PANCREATIC CANCER ACTION NETWORK AND COMMUNITY NEWS

Pancreatic Cancer Action Network news:

Five-year Survival Increases for Third Straight Year
https://www.pancan.org/news/five-year-survival-increases-third-straight-year/

ACS Facts & Figures 2017:

The American Cancer Society released its annual Cancer Facts & Figures report, which highlighted some encouraging news for the pancreatic cancer community. The five-year survival rate for the disease increased, moving from 8 to 9 percent (based on SEER-9 data)! This is the third straight year that the five-year survival rate has climbed, moving us one step closer to achieving our goal to double survival by 2020.

January is National Pancreatic Cancer Trials Awareness Month

We want everyone to know how important pancreatic cancer clinical trials are. For patients who need to make treatment decisions now, clinical trials often provide the best treatment options. At the same time, trial participation helps future patients by contributing to groundbreaking treatment research.

Your Advocacy in Action: New Federal Research Funding to Explore Pancreatic Cancer Immunotherapy

This past month, the National Cancer Institute (NCI) announced a new research funding mechanism to better understand and treat pancreatic cancer. This important commitment to research is the result of your hard work. The NCI will devote $3 million toward the development of a consortium for translational studies of the pancreatic cancer microenvironment and an accompanying resource center.

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/knownyourtumor/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:

Apply now! Pancreatic Cancer Action Network’s 2017 Research Grants Program
https://www.pancan.org/research/grants-program/apply-for-a-pancreatic-cancer-research-grant/
Upcoming deadline:
Early Detection Targeted Grants (will open Dec. 22): Applications due February 22, 2017
We are accepting applications for targeted grants in early detection – for up to $1 million! Please apply today and spread the word. If you or your colleagues do not already receive funding alerts and updates directly from our organization, please email research@pancan.org to be added to our mailing list.

New! 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:

New! 2nd International Conference on Pancreatic Cancer & Liver Diseases
http://pancreas.cmesociety.com/
Meeting: June 12 – 13, 2017, London, UK
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.

New! European Pancreatic Club (EPC) 2017
http://www.epc2017.hu
Meeting: June 28 – July 1, 2017, Budapest, Hungary
Abstract submission deadline: February 25, 2017
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.

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
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
http://pancreasclub.com/annualmeeting/
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_am_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

Aspen Cancer Conference
http://www.aspencancerconference.org/
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.
Other community news:

World-Renowned Surgeon & Researcher to Lead New Pancreatic Cancer Center at NYU Langone
NYU Langone Medical Center has announced that internationally recognized surgeon and scientist Diane M. Simeone, MD, will join its Perlmutter Cancer Center on March 1 to serve as associate director for translational research and to lead its newly established pancreatic cancer center.

AACR Project GENIE Publicly Releases Large Cancer Genomic Data Set
http://www.aacr.org/Newsroom/Pages/News-Release-Detail.aspx?ItemID=994#.WKcpAm8rLIV
The American Association for Cancer Research (AACR) announced the first public release of cancer genomic data aggregated through its initiative known as AACR Project Genomics Evidence Neoplasia Information Exchange (GENIE). The data set includes nearly 19,000 de-identified genomic records collected from patients who were treated at eight international institutions, making it among the largest fully public cancer genomic data sets released to date.

New! 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

Epigenomic Reprogramming During Pancreatic Cancer Progression Links Anabolic Glucose Metabolism to Distant Metastasis

• Journal: Nature Genetics
• Institution(s): Vanderbilt University Medical Center, Nashville, TN, and others
• Corresponding author(s): Andrew Feinberg or Christine Iacobuzio-Donahue
• Pancreatic Cancer Action Network-affiliated authors:
  o Oliver McDonald, MD, PhD: recipient, 2012 The Daniel and Janet Mordecai Foundation – Pathway to Leadership Grant
  o Kathryn Wellen, PhD: recipient, 2014 Career Development Award
  o Christine Iacobuzio-Donahue, MD, PhD: recipient, 2007 Pilot Grant and member, Scientific & Medical Advisory Board
• Major finding: The authors report large-scale reprogramming of chromatin modifications during the natural evolution of distant metastasis. These findings suggest a model whereby linked metabolic-epigenetic programs are selected for enhanced tumorigenic fitness during the evolution of distant metastasis.

Limited Heterogeneity of Known Driver Gene Mutations Among the Metastases of Individual Patients with Pancreatic Cancer
• Journal: Nature Genetics
• Institution(s): Johns Hopkins University School of Medicine, Baltimore, MD, and others
- **Corresponding author(s):** Christine Iacobuzio-Donahue
- **Pancreatic Cancer Action Network-affiliated authors:**
  - Ralph Hruban, MD: member, Emeritus Scientific & Medical Advisory Board
  - Christine Iacobuzio-Donahue, MD, PhD: recipient, 2007 Pilot Grant and member, Scientific & Medical Advisory Board
- **Major finding:** The authors carried out 60× whole-genome sequencing of 26 metastases from four patients with pancreatic cancer. The uniformity of known driver gene mutations among metastases in the same patient has critical and encouraging implications for the success of future targeted therapies in advanced-stage disease.

**Employing Metabolism to Improve the Diagnosis and Treatment of Pancreatic Cancer**
- **Journal:** Cancer Cell
- **Institution(s):** University of Michigan, Ann Arbor, MI
- **Corresponding author(s):** Costas Lyssiotis
- **Pancreatic Cancer Action Network-affiliated authors:** Costas Lyssiotis, PhD: recipient, 2013 Pathway to Leadership Grant
- **Major finding:** In this review, the authors discuss how recent efforts delineating rewired metabolic networks in pancreatic cancer have revealed new in-roads to develop detection and treatment strategies for this dreadful disease.

**PDX1 Dynamically Regulates Pancreatic Ductal Adenocarcinoma Initiation and Maintenance**
- **Journal:** Genes & Development
- **Institution(s):** University of California at San Francisco, San Francisco, CA, and others
- **Corresponding author(s):** Howard Crawford or Matthias Hebrok
- **Pancreatic Cancer Action Network-affiliated authors:**
  - David Dawson, MD, PhD: recipient, 2008 Seena Magowitz – Career Development Award
  - Matthias Hebrok, PhD: recipient, 2011 Abby Sobrato – Innovative Grant and 2008 Michael C. Sandler – Pilot Grant
  - Howard Crawford, PhD: member, Scientific & Medical Advisory Board
- **Major finding:** Here the authors demonstrate diverse functions for pancreatic and duodenal homeobox 1 (PDX1), a transcription factor indispensable for pancreas development, in the progression from normal exocrine cells to metastatic pancreatic ductal adenocarcinoma (PDA). These findings provide insight into the complexity of PDA pathogenesis and advocate a rigorous investigation of therapeutically tractable targets at distinct phases of PDA development and progression.

**Genomic Deletion of Malic Enzyme 2 Confers Collateral Lethality in Pancreatic Cancer**
- **Journal:** Nature
- **Institution(s):** The University of Texas MD Anderson Cancer Center, Houston, TX, and others
- **Corresponding author(s):** Ronald DePinho, Y. Alan Wang or Deepak Nagrath
- **Pancreatic Cancer Action Network-affiliated authors:**
  - Huamin Wang, MD, PhD: recipient, 2007 Skip Viragh – Career Development Award
  - Jason Fleming, MD: co-PI, 2015 Research Acceleration Network Grant and member, Scientific & Medical Advisory Board
  - Giulio Draetta, MD, PhD: PI, 2014 Skip Viragh – Research Acceleration Network Grant
  - Anirban Maitra, MBBS: recipient, 2014 Robert Aronson – Innovative Grant and 2004 Career Development Award and member, Scientific & Medical Advisory Board
• **Major finding:** Mitochondrial malic enzyme deficiency, which results in impaired NADPH production, provides a prime ‘collateral lethality’ therapeutic strategy for the treatment of a substantial fraction of patients diagnosed with this intractable disease.

**Stromal Cues Regulate the Pancreatic Cancer Epigenome and Metabolome**

- **Journal:** PNAS
- **Institution(s):** Salk Institute for Biological Studies, La Jolla, CA, and others
- **Corresponding author(s):** Erik Knudsen or Agnieszka Witkiewicz
- **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 & Medical Advisory Board
  - Alec Kimmelman, MD, PhD: recipient, 2010 Career Development Award
- **Major finding:** The authors’ work suggests the existence of a molecular “AND-gate” such that tumor activation is the consequence of mutant Kras and stromal cues, providing insight into the role of the tumor microenvironment in the origin and treatment of Ras-driven tumors.

**IKBKE Is Required during KRAS-Induced Pancreatic Tumorigenesis**

- **Journal:** Cancer Research
- **Institution(s):** University of Massachusetts Medical School, Worcester, MA, and others
- **Corresponding author(s):** Junhao Mao
- **Pancreatic Cancer Action Network-affiliated authors:**
  - Martin Fernandez-Zapico, MD: recipient, 2007 Carole and Bob Daly – Career Development Award
  - Brian Lewis, PhD: recipient, 2009 Constance Williams – Pilot Grant and 2006 Michael Landon – Career Development Award
- **Major finding:** The authors’ findings highlight the functional importance of the noncanonical IκB-related kinase, IKBKE, in pancreatic cancer, support the evaluation of IKBKE as a therapeutic target in pancreatic ductal adenocarcinoma, and suggest IKBKE inhibition as a strategy to improve efficacy of mTOR inhibitors in the clinic.

**Generation of Patient-derived Xenografts from Fine Needle Aspirates or Core Needle Biopsy**

- **Journal:** Surgery
- **Institution(s):** The University of Texas Health Science Center at Houston, Houston, TX, and others
- **Corresponding author(s):** Jason Fleming
- **Pancreatic Cancer Action Network-affiliated author:** Jason Fleming, MD: co-PI, 2015 Research Acceleration Network Grant and member, Scientific & Medical Advisory Board
- **Major finding:** The authors have found that it is possible to engraft fine needle aspirates and core biopsies of solid tumors in order to generate patient-derived xenografts. This may open up xenografting to a wider cancer patient population than previously possible.

**Alterations of Type II Classical Cadherin Cadherin-10 (CDH10) Is Associated with Pancreatic Ductal Adenocarcinomas**

- **Journal:** Genes, Chromosomes and Cancer
- **Institution(s):** Johns Hopkins Medical Institutions, Baltimore, MD, and others
Corresponding author(s): Shuko Harada
Pancreatic Cancer Action Network-affiliated authors:
- Christine Iacobuzio-Donahue, MD, PhD: recipient, 2007 Pilot Grant and member, Scientific & Medical Advisory Board
- James Eshleman, MD, PhD: recipient, 2011 Innovative Grant
- Ralph Hruban, MD: member, Emeritus Scientific & Medical Advisory Board
- Jonathan Brody, PhD: PI, 2015 Research Acceleration Network Grant and recipient, 2010 Skip Viragh – Career Development Award

Major finding: Taken together, the authors’ data supports the notion that CDH10 is involved in sporadic pancreatic carcinogenesis, and might have a role in rare cases of familial pancreatic cancer. Further functional studies are needed to elucidate the tumor suppressive role of CDH10 in pancreatic carcinogenesis.

Tumour-derived Interleukin 35 Promotes Pancreatic Ductal Adenocarcinoma Cell Extravasation and Metastasis by Inducing ICAM1 Expression
- Journal: Nature Communications
- Institution(s): Tianjin Medical University Cancer Institute and Hospital, Tianjin, China, and others
- Corresponding author(s): He Ren or Jihui Hao
- Major finding: In an orthotopic xenograft model, IL-35 promotes spontaneous pancreatic cancer metastasis in an ICAM1-dependent manner. Together, the authors’ results indicate additional functions of IL-35 in promoting pancreatic ductal adenocarcinoma metastasis through mediating ICAM1 expression.

Pancreatic Cancer Cell Lines as Patient-derived Avatars: Genetic Characterisation and Functional Utility
- Journal: Gut
- Institution(s): University of Arizona, Tucson, AZ, and others
- Corresponding author(s): Erik Knudsen or Agnieszka Witkiewicz
- Major finding: These data illustrate that with the appropriate methods it is possible to develop cell lines that maintain genetic features of pancreatic ductal adenocarcinoma. Such models serve as important substrates for analyzing the significance of genetic variants and create a unique biorepository of annotated cell lines and xenografts that were established simultaneously from same primary tumor. These models can be used to infer genetic and empirically determined therapeutic sensitivities that would be germane to the patient.

Pancreatic Cancer: PDAC Metastases Show Identical Known Driver Gene Mutations
- Journal: Nature Reviews Gastroenterology & Hepatology
- Institution(s): Nature editorial offices, London, UK
- Corresponding author(s): Iain Dickson
- Major finding: In new research published in Nature Genetics, sequencing of treatment-naive metastases from patients with pancreatic ductal adenocarcinoma (PDAC) has revealed identical known driver gene mutations in all lesions from each patient. These findings could have important clinical implications for future therapies in advanced-stage PDAC.

Oncogenes: Coping with Stress
Major finding: Adapting to stress helps tumor cells expressing mutant KRAS to survive and proliferate in adverse conditions and promotes the resistance of these cells to chemotherapy.

Tumour Metabolism: Packed Full of Protein!

Major finding: Altered metabolism promotes the uncontrolled growth of tumors. An important mechanism by which pancreatic cancer cells might achieve this is through the uptake and breakdown of extracellular protein, via macropinocytosis, as a source of amino acids for metabolism.

Pancreatic Cancer: Pancreatic Tumours Derive Amino Acids via Extracellular Protein Uptake

Major finding: Spontaneously arising pancreatic tumors in mice source amino acids from the extracellular environment, according to new research published in the journal *Nature Medicine*. Using microdevices implanted into pancreatic tumors, the researchers show that local inhibition of macropinocytosis reduces amino acid levels in tumor cells but not adjacent healthy tissue.

Tumors Block Pain with CXCL12

Major finding: The chemokine CXCL12 released from early stage pancreatic cancer recruits Schwann cells and suppresses pain signaling.

ETIOLOGY

Rapid Diabetes Deterioration -- Sign of Pancreatic Cancer?
Searchable meeting program: http://www.eccocongress.org/Scientific-Programme/Searchable-Programme#anchorScpr

Meeting: European Cancer Congress 2017
Institution(s): International Prevention Research Institute, Lyon, France
Corresponding author(s): Philippe Autier
- Major finding: Aggravation of diabetes and start of new therapies seem to be an early signal for pancreatic cancer diagnosis for some patients. Thus, use of prescription databases could help develop methodologies which could help identify patients prone to develop a pancreatic cancer in an earlier stage, and also raise awareness for clinicians about diabetes treatment patterns and their relationship with pancreatic cancer.

**Influence of Statins and Cholesterol on Mortality Among Patients with Pancreatic Cancer**


- **Journal:** Journal of the National Cancer Institute
- **Institution(s):** Kaiser Permanente Southern California, Pasadena, CA, and others
- **Corresponding author(s):** Bechien Wu
- **Major finding:** Statin use rather than cholesterol level was associated with lower mortality risk in patients with pancreatic cancer. Statins appear to improve survival through a lipid-independent mechanism.

**Diabetes, Plasma Glucose and Incidence of Pancreatic Cancer: A Prospective Study of 0.5 Million Chinese Adults and a Meta-analysis of 22 Cohort Studies**


- **Journal:** International Journal of Cancer
- **Institution(s):** University of Oxford, Oxford, UK, and others
- **Corresponding author(s):** Christiana Kartsonaki
- **Major finding:** In Chinese and non-Chinese populations, diabetes and higher blood glucose levels among those without diabetes are associated with an increased risk of pancreatic cancer.

**Serum C-peptide, Total and High Molecular Weight Adiponectin, and Pancreatic Cancer: Do Associations Differ by Smoking?**


- **Journal:** Cancer Epidemiology, Biomarkers & Prevention
- **Institution(s):** National Cancer Institute, Rockville, MD, and others
- **Corresponding author(s):** Rachael Stolzenberg-Solomon
- **Major finding:** Associations of biomarkers of insulin secretion and sensitivity with pancreatic ductal adenocarcinoma differ by smoking status. Smoking-induced pancreatic damage may explain the associations in smokers while mechanisms related to insulin resistance associations in non-smokers.

**Dietary Patterns and Pancreatic Cancer Risk: A Meta-Analysis**


- **Journal:** Nutrients
- **Institution(s):** Zhejiang Hospital, Hangzhou, China
- **Corresponding author(s):** Xu-Jiao Chen
- **Major finding:** The results of this meta-analysis demonstrate that healthy and light–moderate drinking patterns may decrease the risk of pancreatic cancer, whereas western-type and heavy drinking patterns may increase the risk of pancreatic cancer. Additional prospective studies are needed to confirm these findings.
EARLY DETECTION, DIAGNOSIS, AND PROGNOSIS

Metabolic Biomarker Signature to Differentiate Pancreatic Ductal Adenocarcinoma from Chronic Pancreatitis
- **Journal**: Gut
- **Institution(s)**: University Medicine, Ernst-Moritz-Arndt-University Greifswald, Greifswald, Germany, and others
- **Corresponding author(s)**: Markus Lerch
- **Major finding**: In patients with chronic pancreatitis with an increased risk for pancreatic cancer, the performance of this metabolite biomarker signature results in a negative predictive value of 99.9% (training set) and 99.8% (test set). In one third of the authors’ patients, the clinical use of this biomarker signature would have improved diagnosis and treatment stratification in comparison to CA19-9.

Factors Associated with Invasive Intraductal Papillary Mucinous Carcinoma of the Pancreas
- **Journal**: JAMA Surgery
- **Institution(s)**: Wakayama Medical University, Wakayama, Japan, and others
- **Corresponding author(s)**: Hiroki Yamaue
- **Major finding**: The measurement of mural nodule size in all types of carcinomas and carcinoembryonic antigen level in the pancreatic juice in mixed and main duct carcinomas might play important roles in predicting invasive intraductal papillary mucinous carcinoma, but further large studies are needed to confirm these results.

Detection of Mutant KRAS and TP53 DNA in Circulating Exosomes from Healthy Individuals and Patients with Pancreatic Cancer
- **Journal**: Cancer Biology & Therapy
- **Institution(s)**: University of Texas MD Anderson Cancer Center, Houston, TX, and others
- **Corresponding author(s)**: Raghu Kalluri
- **Major finding**: This study highlights the value of circulating exosomal DNA for a rapid, low-cost identification of cancer driving mutations. The identification of mutations in intraductal papillary mucinous neoplasm patients and healthy subjects suggests that liquid biopsies may allow potential assessment of cancer risk but with a cautionary note that detection of clinical cancer cannot be assumed.

TREATMENT

Comparison of Adjuvant Gemcitabine and Capecitabine with Gemcitabine Monotherapy in Patients with Resected Pancreatic Cancer (ESPAC-4): A Multicentre, Open-label, Randomised, Phase 3 Trial
- **Journal**: The Lancet
- **Institution(s)**: University of Liverpool, Liverpool, UK, and others
- **Corresponding author(s)**: John Neoptolemos
- **Major finding**: The ESPAC-3 trial showed that adjuvant gemcitabine is the standard of care based on similar survival to and less toxicity than adjuvant 5-fluorouracil/folinic acid in patients with resected pancreatic cancer. The authors conclude that the adjuvant combination of gemcitabine
and capcitabine should be the new standard of care following resection for pancreatic ductal adenocarcinoma.

Five-Year Actual Overall Survival in Resected Pancreatic Cancer: A Contemporary Single-Institution Experience from a Multidisciplinary Perspective
- **Journal:** Annals of Surgical Oncology
- **Institution(s):** Virginia Mason Medical Center, Seattle, WA, and others
- **Corresponding author(s):** Vincent Picozzi
- **Pancreatic Cancer Action Network-affiliated authors:**
  - Vincent Picozzi, MD: Chair and PI, Clinical Trial Consortium and member, Scientific & Medical Advisory Board
  - Margaret Mandelson, PhD: member, Emeritus Scientific & Medical Advisory Board
- **Major finding:** The actual overall survival rates for resected pancreatic cancer shown in this study are reflective of those currently achievable at a tertiary medical center dedicated to this patient population. In considering these results, both frequency and type of adjuvant/neoadjuvant therapy administered in the context of the clinical experience/management techniques of providers administering these treatments will be discussed.

Influence of Preoperative Therapy on Short- and Long-Term Outcomes of Patients with Adenocarcinoma of the Ampulla of Vater
- **Journal:** Annals of Surgical Oncology
- **Institution(s):** The University of Texas MD Anderson Cancer CenterHouston
- **Corresponding author(s):** Matthew Katz
- **Pancreatic Cancer Action Network-affiliated authors:**
  - Huamin Wang, MD, PhD: recipient, 2007 Skip Viragh – Career Development Award
  - Eugene Koay, MD, PhD: recipient, 2014 Skip Viragh – Career Development Award
  - Anirban Maitra, MBBS: recipient, 2014 Robert Aronson – Innovative Grant and 2004 Career Development Award and member, Scientific & Medical Advisory Board
  - Jason Fleming, MD: co-PI, 2015 Research Acceleration Network Grant and member, Scientific & Medical Advisory Board
- **Major finding:** Although these data do not support the routine administration of preoperative therapy to all patients with ampullary cancer, the delivery of preoperative therapy represents an alternative strategy that is associated with excellent short- and long-term outcomes and appears appropriate for a subset of patients.

Tumor-Derived CCL2 Mediates Resistance to Radiotherapy in Pancreatic Ductal Adenocarcinoma
- **Journal:** Clinical Cancer Research
- **Institution(s):** University of Pennsylvania, Philadelphia, PA
- **Corresponding author(s):** Gregory Beatty
- **Pancreatic Cancer Action Network-affiliated author:** Gregory Beatty, MD, PhD: recipient, 2015 Career Development Award and co-PI, Precision Promise Clinical Trial Consortium site
- **Major finding:** Pancreatic ductal adenocarcinoma (PDAC) responds to radiotherapy by producing CCL2, which recruits Ly6C⁺CCR2⁺ monocytes to support tumor proliferation and neovascularization after radiotherapy. Disrupting the CCL2-CCR2 axis in combination with radiotherapy holds promise for improving radiotherapy efficacy in PDAC.

Improving Chimeric Antigen Receptor-Modified T Cell Function by Reversing the Immunosuppressive Tumor Microenvironment of Pancreatic Cancer
Molecular Therapy

Institution(s): Baylor College of Medicine, Houston, TX, and others

Corresponding author(s): Juan Vera

Pancreatic Cancer Action Network-affiliated authors:
  - William Fisher, MD: co-PI, 2016 Translational Research Grant
  - Ann Leen, PhD: PI, 2016 Translational Research Grant

Major finding: To target pancreatic cancer, the authors generated CAR T cells directed against prostate stem cell antigen (PSCA) and demonstrated specific tumor lysis. To protect their cells from the immunosuppressive cytokine IL-4, the authors generated an inverted cytokine receptor in which the IL-4 receptor exodomain was fused to the IL-7 receptor endodomain (4/7 ICR). These findings support the benefit of combining the 4/7 ICR with CAR-PSCA to treat pancreatic cancer, a PSCA-expressing tumor characterized by a dense immunosuppressive environment rich in IL-4.

Systematic Review on the Treatment of Isolated Local Recurrence of Pancreatic Cancer After Surgery; Re-resection, Chemoradiotherapy and SBRT

HPB

Institution(s): University Medical Center Utrecht Cancer Center, The Netherlands, and others

Corresponding author(s): I. Quintus Molenaar

Pancreatic Cancer Action Network-affiliated authors: Joseph Herman, MD, MSc: recipient, 2008 Blum-Kovler – Career Development Award and member, Scientific & Medical Advisory Board

Major finding: In selected patients, treatment of isolated local recurrence following pancreatic resection for pancreatic cancer seems safe, feasible and associated with relatively good survival.

Preclinical Rationale for the Phase III Trials in Metastatic Pancreatic Cancer: Is Wishful Thinking Clouding Successful Drug Development for Pancreatic Cancer?

Pancreas

Institution(s): Vanderbilt University, Nashville, TN, and others

Corresponding author(s): Jordan Berlin

Pancreatic Cancer Action Network-affiliated authors:
  - Jordan Berlin, MD: member, Scientific & Medical Advisory Board
  - Anirban Maitra, MBBS: recipient, 2014 Robert Aronson – Innovative Grant and 2004 Career Development Award and member, Scientific & Medical Advisory Board

Major finding: In this review, the authors attempt to understand how past preclinical data were translated into phase III clinical trials in metastatic pancreatic cancer as described in the article. It remains uncertain how strongly the preclinical data influence the development of clinical regimens but so far the studies developed based on more solid preclinical evidence have been successful.

Macropinocytosis of Nab-paclitaxel Drives Macrophage Activation in Pancreatic Cancer

Cancer Immunology Research

Institution(s): New York University School of Medicine, New York, NY, and others

Corresponding author(s): Dafna Bar-Sagi

Pancreatic Cancer Action Network-affiliated authors:
  - Anirban Maitra, MBBS: recipient, 2014 Robert Aronson – Innovative Grant and 2004 Career Development Award and member, Scientific & Medical Advisory Board
Dafna Bar-Sagi, PhD: recipient, 2014 Innovative Grant and 2008 Pilot Grant, co-PI, 2013 Tempur-Pedic – Inaugural Research Acceleration Network Grant in memory of Tim Miller and member, Scientific & Medical Advisory Board

- **Major finding:** Nab-paclitaxel was internalized by tumor-associated macrophages *in vivo*, and therapeutic doses of nab-paclitaxel alone, and in combination with gemcitabine, increased the MHCI•CD80•CD86+ M1 macrophage population. These data revealed an unanticipated role for nab-paclitaxel in macrophage activation and rationalized its potential use to target immune evasion in pancreatic cancer.

**Resveratrol and Capsaicin Used Together as Food Complements Reduce Tumor Growth and Rescue Full Efficiency of Low Dose Gemcitabine in a Pancreatic Cancer Model**


- **Journal:** Cancer Letters
- **Institution(s):** INSERM, Bordeaux, France
- **Corresponding author(s):** Sandrine Dabernat
- **Major finding:** The authors hypothesized that combined actions of several Bioactive Food Components (BFCs) might provide specific lethal effect towards tumor cells, sparing healthy cells. Human tumor pancreatic cell lines were tested in vitro for sensitivity to resveratrol, capsaicin, piceatannol, and sulforaphane cytotoxic effects. This study raises the possibility to use BFCs as beneficial food complements in the therapy of pancreatic adenocarcinoma, especially for patients unable to receive full doses of chemotherapy.

**Type of Resection (Whipple vs. Distal) Does Not Affect the National Failure to Provide Post-resection Adjuvant Chemotherapy in Localized Pancreatic Cancer**


- **Journal:** Annals of Surgical Oncology
- **Institution(s):** Mayo Clinic, Rochester, MN
- **Corresponding author(s):** Mark Truty
- **Major finding:** Receipt of adjuvant chemotherapy did not vary by type of resection but improved survival independent of procedure performed. Factors other than type of resection appear to be driving the nationwide rates of post-resection adjuvant chemotherapy in localized pancreatic ductal adenocarcinoma.

**Targeted Co-delivery of PTX and TR3 siRNA by PTP Peptide Modified Dendrimer for the Treatment of Pancreatic Cancer**


- **Journal:** Small
- **Institution(s):** Zhejiang University, Hangzhou, China, and others
- **Corresponding author(s):** Guping Tang
- **Major finding:** A new type of tumor-targeted nanovehicle peptide-conjugated PSPG (PSPGP) is successfully synthesized for co-delivery of paclitaxel (PTX) and TR3 small interfering RNA (siRNA). In vitro and in vivo investigations demonstrate that the redox-responsive PSPGP exhibit enhanced endosomal escape and intracellular degradation, which facilitate PTX and TR3 siRNA release, effectively improving the antitumor efficacy.

**Dual Enzymatic Reaction-Assisted Gemcitabine Delivery Systems for Programmed Pancreatic Cancer Therapy**


- **Journal:** ACS Nano
- **Institution(s):** Zhejiang University, Hangzhou, China, and others
- **Corresponding author(s):** Qiao Jin or Jian Ji
• **Major finding:** Compared to free gemcitabine (GEM), the deamination of GEM nanovectors into inactive 2',2'-difluorodeoxyuridine (dFdU) could be greatly suppressed, while the concentration of the activated form of GEM (gemcitabine triphosphate, dFdCTP) was significantly increased in tumor tissue, thus exhibiting superior tumor inhibition activity with minimal side effects.

**Fibroblast Drug Scavenging Increases Intratumoural Gemcitabine Accumulation in Murine Pancreas Cancer**


• **Journal:** Gut
• **Institution(s):** University Medical Centre Goettingen, Goettingen, Germany, and others
• **Corresponding author(s):** Albrecht Neesse
• **Major finding:** The authors’ findings suggest that fibroblast drug scavenging may contribute to the clinical failure of gemcitabine in desmoplastic pancreatic ductal adenocarcinoma. Metabolic targeting of cancer-associated fibroblasts may thus be a promising strategy to enhance the antiproliferative effects of gemcitabine.

**Structural Diversity of Anti-Pancreatic Cancer Capsimycins Identified in Mangrove-derived Streptomyces Xiamenensis 318 and Post-Modification via a Novel Cytochrome P450 Monooxygenase**


• **Journal:** Scientific Reports
• **Institution(s):** Shanghai Jiao Tong University, Shanghai, China
• **Corresponding author(s):** Jun Xu or Min-Juan Xu
• **Major finding:** Polycyclic tetramate macrolactams (PTMs) were identified as distinct secondary metabolites of the mangrove-derived Streptomyces xiamenensis 318. Together with three known compounds—ikarugamycin (1), capsimycin (2) and capsimycin B (3)—two new compounds, capsimycin C (4) with trans-diols and capsimycin D (5) with trans-configurations at C-13/C-14, have been identified. Compounds 1–3 exhibited anti-proliferative activities against pancreatic carcinoma with IC₅₀ values of 1.30–3.37 μM.

**Pancreatic Cancer: Are More Chemotherapy and Surgery Needed?**


**Comment on:** https://www.ncbi.nlm.nih.gov/pubmed/28129987 (above)

• **Journal:** The Lancet
• **Institution(s):** Hôpital Riviera-Chablais, Vevey, Switzerland, and others
• **Corresponding author(s):** Gaël Deplanque
• **Major finding:** We clearly need to provide more surgery for patients especially those with R0 resections since this is the population benefitting most from postoperative chemotherapy in ESPAC-4 with a median survival of 27-9 months in the gemcitabine group, reaching 39-5 months in the combination group versus 23-0 months in the gemcitabine group and 23-7 months in the combination group in R1 patients.

**Targeted Stroma in Pancreatic Cancer: Promises and Failures of Target Therapies**


• **Journal:** Journal of Cellular Physiology
• **Institution(s):** Mashhad University of Medical Sciences, Mashhad, Iran
• **Corresponding author(s):** Seyed Mahdi Hassanian or Amir Avan
• **Major finding:** This review summarizes the current knowledge about pancreatic stellate cells, targeting stroma compartments with particular emphasis on preclinical and clinical trials on targeting of stroma as an option in pancreatic cancer treatment.
Pancreatic Cancer Blocked from Invading Nearby Nerves
Commentary on: https://www.ncbi.nlm.nih.gov/pubmed/27792755
- **Journal:** JAMA
- **Institution(s):** n/a
- **Corresponding author(s):** Tracy Hampton
- **Major finding:** Blocking chemical signals between pancreatic cancer cells and neurons may reduce the cancer cells’ ability to invade surrounding nerves, according to a *PLOS ONE* study. Such perineural invasion may contribute to the high recurrence rate following removal of a pancreatic tumor.

The RAS-Effector Interaction as a Drug Target
- **Journal:** Cancer Research
- **Institution(s):** University of South Alabama, Mobile, AL, and others
- **Corresponding author(s):** Adam Keeton
- **Major finding:** Although RAS proteins are often said to be “undruggable,” there is mounting evidence suggesting it may be feasible to develop direct inhibitors of RAS proteins. Here, the authors review this evidence with a focus on compounds capable of inhibiting the interaction of RAS proteins with their effectors that transduce the signals of RAS and that drive and sustain malignant transformation and tumor growth. These reports of direct-acting RAS inhibitors provide valuable insight for further discovery and development of clinical candidates for RAS-driven cancers involving mutations in RAS genes or otherwise activated RAS proteins.

**News from GI ASCO:**

**CCR2 Blockade Holds Clinical Promise in Advanced or Metastatic Pancreatic Cancer**
- **Abstract:** [http://meetinglibrary.asco.org/content/176997-195](http://meetinglibrary.asco.org/content/176997-195)
- **Meeting:** 2017 Gastrointestinal Cancers Symposium
- **Institution(s):** University of Rochester Medical Center, Rochester, NY, and others
- **Presenting author(s):** Marcus Smith Noel
- **Pancreatic Cancer Action Network-affiliated authors:**
  - Aram Hezel, MD: recipient, 2005 Samuel Stroum – Young Investigator Award
  - David Linehan, MD: PI, 2016 The Shirley Sadoff – Research Acceleration Network-2 Grant and recipient, 2015 Translational Research Grant
  - Andrea Wang-Gillam, MD, PhD: PI, Precision Promise Clinical Trial Consortium site
- **Major finding:** CCX872-B, a potent, selective oral inhibitor of CCR2, added to FOLFIRINOX (5-fluorouracil, leucovorin, irinotecan, and oxaliplatin) was associated with a tumor control rate of 78% at week 12 in a single-arm study of patients with locally advanced or metastatic pancreatic cancer.

**Adding Platinum to Standard of Care Improves Response Rate in Stage IV Pancreatic Cancer**
- **Abstract:** [http://meetinglibrary.asco.org/content/175849-195](http://meetinglibrary.asco.org/content/175849-195)
- **Meeting:** 2017 Gastrointestinal Cancers Symposium
- **Institution(s):** HonorHealth/TGen, Scottsdale, AZ, and others
- **Presenting author(s):** Gayle Jameson
Major finding: Adding a platinum to standard gemcitabine and nab-paclitaxel led to impressive responses and overall survival (OS) rates in a small pilot trial in patients with stage IV pancreatic cancer.

Chemotherapy/Immunotherapy Regimen Active in Treated, Untreated Pancreatic Cancer

Abstract: http://meetinglibrary.asco.org/content/174707-195
- Meeting: 2017 Gastrointestinal Cancers Symposium
- Institution(s): University of California, Los Angeles, Medical Center, Los Angeles, CA, and others
- Presenting author(s): Zev Wainberg
- Major finding: Encouraging clinical activity with limited toxicity in patients with metastatic pancreatic cancer will lead to further evaluation of nivolumab (Opdivo) plus nab-paclitaxel with gemcitabine, investigators reported.

Phase 2 Trials in Pancreatic Cancer: Missing the Mark

Abstract: http://meetinglibrary.asco.org/content/176314-195
- Meeting: 2017 Gastrointestinal Cancers Symposium
- Institution(s): Prince of Wales Hospital, Randwick, Australia, and others
- Presenting author(s): Monica Tang
- Major finding: Many new agents show promise in phase 2 pancreatic cancer studies, but the promise all too often fizzles out during phase 3 trials. And that's if they even make it to the phase 3 level. Despite a great number of phase 2 studies, only 15% have gone on to phase 3 for the treatment of locally advanced and metastatic pancreatic cancer.

Meeting Slides: 2017 Gastrointestinal Cancers Symposium
http://shop.asco.org/gisl17_meeting-slides-2017-gastrointestinal-cancers-symposium/?cmpid=ts_gi_mtgslides_etoc_all_01-24-17_mtgslides

Do you need to download the slides from the 2017 Gastrointestinal Cancers Symposium (GI) presentations? The Meeting Slide Library provides you the ability to download all the slides that are included in the 2017 GI Virtual Meeting presentations. The slides are high-resolution images suitable for use in your presentations.

Industry news:

Halozyme Announces Phase 2 Study in Advanced Pancreas Cancer Meets Key Endpoints
- Company: Halozyme Therapeutics, Inc., San Diego, CA
- Major finding: Halozyme Therapeutics, Inc. reported topline results from the combined analysis of Stages 1 and 2 and Stage 2 alone of its HALO 202 study, a Phase 2 randomized, multi-center clinical trial of lead investigational drug PEGPH20 in combination with ABRAXANE® (nab-paclitaxel) and gemcitabine in stage IV pancreas cancer patients. PEGPH20 is an investigational PEGylated form of Halozyme's proprietary recombinant human hyaluronidase under clinical development for the potential systemic treatment of tumors that accumulate hyaluronan.
Celyad Announces Registration of the First Pancreatic Cancer Patient in its CAR-T NKR-2 THINK Trial in Belgium


- **Company:** Celyad, Mont-Saint-Guibert, Belgium
- **Major finding:** Celyad, a leader in the discovery and development of engineered cell-based therapies, announced the activation of a second clinical site in Belgium for the THINK trial, with the registration of a pancreatic cancer patient at Cliniques Universitaires Saint-Luc (UCL). THINK (THerapeutic Immunotherapy with NKR-2) is a multinational (EU/US) open-label Phase Ib study to assess the safety and clinical activity of multiple administrations of autologous CAR-T NKR-2 cells in seven refractory cancers, including five solid tumors (colorectal, ovarian, bladder, triple-negative breast and pancreatic cancers) and two hematological tumors (acute myeloid leukemia and multiple myeloma).

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

Cancer Statistics, 2017


- **Journal:** CA: A Cancer Journal for Clinicians
- **Institution(s):** American Cancer Society, Atlanta, GA
- **Corresponding author(s):** Rebecca Siegel
- **Major finding:** Each year, the American Cancer Society estimates the numbers of new cancer cases and deaths that will occur in the United States in the current year and compiles the most recent data on cancer incidence, mortality, and survival.