing Pancreatic Cancer


- **Journal:** Cancer Letters
- **Institution(s):** Indiana University School of Medicine, Indianapolis, IN
- **Corresponding author(s):** Xianyin Lai or Murray Korc
- **Major finding:** The authors report that exosomal glypican-1 (GPC1) is not diagnostic for pancreatic ductal adenocarcinoma (PDAC), whereas high exosomal levels of microRNA-10b, (miR-10b), miR-21, miR-30c, and miR-181a and low miR-let7a readily differentiate PDAC from normal control and chronic pancreatitis (CP) samples. Thus, the authors’ exosomal miR signature is superior to exosomal GPC1 or plasma CA 19-9 levels in establishing a diagnosis of PDAC and differentiating between PDAC and CP.
Quantitative Proteomic Analysis of Serum Exosomes from Patients with Locally Advanced Pancreatic Cancer Undergoing Chemoradiotherapy
- **Journal:** Journal of Proteome Research
- **Institution(s):** University of Michigan Medical Center, Ann Arbor, MI
- **Corresponding author(s):** David Lubman
- **Major finding:** In this work, the authors isolated exosomes from the serum of 10 patients with locally advanced pancreatic cancer at serial time points over a course of therapy, and quantitative analysis was performed using the iTRAQ method. Their data show that exosomes can be reliably extracted from patient serum and analyzed for protein content. The differential loading of exosomes during a course of therapy suggests that exosomes may provide novel insights into the development of treatment resistance and metastasis.

Pancreatic Cancer: Tumour-derived EVs for Diagnosis
Review of: http://www.nature.com/articles/s41551-016-0021 (above)
- **Journal:** Nucleic Acids Research
- **Institution(s):** Nature editorial office, London, UK
- **Corresponding author(s):** Katrina Ray
- **Major finding:** A quick, ultrasensitive, blood-based extracellular vesicle (EV) biomarker assay for the detection of pancreatic cancer is reported in a pilot study published in *Nature Biomedical Engineering*. The test distinguished all stages of pancreatic cancer from pancreatitis, and showed promise in detecting early responses to neoadjuvant therapy.

Precision Diagnostics: Moving Towards Protein Biomarker Signatures of Clinical Utility in Cancer
- **Journal:** Nature Reviews Cancer
- **Institution(s):** Lund University, Lund, Sweden
- **Corresponding author(s):** Carl Borrebaeck
- **Major finding:** This Opinion article focuses on the progress being made in identifying protein biomarker signatures of clinical utility, using blood-based proteomics.

**TREATMENT**

Interferon-based Chemoradiation Followed by Gemcitabine for Resected Pancreatic Adenocarcinoma: Long-term Follow-up
- **Journal:** HPB
- **Institution(s):** Washington University School of Medicine, St. Louis, MO, and others
- **Corresponding author(s):** William Hawkins
- **Pancreatic Cancer Action Network-affiliated authors:**
  - David Linehan, MD: PI, 2016 The Shirley Sadoff – Research Acceleration Network-2 Grant and recipient, 2015 Translational Research Grant
  - William Hawkins, MD: recipient, 2016 Translational Research Grant and 2005 Skip Viragh – Career Development Award
- **Major finding:** Adjuvant interferon-based chemoradiation for pancreatic ductal adenocarcinoma improves long-term survival compared to standard therapy. However, recurrence rates and long-term complications remain high, thus further studies are indicated to assess patient characteristics that indicate a favorable treatment profile.
Multivalent Small-Molecule Pan-RAS Inhibitors
- **Journal:** Cell
- **Institution(s):** Columbia University, New York, NY, and others
- **Corresponding author(s):** Brent Stockwell
- **Pancreatic Cancer Action Network-affiliated author:** Kenneth Olive, PhD: recipient, 2011 Tempur-Pedic Retailers – Career Development Award
- **Major finding:** These findings suggest that pan-RAS inhibition may be an effective therapeutic strategy for some cancers and that structure-based design of small molecules targeting multiple adjacent sites to create multivalent inhibitors may be effective for some proteins.

ACR Appropriateness Criteria® Resectable Pancreatic Cancer
- **Journal:** American Journal of Clinical Oncology
- **Institution(s):** University of Texas Health Science Center at San Antonio, San Antonio, TX, and others
- **Corresponding author(s):** William Jones
- **Pancreatic Cancer Action Network-affiliated author:** Joseph Herman, MD, MSc: recipient, 2008 Blum-Kovler – Career Development Award
- **Major finding:** The American College of Radiology Appropriateness Criteria are evidence-based guidelines for specific clinical conditions that are reviewed annually by a multidisciplinary expert panel. The guideline development and revision include an extensive analysis of current medical literature from peer reviewed journals and the application of well-established methodologies (RAND/UCLA Appropriateness Method and Grading of Recommendations Assessment, Development, and Evaluation or GRADE) to rate the appropriateness of imaging and treatment procedures for specific clinical scenarios. In those instances where evidence is lacking or equivocal, expert opinion may supplement the available evidence to recommend imaging or treatment.

Targeting Neoantigens to Augment Antitumour Immunity
- **Journal:** Nature Reviews Cancer
- **Institution(s):** The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD
- **Corresponding author(s):** Elizabeth Jaffee
- **Pancreatic Cancer Action Network-affiliated authors:**
  - Eric Lutz, PhD: recipient, 2013 Career Development Award
  - Elizabeth Jaffee, MD: member, Emeritus Scientific & Medical Advisory Board
- **Major finding:** In this Review the authors discuss the emerging evidence that neoantigens are recognized by the immune system and can be targeted to increase antitumor immunity. They also provide a framework for personalized cancer immunotherapy through the identification and selective targeting of individual tumor neoantigens, and present the potential benefits and obstacles to this approach of targeted immunotherapy.

BET Inhibitors Block Pancreatic Stellate Cell Collagen I Production and Attenuate Fibrosis in vivo
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5291732/
- **Journal:** JCI Insight
- **Institution(s):** Northwestern University, Chicago, IL, and others
- **Corresponding author(s):** Hidayatullah Munshi
Pancreatic Cancer Action Network-affiliated author: Paul Grippo, PhD: recipient, 2007 Nancy Daly Riordan – Career Development Award

Major finding: In this report, the authors show that members of the bromodomain and extraterminal (BET) family of proteins are expressed in primary pancreatic stellate cells (PSCs) isolated from human pancreatic ductal adenocarcinoma tumors, with BRD4 positively regulating, and BRD2 and BRD3 negatively regulating, collagen I expression in primary cancer-associated PSCs. The authors’ results demonstrate that BET inhibitors regulate fibrosis by modulating the activation and function of cancer-associated PSCs.

Updated Results from GEST Study: A Randomized, Three-arm Phase III Study for Advanced Pancreatic Cancer

- Journal: Journal of Cancer Research and Clinical Oncology
- Institution(s): National Cancer Center Hospital, Tokyo, Japan, and others
- Corresponding author(s): Takuji Okusaka
- Major finding: The authors’ survey reconfirmed the non-inferiority of S-1 to gemcitabine and showed S-1 can be used as one of the standard treatment options for advanced pancreatic cancer.

A Phase II Study to Evaluate LY2603618 in Combination with Gemcitabine in Pancreatic Cancer Patients

- Journal: BMC Cancer
- Institution(s): Institut Català d’Oncologia-IDIBELL, Barcelona, Spain, and others
- Corresponding author(s): Emiliano Calvo
- Major finding: The aim of this study was to determine whether checkpoint kinase 1 inhibitor (CHK1), LY2603618, and gemcitabine prolong overall survival (OS) compared to gemcitabine alone in patients with unresectable pancreatic cancer. LY2603618/gemcitabine was not superior to gemcitabine for the treatment of patients with pancreatic cancers.

Gemcitabine-erlotinib versus Gemcitabine-erlotinib-capecitabine in the First-line Treatment of Patients with Metastatic Pancreatic Cancer: Efficacy and Safety Results of a Phase IIb Randomised Study from the Spanish TTD Collaborative Group

- Journal: European Journal of Cancer
- Institution(s): Virgen de la Salud Hospital, Toledo, Spain, and others
- Corresponding author(s): Antonio Irigoyen
- Major finding: Progression-free survival with gemcitabine-erlotinib-capecitabine was not significantly different to that with gemcitabine-erlotinib in patients with metastatic pancreatic cancer. Skin rash strongly predicted erlotinib efficacy.

Management of Severe Pancreatic Fistula After Pancreatoduodenectomy

- Journal: JAMA Surgery
- Institution(s): University Medical Center Utrecht, Utrecht, the Netherlands, and others
- Corresponding author(s): I. Quintus Molenaar
- Major finding: In this propensity-matched cohort, catheter drainage as first intervention for severe pancreatic fistula after pancreatectoduodenectomy was associated with a better clinical outcome, including lower mortality, compared with primary relaparotomy.
Pancreatic Cancer: Addition of Capecitabine Prolongs Overall Survival
- Journal: *Nature Reviews Clinical Oncology*
- Institution(s): Nature editorial office, London, UK
- Corresponding author(s): Peter Sidaway
- Major finding: Data from a phase III trial in patients with resected pancreatic ductal adenocarcinoma (PDAC), who generally have a poor prognosis, indicate that patients receiving adjuvant capecitabine plus gemcitabine have a superior median overall survival duration compared with patients receiving gemcitabine alone (28.0 months versus 25.5 months).

A Multidisciplinary Approach to Pancreas Cancer in 2016: A Review
- Journal: *The American Journal of Gastroenterology*
- Institution(s): Indiana University School of Medicine, Indianapolis, IN
- Corresponding author(s): Stuart Sherman
- Major finding: In this article, the authors review their multidisciplinary approach for patients with pancreatic cancer. Specifically, they review the epidemiology, diagnosis and staging, biliary drainage techniques, selection of patients for surgery, chemotherapy, radiation therapy, and discuss other palliative interventions. The areas of active research investigation and where their knowledge is limited are emphasized.

Tackling Pancreatic Cancer with Metronomic Chemotherapy
- Journal: *Cancer Letters*
- Institution(s): Sapienza University, Rome, Italy
- Corresponding author(s): Adriana Romiti
- Major finding: Metronomic chemotherapy (MCT), which consists in the administration of continuous, low-dose anticancer drugs, has demonstrated the ability to suppress tumor growth. Here the authors discuss evidence arising from preclinical and clinical studies regarding the use of MCT in pancreatic cancer. Further studies are awaited to confirm both preclinical findings and the preliminary clinical data.

MicroRNA-155 Controls Exosome Synthesis and Promotes Gemcitabine Resistance in Pancreatic Ductal Adenocarcinoma
- Journal: *Scientific Reports*
- Institution(s): Osaka University, Osaka, Japan
- Corresponding author(s): Hidetoshi Eguchi
- Major finding: In this study, the authors revealed that the loop conferred chemoresistance in pancreatic ductal adenocarcinoma (PDAC) cells. The loop was as follows; 1, The long-term exposure of gemcitabine (GEM) increased miR-155 expression in PDAC cells. 2, The increase of miR-155 induced two different functions: exosome secretion and chemoresistance ability via facilitating the anti-apoptotic activity. 3, Exosome deliver the miR-155 into the other PDAC cells and induce the following function. This mechanism represents a novel therapeutic target in GEM treatment to PDAC.

Cancer Cell Mitochondria Targeting by Pancratistatin Analogs is Dependent on Functional Complex II and III
- Journal: *Scientific Reports*
Institution(s): University of Windsor, Windsor, Ontario, Canada

Corresponding author(s): Siyaram Pandey

Major finding: The compound pancratistatin (PST) has been shown to selectively induce apoptosis in cancer cells. This work provides a scaffold for characterizing distinct mitochondrial and metabolic features of cancer cells and reveals several lead compounds with high therapeutic potential.

Synthesis of ent-BE-43547A; Reveals a Potent Hypoxia-selective Anticancer Agent and Uncovers the Biosynthetic Origin of the APD-CLD Natural Products

Journal: Nature Chemistry

Institution(s): Aarhus University, Aarhus, Denmark

Corresponding author(s): Thomas Poulsen or Thomas Tørring

Major finding: Here the authors demonstrate that the BE-43547 subclass of the APD-CLD (amidopentadienoate-containing cyclolipodepsipeptides) natural products possesses highly hypoxia-selective growth-inhibitory activity against pancreatic cancer cells. Their studies underline the exciting possibilities for the further development of the anticancer activities of these natural products.

FAK-inhibition Opens the Door to Checkpoint Immunotherapy in Pancreatic Cancer

Commentary on: https://www.ncbi.nlm.nih.gov/pubmed/27376576

Journal: Journal for ImmunoTherapy of Cancer

Institution(s): University of Edinburgh, Edinburgh, UK

Corresponding author(s): Alan Serrels

Major finding: Recently, Jiang and colleagues identified a key role for FAK in regulating the composition of the fibrotic and immuno-suppressive pancreatic tumor niche, and showed that FAK inhibitors can be used in combination with immune checkpoint blockade and gemcitabine chemotherapy to significantly delay pancreatic tumor progression. This study further supports the use of FAK inhibitors in combination with immunotherapy.

Industry news:

Boston Biomedical Initiates CanStem111P: A Global Phase 3 Study Investigating Cancer Stemness Inhibitor Napabucasin in Patients With Metastatic Pancreatic Cancer

Company: Boston Biomedical. Cambridge, MA

Major finding: Boston Biomedical, an industry leader in the development of next-generation cancer therapeutics designed to inhibit cancer stemness pathways, has initiated dosing of the first patient in a new global phase 3 study, CanStem111P. The study will investigate napabucasin – an orally administered, first-in-class, investigational agent designed to inhibit cancer stemness pathways by targeting STAT3 – in combination with standard of care (nab-paclitaxel plus gemcitabine) in patients with metastatic pancreatic cancer.

Bellicum Announces Initiation of Patient Dosing with Controllable CAR T-Cell Product Candidate

Company: Bellicum Pharmaceuticals, Inc., Houston, TX

Major finding: Bellicum Pharmaceuticals, Inc., a leader in developing novel, controllable cellular immunotherapies for cancers and orphan inherited blood disorders, announced it has dosed the
first patient with BPX-601, the first CAR T-cell product candidate to enter clinical studies that is designed to enable control over the expansion and stimulation of the cells. BPX-601 targets solid tumors that express PSCA (prostate stem cell antigen), with an initial indication in non-resectable pancreatic cancer.

MabVax Therapeutics Announces FDA Authorization to Proceed with MVT-1075 in a Phase I Clinical Trial for the Treatment of Pancreatic Cancer


- **Company:** MabVax Therapeutics Holdings, Inc., San Diego, CA
- **Major finding:** MabVax Therapeutics Holdings, Inc., a clinical-stage oncology drug development company, announces that it has received notice from the U.S. Food and Drug Administration (FDA) authorizing the initiation a Phase I clinical trial with MVT-1075 as a therapeutic treatment for pancreatic cancer. MVT-1075 (177Lu-CHX-A*-DTPA-HuMab5B1) is the Company’s novel fully human antibody radioimmunotherapy (RIT). MabVax plans to initiate the phase I clinical trial in patients with recurrent pancreatic cancer and other CA19-9 positive malignancies the first half in 2017.

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

European Cancer Mortality Predictions for the Year 2017, with Focus on Lung Cancer

https://academic.oup.com/annonc/article/3044179/European

- **Journal:** Annals of Oncology
- **Institution(s):** Università degli Studi di Milano, Milan, and others
- **Corresponding author(s):** Carlo La Vecchia
- **Major finding:** The authors predicted cancer mortality figures in the European Union (EU) for the year 2017 using most recent available data, with a focus on lung cancer. Mortality rates for all selected cancer sites are predicted to decline, except pancreatic cancer in both sexes and lung cancer in women. European cancer mortality projections for 2017 confirm the overall downward trend in rates, with a stronger pattern in men.

Socio-economic Status Influences the Likelihood of Undergoing Surgical Treatment for Pancreatic Cancer in the Netherlands


- **Journal:** HPB
- **Institution(s):** Catharina Hospital, Eindhoven, The Netherlands, and others
- **Corresponding author(s):** Ignace H.J.T. de Hingh
- **Major finding:** The influence of socio-economic status (SES) on surgical treatment and survival was investigated in the Netherlands, a country with a widely accessible healthcare system. SES in pancreatic cancer patients determined the likelihood for surgery. However, SES had no influence on survival. It is important to provide more insights in the causes of these inequalities to minimalize the effects of SES in pancreatic cancer care.