PANCREATIC CANCER NEWS & UPDATES – APRIL 2012

PANCREATIC CANCER ACTION NETWORK AND COMMUNITY NEWS

Share your federal funding experiences: Help our advocacy efforts

http://www.pancan.org/section_research/resources_for_scientists/form_funding_experiences.php

Have you struggled to receive grants from the NCI or other federal institutions? Have you been successful? We're looking for information to help us understand what is working well for pancreatic cancer researchers and what could be improved (including, but not limited to, funding levels). We will use this information in our public policy efforts. Please click above and share your stories (they can be submitted anonymously).

Funding opportunities: FY12 Peer Reviewed Cancer Research Program (PRCRP)

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

Visionary Postdoctoral Fellow Award: http://cdmrp.army.mil/funding/pa/12prcrpvpfa_pa.pdf

Career Development Award: http://cdmrp.army.mil/funding/pa/12prcrpcda_pa.pdf

The Congressionally Directed Medical Research Programs at the Department of Defense announced 2012 cancer funding opportunities. Both funding mechanisms' program announcements (linked above) include pancreatic cancer as a topic area. Pre-application deadlines are June 19 for both types of grants.

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."

Funding opportunity: Caring for Carcinoid Foundation-AACR Grant: Pancreatic Neuroendocrine Tumor

http://www.aacr.org/home/scientists/aacr-research-funding/current-funding-opportunities-for-independent-researchers.aspx#CFCF

The application deadline is June 16, 2012 for the Caring for Carcinoid Foundation-AACR Grant for Carcinoid Tumor and Pancreatic Neuroendocrine Tumor Research grants. Please click the above link for eligibility criteria and additional information.

Call for abstracts - APA/IAP Joint Annual Meeting

http://www.american-pancreatic-association.org/index.php?option=com_content&view=article&id=34&Itemid=38

The 2012 Annual Meeting of the American Pancreatic Association (APA) will be held jointly with the International Association of Pancreatology (IAP), and will take place at the Eden Roc Renaissance in Miami Beach, FL, October 31 – November 3, 2012. Abstract submission is now open, and the deadline is Monday, June 25, 2012. The young investigator travel award application (http://www.american-pancreatic-association.org/index.php?option=com_content&view=article&id=28&Itemid=26) is also due on June 25.

Finding hope in the fight against pancreatic cancer

http://www.huffingtonpost.com/terrence-meck/pancreatic-cancer-action-network_b_1397079.html

Pancreatic Cancer Action Network Board of Directors member Terrence Meck wrote this heartfelt piece for the *Huffington Post* following his experiences at Community Outreach Leadership Training and his first official Board meeting.

BIOLOGY OF CANCER

Oncogenic Kras maintains pancreatic tumors through regulation of anabolic glucose metabolism

http://www.ncbi.nlm.nih.gov/pubmed/22541435

Pancreatic Cancer Action Network write-up:
http://www.pancan.org/section_research/strategic_research_program/news/topic_new_role_discovered_for_protein.php

Dana-Farber press release: http://www.dana-farber.org/Newsroom/News-Releases/advanced-pancreatic-tumors-depend-on-continued-oncogene-activity.aspx

Alec Kimmelman, MD, PhD (2010 Career Development Award) is co-corresponding author on this important publication in *Cell*. Another author on the paper is Aram Hezel, MD (2005 Samuel Stroum Young Investigator Award). The paper describes an inducible model of K-Ras driven pancreatic cancer, whereby mutant K-Ras expression can be turned off once the tumor forms. A novel finding was that mutant K-Ras drives glucose intermediates towards the hexosamine biosynthesis and pentose phosphate pathways, revealing potential therapeutic targets.

The deubiquitinase USP9X suppresses pancreatic ductal adenocarcinoma

http://www.nature.com/nature/journal/vaop/ncurrent/full/nature11114.html

CRUK press release: http://info.cancerresearchuk.org/news/archive/pressrelease/2012-04-29-pancreatic-cancer-treatment-hope?view=n-and-r-homepage

This *Nature* paper is out of the laboratory of Dave Tuveson, MD, PhD (2003 Career Development Award and Emeritus Scientific Advisory Board), and includes collaboration from Ralph Hruban, MD (Emeritus Scientific Advisory Board) and Christine Iacobuzio-Donahue, MD, PhD (2007 Pilot Grant and Scientific Advisory Board). This study has picked up a great deal of media attention. Dr. Tuveson and colleagues utilized the *Sleeping Beauty* transposon system to introduce interruptions of various genes in a mutant K-Ras driven mouse model of pancreatic cancer. They found that loss of *Usp9x* enhanced transformation of pancreas cells and protected from anoikis. The authors hypothesize that *Usp9x* is modified by epigenetic regulation, likely methylation.

NF-κB pathway-mediated positive feedback loop amplifies Ras activity to pathological levels in mice
http://www.ncbi.nlm.nih.gov/pubmed/22406536
Craig Logsdon, PhD (Scientific Advisory Board) is the senior author on this *JCI* article, which also features Huamin Wang, MD, PhD (2007 Skip Viragh Career Development Award). The team at MD Anderson report that, in the presence of physiological levels of oncogenic K-Ras, inflammation stimulation involving NF-κB pushes mutant K-Ras to pathological levels, facilitating formation of PanINs.

Intratumoral delivery of CpG-conjugated anti-MUC1 antibody enhances NK cell anti-tumor activity
http://www.ncbi.nlm.nih.gov/pubmed/22543528
This study was conducted in the laboratory of Pinku Mukherjee, PhD (2007 Pilot Grant), and addresses the potential of utilizing antibody-directed cellular toxicity as a treatment strategy for pancreatic cancer. Dr. Mukherjee and colleagues coated pancreatic cancer cells with an antibody targeting mucin-1, and then determined that the presence of both natural killer cells and macrophages was necessary to elicit cell killing.

Acquisition of resistance of pancreatic cancer cells to 2-methoxyestradiol
http://www.ncbi.nlm.nih.gov/pubmed/22547077
This *Molecular Cancer Research* article describes a potential mechanism of pancreatic cancer cells' drug resistance. In the investigators' model, pancreatic cancer cells were exposed to 2-methoxyestradiol to induce reactive oxygen species. Over time, the cells developed resistance, and the authors determined that the mitochondrial protein manganese superoxide dismutase was upregulated in the resistant cells, suggesting its role in the detoxification of reactive oxygen species generated by the drug. Consistent with this hypothesis, inhibiting manganese superoxide dismutase led to the cells being sensitive to 2-methoxyestradiol again.

BART inhibits pancreatic cancer cell invasion by PKCα inactivation through binding to ANX7
http://www.ncbi.nlm.nih.gov/pubmed/22532868
Published in *PLoS One*, this paper looks at the binder of Arl two (BART) protein and its role in inhibiting invasion of pancreatic cancer cells. The authors' data suggest that BART binds to the GTPase annexin7 (ANX7), which then blocks the activity of PKC and inhibits cell invasion.

Cysteamine suppresses invasion, metastasis and prolongs survival by inhibiting MMPs
http://www.ncbi.nlm.nih.gov/pubmed/22532830
The experiments for this *PLoS One* paper were conducted at the FDA. Cysteamine is an anti-oxidant aminothiol that is commonly used to treat nephropathic cystinosis, and has also been shown to have chemo-sensitization and radioprotection properties. Here, the research team determined that cysteamine inhibited invasion and metastasis in a xenograft mouse model of pancreatic cancer, via decreasing the activity of matrix metalloproteinases (MMPs).

CDK-4 inhibitor P276 sensitizes pancreatic cancer cells to gemcitabine induced apoptosis
http://www.ncbi.nlm.nih.gov/pubmed/22532602
This *Molecular Cancer Therapeutics* article is out of University of Kansas Medical Center. The researchers explore a novel cyclin dependent kinase (CDK) inhibitor, P276. Their data suggest that P276 sensitizes pancreatic cancer cells to gemcitabine, via inhibition of the PI3K/Akt/mTor signaling cascade.

Involvement of the mitochondrial pathway in bruceine D-induced apoptosis
http://www.ncbi.nlm.nih.gov/pubmed/22552257
Researchers at the Chinese Institute of Hong Kong extracted bruceine D, a quassinoid, out of a commonly used Chinese medicinal herb called B. javanica. Their data suggest that bruceine D blocks proliferation and induces cell death specifically of the Capan-2 pancreatic cancer cell line, without similar effects in a hepatocyte cell line or normal pancreas cells.

ETIOLOGY

Dietary fructose, carbohydrates, glycemic indices and pancreatic cancer risk
http://www.ncbi.nlm.nih.gov/pubmed/22539563
American Institute for Cancer Research blog: http://blog.aicr.org/2012/05/02/carbs-and-pancreatic-cancer-why-null-findings-matter/
Published in *Annals of Oncology*, this meta-analysis looks at cohort studies that studied the link between dietary carbohydrates, glycemic load, and glycemic index, and pancreatic cancer. Based on the ten cohort studies that were analyzed, the authors did not find a link between risk of pancreatic cancer and diets high in glycemic index, glycemic load, total carbohydrates, or sucrose. A potential link with fructose intake will warrant further studies.

Nicotine, IFN-gamma and retinoic acid mediated induction of MUC4 requires E2F1 and STAT-1
http://www.ncbi.nlm.nih.gov/pubmed/22537161
This *Molecular Cancer* paper explores a potential mechanism by which smoking can contribute to the development of pancreatic cancer. The authors found that interferon-gamma and retinoic acid could collaborate with nicotine in elevating the expression of the transmembrane mucin MUC4, a protein involved in the progression and invasion of pancreatic cancer.

PREVENTION

Atorvastatin inhibits pancreatic carcinogenesis and increases survival
http://www.ncbi.nlm.nih.gov/pubmed/22549877
This *Molecular Carcinogenesis* paper out of Northwestern University discusses use of the HMG-CoA reductase inhibitor atorvastatin as a chemopreventive agent against pancreatic cancer. Atorvastatin was administered to LSL-Kras(G12D) -LSL-Trp53(R172H)-Pdx1-Cre mice, which are genetically programmed to develop pancreatic cancer. Indeed, mice treated with atorvastatin showed reductions in tumor volume and proliferation, and enhanced survival.

EARLY DETECTION, DIAGNOSIS, AND PROGNOSIS

Frequent detection of pancreatic lesions in asymptomatic high-risk individuals
http://www.ncbi.nlm.nih.gov/pubmed/22245846
Johns Hopkins press release:
http://www.hopkinsmedicine.org/news/media/releases/detectable_pancreatic_lesions_common_in_people_at_high_risk_for_hereditary_pancreatic_cancer
Mimi Canto, MD (Medical Advisory Board) led a multi-institutional and multi-disciplinary team that also included Ralph Hruban, MD (Emeritus Scientific Advisory Board) and Gloria Petersen, PhD (Scientific Advisory Board). The study explores screening strategies for individuals at high risk for developing pancreatic adenocarcinoma. The data suggest that small precancerous cysts are frequently detected in

asymptomatic high risk individuals, and these cysts are often curable. Endoscopic ultrasound and MRI were found to be superior detection modalities when compared to CT.

Mucin 16 expression in human tissues and cell lines and correlation with clinical outcome
http://www.ncbi.nlm.nih.gov/pubmed/22542127
Included among the authors on this *Human Pathology* study is Anirban Maitra, MD (2004 Career Development Award and member, Scientific Advisory Board). This study evaluates mucin 16 (also known as cancer antigen 125), used as a biomarker for ovarian cancer detection and progression, in adenocarcinomas of the pancreas, esophagus, stomach, and colon. Mucin 16 expression proved to have a strong, independent association with poor prognosis in pancreatic cancer.

The protein survivin could be a useful biomarker for pancreatic cancer
http://medicalxpress.com/news/2012-04-protein-survivin-biomarker-pancreatic-cancer.html
AACR abstract: http://www.abstractsonline.com/Plan/ViewAbstract.aspx?sKey=6460248f-0b47-40b8-81bb-ed0702ab40e0&cKey=3dae0f5f-e9d6-4d12-8f9e-9ab9f8beb102&mKey=%7b2D8C569E-B72C-4E7D-AB3B-070BEC7EB280%7d
Presented at the American Association for Cancer Research Annual Meeting and conducted at Fox Chase Cancer Center, this study evaluates survivin as a biomarker for pancreatic adenocarcinoma. The team's findings indicate that survivin could provide information about prognosis or diagnosis, but further experimentation will be necessary.

Diagnosis of pancreatic ductal adenocarcinoma and chronic pancreatitis by microRNA abundance
http://www.ncbi.nlm.nih.gov/pubmed/22511932
This *PLoS One* article describes analyses of tissue and blood samples of individuals with pancreatic cancer, chronic pancreatitis, and healthy controls. RT-PCR experiments revealed variations in the abundance of various microRNA molecules, characteristic of each group of subjects.

Metastatic lymph node ratio as an important prognostic factor in pancreatic ductal adenocarcinoma
http://www.ncbi.nlm.nih.gov/pubmed/22317758
Scientists at Freeman Hospital in Newcastle upon Tyne did an analysis of outcomes of pancreatic cancer patients who underwent pancreaticoduodenectomy. The authors found that the metastatic to resected lymph node ratio was an accurate predictor of patient prognosis.

Comparison of the influence of plastic & fully covered metal biliary stents on the accuracy of EUS-FNA
http://www.ncbi.nlm.nih.gov/pubmed/22526586
Siddiqui and colleagues prepared this *Digestive Diseases and Sciences* study to determine whether biliary plastic or fully covered self-expanding metal stents influences the diagnosis of pancreatic cancer via EUS-FNA. A retrospective cohort trial showed that EUS-FNA was accurate and safe, regardless of the presence of a plastic or metal stent.

TNM staging of neoplasms of the endocrine pancreas: Results from a large international cohort study
http://www.ncbi.nlm.nih.gov/pubmed/22525418
Published in *JNCI*, this large collaborative study compares staging of pancreatic neuroendocrine tumors based on the European Neuroendocrine Tumor Society (ENETS) and the International Union for Cancer

Control/American Joint Cancer Committee/World Health Organization (UICC/AJCC/WHO) classifications. The authors conclude that the ENETS TNM staging system is superior.

Abcodia collaboration on pancreatic cancer

http://www.businessweekly.co.uk/biomedtech-/13951-abcodia-collaboration-on-pancreatic-cancer

Abcodia, based in Cambridge, England, has formed a collaboration with BIOUNIVERSA Srl, out of the University of Salerno in Italy. The companies will work together to develop an immuno-diagnostic test that recognizes the biomarker BAG3 in patient serum. Early data suggest that elevated BAG3 represents an early indicator of pancreatic tumor development.

Trovagene announces validation program for trans-renal K-RAS mutation detection

http://www.marketwatch.com/story/trovagene-announces-validation-program-for-trans-renal-k-ras-mutation-detection-in-pancreatic-cancer-2012-04-30-125000

Located in San Diego, Trovagene, Inc. announced a PCR-based diagnostic test to detect K-RAS mutation in the urine of individuals with pancreatic cancer.

Staging of pancreatic cancer

http://apps.pathology.jhu.edu/blogs/pancreas/?p=147

Ralph Hruban, MD (Emeritus Scientific Advisory Board) wrote this piece for the Pancreatic Cancer Blog at Johns Hopkins, discussing the staging of pancreatic tumors.

TREATMENT

The following articles describe work presented at the 103rd Annual American Association for Cancer Research that took place in April in Chicago:

Two drug combo slows advanced pancreatic cancer

http://newsblog.mayoclinic.org/2012/04/02/two-drug-combo-slows-advanced-pancreatic-cancer/

AACR abstract: http://www.abstractsonline.com/Plan/ViewAbstract.aspx?sKey=21a1ec6b-0397-4425-b223-31844c6077c3&cKey=edf55bb0-41e9-4d4e-8f01-368a2ebeee69&mKey=%7b2D8C569E-B72C-4E7D-AB3B-070BEC7EB280%7d

This abstract describes a multi-center study of the Threshold compound TH-302 in combination with gemcitabine in patients with advanced pancreatic adenocarcinoma. TH-302 is a bioactivated compound that is converted to a toxic drug in conditions of low oxygen. Median progression-free survival of patients treated with gemcitabine alone was 3.6 months, vs. 5.6 months in patients treated with the combination of gemcitabine and TH-302.

Pancreatic cancer clinical trial results released

http://medicalxpress.com/news/2012-04-pancreatic-cancer-clinical-trial-results.html

AACR abstract: http://www.abstractsonline.com/Plan/ViewAbstract.aspx?sKey=fdef3932-134b-47f6-969f-fa9e84e0328a&cKey=0c39a586-b16e-4da0-bf79-fe9035f2c0cc&mKey=%7b2D8C569E-B72C-4E7D-AB3B-070BEC7EB280%7d

This presentation described progress on one of the Stand Up To Cancer Pancreatic Cancer Dream Team projects. The Phase II clinical trial taking place at TGen is called "Therapy Selected by Tumor Molecular Profiling in Patients with Previously Treated Metastatic Pancreatic Cancer." Biopsies from patients were

molecularly profiled and then xenografted into mice, and treatment options were selected based on genetic changes, and evaluated in the mice. Patient accrual is complete at this point.

Vaccine injections given directly into pancreatic cancer tumors associated with stable disease
http://www.news-medical.net/news/20120405/Vaccine-injections-given-directly-into-pancreatic-cancer-tumors-associated-with-stable-disease.aspx
AACR abstract: http://www.abstractsonline.com/Plan/ViewAbstract.aspx?sKey=d4ec7242-a302-4299-90ab-a5c108389a77&cKey=adaf0f7b-f664-4cb3-af3b-4707177b1b06&mKey=%7b2D8C569E-B72C-4E7D-AB3B-070BEC7EB280%7d
Researchers at the Cancer Institute of New Jersey and NCI teamed up to undertake a Phase I clinical trial of endoscopic ultrasound-guided intratumoral poxvirus vaccines in patients with locally advanced inoperable pancreatic adenocarcinoma. Early evidence suggests that poxvirus vaccines are tolerable and may lead to stable disease in some patients.

Immunomedics develops bispecific hexavalent antibodies for diverse epithelial cancers
http://www.marketwatch.com/story/immunomedics-develops-bispecific-hexavalent-antibodies-for-diverse-epithelial-cancers-2012-04-02
AACR abstract: http://www.abstractsonline.com/Plan/ViewAbstract.aspx?sKey=8101555a-8ecf-4d0a-9307-d3d7adbe97e7&cKey=19669da7-bebc-401c-9e70-6ed3af352187&mKey=%7b2D8C569E-B72C-4E7D-AB3B-070BEC7EB280%7d
This release discusses two novel antibodies being developed by Immunomedics, Inc., and antibody-SN-38 conjugates (presented at AACR). The antibodies are being tested in pancreatic and other solid tumors, and combine an antibody against insulin-like growth factor 1 receptor with an antibody targeting either trophoblast cell-surface marker or carcinoembryonic antigen cell adhesion molecule 6. The SN-38 studies involve conjugation of irinotecan with antibodies to facilitate specific drug delivery.

CureFAKtor Pharmaceuticals demonstrates novel FAK inhibitor disrupts FAK-VEGFR3 interaction
http://www.marketwatch.com/story/curefaktor-pharmaceuticals-demonstrates-novel-focal-adhesion-kinase-fak-inhibitor-disrupts-fak-vegfr3-interaction-and-inhibits-pancreatic-tumor-growth-2012-04-03
AACR abstract: http://www.abstractsonline.com/Plan/ViewAbstract.aspx?sKey=c3391e58-3794-4d96-b3ff-fddecd9edcdb&cKey=9fe8e6fc-819e-4044-b4e6-ff3335bdc559&mKey=%7b2D8C569E-B72C-4E7D-AB3B-070BEC7EB280%7d
Research taking place at Roswell Park Cancer Institute evaluated focal adhesion kinase (FAK) inhibitors developed by CureFAKtor Pharmaceuticals, LLC. Their novel FAK inhibitor C4 was found to have efficacy as a mono-therapy, and in combination with gemcitabine, in mouse models of pancreatic cancer. The authors conclude that targeting the FAK-VEGFR3 interaction represents a promising treatment strategy.

New boost for pancreatic cancer therapy: additional compounds help first-line drug kill cancer cells
http://www.fccc.edu/information/news/press-releases/2012/2012-04-02-aacr-beeharry.php.html
AACR abstract: http://www.abstractsonline.com/Plan/ViewAbstract.aspx?sKey=4271b2f9-92ba-4669-8495-0c807492f8ce&cKey=2190b068-eff1-43d4-aa91-94e5ec13dd26&mKey=%7b2D8C569E-B72C-4E7D-AB3B-070BEC7EB280%7d
This AACR presentation described work at Fox Chase Cancer Center related to favorable "collateral damage" caused by kinase inhibitors. The abstract states, "… unintended targets of kinase inhibitors may in fact play a greater role in achieving the desired biological effects of the drug."

TetraLogic Pharmaceuticals announces presentation of preclinical data on birinapant (TL32711)
http://www.marketwatch.com/story/tetralogic-pharmaceuticals-announces-presentation-of-preclinical-data-on-birinapant-tl32711-in-pancreatic-cancer-and-lymphoma-at-the-103rd-aacr-annual-meeting-2012-2012-04-03
AACR abstract: http://www.abstractsonline.com/Plan/ViewAbstract.aspx?sKey=bbabd562-dba8-471f-b72d-5d6eaa90b19d&cKey=32a2fb78-01c5-4d22-bca8-ea0a2044b51f&mKey=%7b2D8C569E-B72C-4E7D-AB3B-070BEC7EB280%7d
Researchers at Roswell Park also teamed up with TetraLogic Pharmaceuticals to evaluate the Smac mimetic drug candidate birinapant (formerly TL32711) in pancreatic cancer. Birinapant acts as an antagonist of inhibitor of apoptosis (IAPs), promoting apoptotic cell death. Promising preclinical findings encourage the development of clinical trials of this compound in pancreatic cancer patients.

CytRx's INNO-206 to be featured in two presentations
http://www.marketwatch.com/story/cytrxs-inno-206-to-be-featured-in-two-presentations-at-the-american-association-for-cancer-research-aacr-2012-annual-meeting-2012-03-27?reflink=MW_news_stmp
AACR abstracts: http://www.abstractsonline.com/Plan/ViewAbstract.aspx?sKey=43002f9a-df27-4e50-967a-7a0d201aa85e&cKey=8273344d-808e-4488-9e3f-aba9175f20c0&mKey=%7b2D8C569E-B72C-4E7D-AB3B-070BEC7EB280%7d
http://www.abstractsonline.com/Plan/ViewAbstract.aspx?sKey=43002f9a-df27-4e50-967a-7a0d201aa85e&cKey=a6c8310c-641e-4997-9fd4-15dddae56489&mKey=%7b2D8C569E-B72C-4E7D-AB3B-070BEC7EB280%7d
INNO-206 is an acid-sensitive albumin-binding prodrug of doxorubicin. INNO-206 was invented by Dr. Felix Krantz at the Tumor Biology Center in Freiburg, Germany. The studies presented involve combining INNO-206 with doxorubicin or an albumin-binding prodrug of methotrexate in pancreatic cancer cells and xenograft models of the disease.

New 'super' aspirin shrinks tumours for 11 different cancers
http://www.dailymail.co.uk/health/article-2112723/New-super-aspirin-shrinks-tumours-11-different-cancers.html?ito=feeds-newsxml
AACR abstract: http://www.abstractsonline.com/Plan/ViewAbstract.aspx?sKey=006808e0-d434-462e-a212-fec7cb51c072&cKey=9616167b-3400-4a61-97d6-c4334554ee82&mKey=%7b2D8C569E-B72C-4E7D-AB3B-070BEC7EB280%7d
Vannini and colleagues report on a "super" aspirin that may be more effective at treating cancers, without the side effects common to aspirin. Their lead NSAID-based compound, NOSH-1 (nitric oxide-,

hydrogen sulfide-releasing), was found to inhibit the growth of several types of cancer cells, including pancreatic, without toxicity to normal cells.

Nutritional supplement works against some pancreatic cancer cells in mice
http://www.newswise.com/articles/nutritional-supplement-works-against-some-pancreatic-cancer-cells-in-mice
AACR abstract: http://www.abstractsonline.com/Plan/ViewAbstract.aspx?sKey=be31a638-18b2-47f3-a9a2-8ed8f860530d&cKey=702cdec7-f502-4f21-afb7-c3fc460a4542&mKey=%7b2D8C569E-B72C-4E7D-AB3B-070BEC7EB280%7d
A research team led by pathologist Dr. Ruth Lupu at Mayo Clinic looked at nutritional supplement gamma-linolenic acid (GLA), a poly-unsaturated fatty acid (PUFA) of the n-6 PUFA family, as a cytotoxic agent. They found that GLA was effective, in combination with gemcitabine, against pancreatic cancer cells that express the fatty acid synthase (FASN) gene.

Treatment news not presented at AACR:
A Phase I/II trial of intensity modulated radiation dose escalation with fixed-dose rate gemcitabine
http://www.ncbi.nlm.nih.gov/pubmed/22543215
Among the authors on this study is Diane Simeone, MD (2010 The Randy Pausch Family Innovative Grant and member, Scientific Advisory Board). The paper describes a Phase I/II clinical trial conducted at the University of Michigan, seeking a maximum tolerated dose of intensity modulated radiation therapy (IMRT) in conjunction with fixed-dose rate gemcitabine (FDR-G) in patients with unresectable pancreatic cancer. Their results suggest that more intense, high-dose radiation therapy can safely be administered along with FDR-G.

Therapeutic potential of amanitin-conjugated anti-epithelial cell adhesion molecule antibody
http://www.ncbi.nlm.nih.gov/pubmed/22457476
Media: http://www.sciencedaily.com/releases/2012/04/120402112934.htm
JNCI published this paper out of the German Cancer Research Center in Heidelberg. The authors evaluated the therapeutic potential of monoclonal antibodies against epithelial cell adhesion molecule (EpCAM), conjugated to amanitin, a fungal toxin that inhibits DNA transcription. This treatment strategy showed promising in experiments in mice xenografted with pancreatic cancer cells.

Meta-analysis of Phase III randomized trials of molecular targeted therapies
http://www.ncbi.nlm.nih.gov/pubmed/22404265
This paper is published in *HPB: The Official Journal of the Hepato-Pancreato-Biliary Association*. The authors conducted a meta-analysis of clinical trials studying gemcitabine in combination with various molecular targeted therapies in patients with advanced pancreatic cancer. Findings suggested that addition of molecular targeted therapies has not yet enhanced patient survival time, while causing an increase in adverse events.

XELOX versus FOLFOX4 as second line chemotherapy in advanced pancreatic cancer
http://www.ncbi.nlm.nih.gov/pubmed/22534542
This clinical trial was designed to compare the FOLFOX4 (folinic acid, 5-FU, oxaliplatin) and XELOX (capecitabine, oxaliplatin) treatment regimens in patients with previously gemcitabine-treated,

advanced pancreatic cancer. The results suggested that oxaliplatin-based therapies were an acceptable strategy following gemcitabine failure, and the investigators observed similar outcome and toxicity between patients treated with FOLFOX4 or XELOX.

Phase I trial of gemcitabine and candesartan combination therapy in normotensive patients: GECA1
http://www.ncbi.nlm.nih.gov/pubmed/22515232
The investigators retrospectively looked at clinical trials where advanced pancreatic cancer patients were treated with gemcitabine, while also receiving the renin-angiotensin inhibitor candesartan. Patients with the combined treatment showed better outcomes, and the researchers determined the appropriate dose of candesartan for pancreatic cancer patients with normal blood pressure.

A 2-cohort phase 1 study of weekly oxaliplatin & gemcitabine, then oxaliplatin, gemcitabine, erlotinib
http://www.ncbi.nlm.nih.gov/pubmed/22547007
This *American Journal of Clinical Oncology* article describes a multi-institutional two-cohort clinical trial to determine maximum tolerated dose of oxaliplatin and gemcitabine with concurrent radiotherapy, then oxaliplatin, gemcitaibine, and erlotinib with radiotherapy in the treatment of locally advanced and low-volume metastatic pancreatic cancer patients.

Adjuvant and neoadjuvant treatment in pancreatic cancer
http://www.ncbi.nlm.nih.gov/pubmed/22529684
Researchers at the Mayo Clinic reviewed variations in standards of care for pancreatic cancer patients, newer treatment options available to advanced pancreatic cancer patients, and discussed future strategies for the neoadjuvant and adjuvant treatment of this disease in its earlier stages.

How is gene transfection able to improve current chemotherapy? The role of combined therapy
http://www.ncbi.nlm.nih.gov/pubmed/22414080
This chapter of *Current Medicinal Chemistry* is devoted to various strategies involving gene transfer to enhance the effectiveness of chemotherapy and minimize side effects in different types of solid tumors, including pancreatic.

Phase 1/2a, dose-escalation, safety, pharmacokinetic and preliminary efficacy study of BC-819
http://www.ncbi.nlm.nih.gov/pubmed/22498722
This study involved intra-tumoral injection of BC-819, a DNA plasmid that expresses diphtheria toxin in cells that express H19, such as pancreatic cancer cells. Results of this phase 1/2a trial suggest that local administration of BC-819 in combination with systemic chemotherapy may show efficacy in the treatment of unresectable, locally advanced, non-metastatic pancreatic cancer.

The role of chemoradiation for patients with resectable or potentially resectable pancreatic cancer
http://www.ncbi.nlm.nih.gov/pubmed/22500684
Kimple *et al* look at literature and studies relating to the best adjuvant treatment options for patients with resectable or borderline resectable pancreatic cancer. Thus far, conclusions cannot be drawn as to the optimal adjuvant treatment plan.

Laparoscopic distal pancreatectomy is associated with significantly less overall morbidity
http://www.ncbi.nlm.nih.gov/pubmed/22511003
Annals of Surgery published this systematic review and meta-analysis of laparoscopic distal vs. open distal pancreactomy. The authors found that the laparoscopic procedure is equally effective and involves fewer complications.

Threshold Pharmaceuticals earns $20 million milestone payment from Merck KGaA
http://www.marketwatch.com/story/threshold-pharmaceuticals-earns-20-million-milestone-payment-from-merck-kgaa-for-positive-results-from-phase-2-trial-of-th-302-in-pancreatic-cancer-2012-04-11?reflink=MW_news_stmp
Based on the preset milestone of positive results from a Phase 2 trial of TH-302 (hypoxia-inducible drug) in pancreatic cancer patients (see AACR abstract above), Threshold Pharmaceuticals will receive $20 million from Merck KGaA in Germany.

Advancing the quality of pancreatic cancer care
http://qualitymeasures.ahrq.gov/expert/expert-commentary.aspx?f=rss&id=36833
Dr. Karl Bilimoria wrote this expert commentary for the Agency for Healthcare Research and Quality. Dr. Bilimoria discusses metrics to rate hospitals and physicians in the care of pancreatic cancer patients, especially related to surgery, so that comparisons and improvements can be made.

Stifling new cures: The true cost of lengthy clinical drug trials
http://www.manhattan-institute.org/html/fda_05.htm
This Project FDA Report discusses the clinical trial system in the US, and offers suggestions and a plea to Congress to help make improvements.

Drug shortages compromise oncology research
http://www.medscape.com/viewarticle/762488?src=mp&spon=38
Medscape Oncology News published this article to discuss recent shortages in oncology drugs, and how the impact these have had on the design and implementation of clinical trials.

CANCER CONTROL, SURVIVORSHIP, AND OUTCOMES RESEARCH

A progressive postresection walking program significantly improves fatigue and health-related QOL
http://www.ncbi.nlm.nih.gov/pubmed/22321518
Patients treated at Thomas Jefferson University for pancreas and periampullary cancer were prospectively divided into two groups and evaluated for quality of life after surgical resection. Patients in the "intervention group" participated in a home walking program, and showed a significant improvement in fatigue levels, physical functioning, and health-related quality of life.

Impact of gemcitabine chemotherapy & 3-dimensional conformal radiation therapy/5-FU on QOL
http://www.ncbi.nlm.nih.gov/pubmed/22543205
A team of Australian researchers sought to evaluate quality of life (QOL) of pancreatic cancer patients receiving chemoradiation. The authors discovered that QOL status differed between patients with locally advanced disease, and those who were able to receive surgery. In both cases, however, the chemoradiation regimen was tolerable from a QOL standpoint.

A multi-institutional study of pancreatic cancer in Texas: Race predicts treatment and survival
http://www.ncbi.nlm.nih.gov/pubmed/22526908
This *Annals of Surgical Oncology* paper looked at a group of individuals in Harris County, TX, to determine whether people from the same location showed differential diagnosis and outcome of pancreatic cancer. Even upon adjusting for covariates, African-American patients showed the poorest survival, compared to Hispanic or white.

Suicide and cardiovascular death after a cancer diagnosis
http://www.ncbi.nlm.nih.gov/pubmed/22475594
Media: http://www.huffingtonpost.com/dr-douglas-fields/cancer-suicide_b_1425425.html
The *New England Journal of Medicine* published this paper out of Karolinska Institutet in Sweden. The work was conducted in a large historical cohort study, and the results suggested that individuals diagnosed with cancer had a higher risk of death by suicide or cardiovascular disease than those who were not diagnosed. Pancreatic cancer, in addition to liver and esophageal, was found to be associated with the highest increase in suicide rates.

How cancer patients value hope, implications for cost-effectiveness of high-cost cancer therapies
http://www.ncbi.nlm.nih.gov/pubmed/22492883
Media: http://www.eurekalert.org/pub_releases/2012-04/uosc-cpp040912.php
The April issue of *Health Affairs* (http://content.healthaffairs.org/content/31/4.toc) was devoted to cancer costs. This article reports that a large majority of cancer patients surveyed would opt for treatment options considered "hopeful gambles," instead of "safe bets," even if the therapy which provides greater hope is costlier.