PANCREATIC CANCER NEWS & UPDATES – MARCH 2011

PANCREATIC CANCER ACTION NETWORK NEWS

Nearly $3 million in research grants awarded

http://www.pancan.org/section_research/research_grants_program/

Press release:

http://www.pancan.org/section_about/news_press_center/2011_press_releases/03_25_11_pr.php

The 2011 grant recipients have been announced. The Pancreatic Cancer Action Network, in partnership with the American Association for Cancer Research (AACR), will award ten awards for nearly $3 million in research grant funding this year. Since the program's inception in 2003, we have now reached the milestone of over $10 million in research grant funding distributed. Welcome to our new grantees!

Informative webinar on Open Access Publishing

http://www.pancan.org/section_research/research_grants_program/ *(scroll down to Open Access Publishing Webinar to see each speaker's slides)*

The Pancreatic Cancer Action Network hosted an informative webinar on Open Access Publishing on March 16, 2011, featuring Ms. Heather Joseph (Scholarly Publishing and Academic Resources [SPARC]), Dr. Gary Ward (University of Vermont), and Dr. Tony Hollingsworth (University of Nebraska Medical Center).

Pancreatic Cancer Action Network researcher involved in breakthrough finding

http://www.pancan.org/section_research/scientific_strategy/topic_malaria_drug_march_2011.php

Please find more information and the scientific abstract below in the Treatment section

Alec Kimmelman, MD, PhD (2010 Pancreatic Cancer Action Network – AACR Career Development Award) conducted research suggesting that a malaria drug may be effective to treat pancreatic cancer. Pancreatic cancer cells were observed to display an unexpected dependence on the process of autophagy, causing the researchers to hypothesize that inhibition of autophagy with chloroquine might block the cells' growth. This promising story received considerable media attention – congratulations and best wishes to Dr. Kimmelman and his colleagues!

Grant recipient to become president of the American Association for Cancer Research

http://www.aacr.org/home/public--media/aacr-in-the-news.aspx?d=2309

Frank McCormick, PhD (2010 Fredman Family Foundation – Pancreatic Cancer Action Network – AACR Innovative Grant) was named President-Elect of the AACR. Dr. McCormick's one-year term of presidency will begin at the 103rd Annual Meeting in April 2012.

Scientific Advisory Board chair to direct new cancer centre
http://www.cambridge-news.co.uk/Health-and-Beauty/Health-News/Hope-for-pancreatic-cancer-patients.htm
The Cambridge Pancreatic Cancer Centre opened on March 28, 2011, and will be directed by David Tuveson, MD, PhD (Scientific Advisory Board chair; 2003 Pancreatic Cancer Action Network – AACR Career Development Award). The centre's work will focus on conducting clinical trials of therapies and diagnostics for pancreatic cancer.

BIOLOGY OF CANCER

Characterization of alternative spliceoforms and the RNA splicing machinery in pancreatic cancer
http://www.ncbi.nlm.nih.gov/pubmed/21178653
This article, co-authored by Teri Brentnall, MD (Scientific Advisory Board), describes a spliceoform-specific microarray and polymerase chain reaction utilized to evaluate all known splice variants in human pancreatic cancer cell lines. Validation of altered spliceoforms was verified in primary cancer specimens and normal pancreatic ductal cells. A statistically significant reduction in alternative splicing was found in the pancreatic cancer cell lines compared with near-normal pancreas cells.

CNT1 expression influences proliferation and chemosensitivity in drug-resistant pancreatic cancer cells
http://www.ncbi.nlm.nih.gov/pubmed/21343396
This *Cancer Research* article looks at the role of human concentrative nucleoside transporter-1 (hCNT1) in determining chemosensitivity of human pancreatic cancer cells to gemcitabine. The investigators found that expression of hCNT1 was frequently reduced in pancreatic tumors and cancer cell lines, as compared with normal pancreas. They found that constitutive expression of hCNT1 in pancreatic cancer cells led to clonogenic survival and increased the transport and response to gemcitabine, suggesting a tumor suppressive role for hCNT1.

Farnesoid X receptor promotes cell migration and invasion
http://www.ncbi.nlm.nih.gov/pubmed/21364590
JY Lee and colleagues report on the expression of the farnesoid X receptor (FXR) in pancreatic cancer tissue samples with or without lymph node metastasis. Their data suggest that FXR over-expression in patients with lymph node metastasis is indicative of poor prognosis. Down-regulation and inhibition of FXR led to a marked reduction in cell migration and invasion. Overall, these findings indicate that FXR over-expression plays an important role in lymphatic metastasis of pancreatic cancer and that down-regulation of FXR may be an approach for inhibition of pancreatic tumor progression.

Pancreatic tumor suppression by BITC is associated with inhibition of PI3K/AKT/FOXO pathway
http://www.ncbi.nlm.nih.gov/pubmed/21350002
Scientists at Texas Tech sought to elucidate the molecular mechanism of benzyl isothiocyanate (BITC)'s inhibition of pancreatic cancer cells. Data presented in this *Clinical Cancer Research* publication suggested that the PI3K/AKT/FOXO pathway is involved in BITC-mediated apoptosis in pancreatic cancer xenograft models.

Activated Kras(G12D) is associated with invasion and metastasis through inhibition of E-cadherin
http://www.ncbi.nlm.nih.gov/pubmed/21364589
In this *British Journal of Cancer* publication, University of Nebraska researchers explored the repercussions of silencing oncogenic Kras expression (via shRNA) in pancreatic cancer cell lines. Effects of Kras knockdown included decreased motility, invasion, and anchorage- dependent and independent growth. The authors also observed that Kras knockdown led to increased expression of E-cadherin at both the mRNA and protein levels, suggesting that one of the functions of oncogenic Kras may be inhibition and down-regulation of E-cadherin.

Nestin is a novel target for suppressing pancreatic cancer cell migration, invasion and metastasis
http://www.ncbi.nlm.nih.gov/pubmed/21258211
This study published in *Cancer Biology & Therapy* looks at nestin, a class VI intermediate filament, which is expressed in 30 percent of pancreatic ductal adenocarcinoma cases. The authors utilized shRNA technology to down-regulate nestin expression in pancreatic cancer cell lines, and observed decreases in cell migration, invasion, and metastasis.

Suppression of the uPAR-uPA system retards angiogenesis, invasion and in vivo tumor development
http://www.ncbi.nlm.nih.gov/pubmed/21389187
University of Illinois College of Medicine researchers examined the outcome of inhibiting the uPAR-uPA system in pancreatic cancer cells. Simultaneously down-regulating both uPAR and uPA by RNAi in pancreatic cancer cells led to decreased angiogenesis and proliferation, and an increase in apoptosis.

TBK1 directly engages Akt/PKB survival signaling to support oncogenic transformation
http://www.ncbi.nlm.nih.gov/pubmed/21329883
This *Molecular Cell* paper explores the activation of TBK1 and its role in cancer. TBK1, an innate immune signaling kinase, was found to directly active AKT by phosphorylation. The authors discovered and characterized a 6-aminopyrazolopyrimidine derivative, a selective low-nanomolar TBK1 inhibitor, allowing investigation into perturbing TBK1. If mouse experiments are successful, then the researchers plan to test TBK1 inhibition in pancreatic and non-small cell lung cancer.

Anti-tumor activity of a novel compound-CDF is mediated by regulating miR-21, miR-200, and PTEN
http://www.ncbi.nlm.nih.gov/pubmed/21408027
A novel synthetic analog of curcumin, called 3,4-difluoro-benzo-curcumin (or difluorinated-curcumin, CDF), induced pancreatic cancer cell growth inhibition and induction of apoptosis. Sphere-forming pancreatic cancer cells with stem cell like behavior were specifically inhibited by CDF.

ETIOLOGY

Association of alcohol intake with pancreatic cancer mortality in never smokers
http://www.ncbi.nlm.nih.gov/pubmed/21403041
This *Archives of Internal Medicine* paper received considerable media attention this month. Researchers at the ACS scrutinized data from the Cancer Prevention Study II, a prospective study of US adults aged 30 and above, which included 6,847 pancreatic cancer deaths among over one million participants.

Multivariable-adjusted relative risk analyses suggested that consumption of three of more drinks (liquor, not beer or wine) per day was associated with increased risk of death from pancreatic cancer in never- and ever- smokers.

Calmodulin protects against alcohol-induced pancreatic trypsinogen activation
http://www.ncbi.nlm.nih.gov/pubmed/21436055
Research taking place at Cardiff University was published in this *PNAS* article. The scientists looked at the actions of alcohol on intracellular calcium channels in pancreatic acinar cells. The calcium sensor calmodulin (at a normal intracellular concentration) markedly reduced ethanol-induced calcium release and trypsinogen activation in permeabilized cells. These data suggest that calmodulin can play a role in protecting pancreatic cells from damaged induced by alcohol consumption.

Glucose metabolism gene variations modulate the risk of pancreatic cancer
http://www.ncbi.nlm.nih.gov/pubmed/21411499
Researchers retrospectively looked at genotypes of glucose metabolism genes in pancreatic cancer cases. They examined 26 single nucleotide polymorphisms of five glucose metabolism genes in 706 pancreatic cancer patients and 706 cancer-free individuals. Results showed that the R844K GA/AA genotype of hexokinase 2 was associated with a reduced risk of pancreatic cancer among non-diabetic individuals, but an increased risk among those with diabetes.

Serum C-reactive protein and risk of pancreatic cancer in two nested, case-control studies
http://www.ncbi.nlm.nih.gov/pubmed/21173171
Epidemiologists at the NCI explored the association between C-reactive protein (CRP) concentrations and pancreatic adenocarcinoma risk. CRP concentrations did not appear to be correlated with pancreatic cancer risk in the studies analyzed. The authors' findings highlight the importance of investigating more specific biomarkers for inflammation that may reflect the biological mechanisms underlying pancreatic cancer in prospective cohort studies.

Coffee consumption and risk of cancers: a meta-analysis of cohort studies
http://www.ncbi.nlm.nih.gov/pubmed/21406107
Yu, *et al* studied 59 studies, consisting of 40 independent cohorts, that reported relative risks and corresponding 95 percent confidence intervals of various cancers with respect to coffee consumption. Findings from this meta-analysis suggest that coffee consumption may reduce the total cancer incidence and it also has an inverse association with some type of cancers, including pancreatic.

Coffee, decaffeinated coffee, tea, and pancreatic cancer risk: two Italian case-control studies
http://www.ncbi.nlm.nih.gov/pubmed/21403521
On a similar note, this study did a pooled analysis of two Italian case-control studies, examining the association between coffee, decaffeinated coffee, and tea consumption and pancreatic cancer risk. They found a lack of relationship with dose and duration weighs against a causal association between coffee and pancreatic cancer, which is in agreement with most evidence on the issue.

EARLY DETECTION, DIAGNOSIS, AND PROGNOSIS

Mass spectrometric assay for analysis of haptoglobin fucosylation in pancreatic cancer

http://www.ncbi.nlm.nih.gov/pubmed/21417406

Diane Simeone, MD (2010 The Randy Pausch Family – Pancreatic Cancer Action Network – AACR Innovative Grant) is co-author on this study out of Dr. David Lubman's laboratory at the University of Michigan. The authors describe a mass spectrometric method to elucidate the N-glycan structures of serum glycoproteins and utilize fucosylated glycans as potential markers for pancreatic cancer. This study demonstrates that a serum assay based on haptoglobin fucosylation patterns using mass spectrometric analysis may serve as a novel method for the diagnosis of pancreatic cancer.

Overexpression of CXCL5 is associated with poor survival in patients with pancreatic cancer

http://www.ncbi.nlm.nih.gov/pubmed/21356384

A research team at UCLA, including Dave Dawson, MD, PhD (2008 Seena Magowitz – Pancreatic Cancer Action Network – AACR Career Development Award), looked at expression of epithelial neutrophil-activating peptide-78 (CXCL5), a member of the CXC chemokine family, in pancreatic cancer samples. They found that CXCL5 expression was high in human pancreatic cancer cases, compared to paired normal pancreas tissue as a control. Over-expression of CXCL5 was found to be significantly correlated with poorer tumor differentiation, advanced clinical stage, and shorter patient survival. Down-regulation of CXCL5 or its receptor CXCR2 with siRNA blocked pancreatic cancer growth in a xenograft mouse model.

Meta-analysis of immunohistochemical prognostic markers in resected pancreatic cancer

http://www.ncbi.nlm.nih.gov/pubmed/21448172

This objective of this study published in the *British Journal of Cancer* was to conduct a systematic review of literature evaluating p53, p16, smad4, bcl-2, bax, vascular endothelial growth factor (VEGF), and epidermal growth factor receptor (EGFR) expression as prognostic factors in resected pancreatic adenocarcinoma and to conduct a subsequent meta-analysis to quantify the overall prognostic effect. VEGF emerged as the most potentially informative prognostic marker, significantly and reproducibly representing adverse prognosis in resected pancreatic cancer.

Cystic precursors to invasive pancreatic cancer

http://www.ncbi.nlm.nih.gov/pubmed/21383670

Authors of this *Nature Reviews Gastroenterology and Hepatology* review article include Anirban Maitra, MD (2004 Pancreatic Cancer Action Network – AACR Career Development Award) and Ralph Hruban, MD (Scientific Advisory Board). The article reports that, despite progress in imaging and clinical guidelines, sensitive and specific tests have not yet been developed that can reliably predict the histology and biological properties of a cystic lesion. Such biomarkers are urgently needed, as noninvasive precursors of pancreatic cancer are curable, while the vast majority of invasive pancreatic adenocarcinomas are not.

Invasive carcinoma arising in intraductal papillary mucinous neoplasms of the pancreas
http://www.ncbi.nlm.nih.gov/pubmed/21422912
Two distinct histological subtypes of invasive carcinomas arising in IPMNs have been described, colloid carcinoma and tubular carcinoma. Previous reports have suggested prognostic differences between these two subtypes, but a matched comparison of colloid carcinoma, tubular carcinoma, and conventional pancreatic adenocarcinoma had not been previously reported. In this study, the colloid carcinoma histological subtype of invasive IPMN had a more statistically favorable survival outcome than the tubular subtype. Patients with invasive tubular IPMN had no statistically significant difference in survival from matched patients with conventional ductal pancreatic carcinoma.

Cyst fluid interleukin-1{beta} levels predict the risk of carcinoma in IPMNs of the pancreas
http://www.ncbi.nlm.nih.gov/pubmed/21266527
Maker, *et al* performed a multiplex sandwich immunoassay of pancreatic cyst fluid aspirates collected from resected intraductal papillary mucinous neoplasm (IPMN) cases. Patients were stratified as low-risk, moderate dysplasia, high-risk, or carcinoma. Data suggested that interleukin (IL) IL5 and IL8 were higher in patients with high-risk disease, than low-risk. IL1{beta} was also found to be higher in cyst fluid from patients with high-risk dysplasia or cancer, and remained a significant predictor after multivariate analysis. They therefore conclude that IL1{beta} may be able to act as a biomarker to differentiate low- from high-risk IPMN.

The duration of symptoms predicts the presence of malignancy in resected cases of pancreatic IPMN
http://www.ncbi.nlm.nih.gov/pubmed/21380634
Research taking place at the Virginia Mason Medical Center in Seattle examined 210 histologically confirmed intraductal papillary mucinous neoplasm (IPMN) cases. The research team calculated time from the first clinical symptom to malignant detection (resection), and compared rates of malignant detection in main vs side-branch duct location. Presence of symptoms followed by main pancreatic duct location had a significantly shorter elapsed time to malignant detection.

Metabolites of purine nucleoside phosphorylase have the potential to delineate pancreatic cancer
http://www.ncbi.nlm.nih.gov/pubmed/21448452
This *PLoS One* article describes efforts to detect novel biomarkers of pancreatic cancer by using label-free mass spectrometry coupled to 1D-SDS-PAGE and Strong Cation-Exchange Chromatography (SCX). Among the positive results were alpha synuclein (aSyn) and the metabolic enzyme purine nucleoside phosphorylase (NP). Levels of NP and its downstream metabolites, guanosine and adenosine, were detectable in serum of pancreatic cancer patients. Overall, this study describes elevated levels of aSyn in pancreatic ductal adenocarcinoma, as well as highlights the potential of evaluating NP protein expression and levels of its downstream metabolites to develop a multiplex panel for non-invasive detection of pancreatic cancer.

High EGFR mRNA expression is a prognostic factor for reduced survival in pancreatic cancer
http://www.ncbi.nlm.nih.gov/pubmed/21243324
The authors of this *International Journal of Oncology* paper aimed to look at EGFR mRNA levels in pancreatic cancer patients' tissue samples. EGFR expression was found to be a statistically significant indicator of poor prognosis in patients who had received adjuvant gemcitabine-based chemotherapy.

The authors conclude that quantitative analysis of EGFR mRNA expression using FFPE tissue samples and microdissected neoplastic cells from EUS-FNA cytological specimens could be useful in predicting prognosis and sensitivity to gemcitabine in pancreatic cancer patients.

Differential expression of ERCC1 in pancreas adenocarcinoma
http://www.ncbi.nlm.nih.gov/pubmed/21360249
Although increased expression of excision repair cross-complementing gene-1 (ERCC1) has been shown to be associated with decreased survival in other cancer types, its expression levels had not been previously measured in pancreatic cancer. Here, researchers at Emory University evaluated ERCC1 expression in tumor samples from 95 patients who underwent pancreaticoduodenectomy for pancreatic cancer. The authors conclude that pancreatic cancer exhibits differential expression of ERCC1, with high ERCC1 expression associated with reduced recurrence-free and overall survival after resection.

Ep-CAM is a significant prognostic factor in pancreatic cancer patients by suppressing cell activity
http://www.ncbi.nlm.nih.gov/pubmed/21399662
Published in *Oncogene*, this study explored epithelial cell adhesion molecule (Ep-CAM) expression in pancreatic cancer. When Ep-CAM was transfected into pancreatic cancer cells, one of the cell lines examined showed a significant decrease in proliferation rates. Moreover, examination of clinical specimens revealed that Ep-CAM was associated with a better prognosis among patients who had undergone a surgical resection.

Detection of the pancreatic cancer marker MUC4 in serum using surface-enhanced Raman scattering
http://www.ncbi.nlm.nih.gov/pubmed/21391573
The mucin protein MUC4 has been shown to be expressed on the surface of pancreatic cancer cells, while absent from normal pancreas and pancreatitis samples. However, conventional detection methods (ELISA, RIA) have not been effective at detecting serum MUC4 levels. Here, researchers at Iowa State University present data suggesting that a surface-enhanced Raman scattering (SERS)-based immunoassay could detect serum MUC4 levels. Sera from pancreatic cancer patients showed higher SERS response for MUC4 than sera from healthy controls or patients with benign pancreatic disease.

A prognostic model to identify patients who could benefit from second-line chemotherapy
http://www.ncbi.nlm.nih.gov/pubmed/21382702
This Korean group has concluded that advanced pancreatic cancer patients with ECOG performance status 0-1, albumin level of at least 3.5mg/dl, and who showed response to first-line chemotherapy may benefit from second-line chemotherapy.

Overall survival of patients improved with an increase in 2nd-line chemotherapy after gemcitabine
http://www.ncbi.nlm.nih.gov/pubmed/21386638
This retrospective data analysis suggested that overall survival closely correlated with second-line chemotherapy in patients with advanced pancreatic cancer.

TREATMENT

Pancreatic cancers require autophagy for tumor growth

http://www.ncbi.nlm.nih.gov/pubmed/21406549

Research primarily conducted in the Dana-Farber Cancer Institute laboratory of Alec Kimmelman, MD, PhD (2010 Pancreatic Cancer Action Network – AACR Career Development Award) led to this *Genes and Development* publication. Another collaborator on the study was Nabeel Bardeesy, recipient of a 2008 Randy Pausch – Pancreatic Cancer Action Network – AACR Pilot Grant. Their findings suggested that, rather than behaving as a response to toxins or other cellular stress, the autophagy mechanism was constitutively activated in pancreatic cancer cells. In fact, even cells in a dish, bathed in nutrients, were still undergoing autophagy. The malaria drug chloroquine acts to inhibit autophagy, and the authors saw a response in pancreatic cancer cell lines, xenograft mouse models, and genetically engineered mouse models upon treatment with chloroquine. At least two clinical trials are underway to examine this drug's effectiveness in human patients.

CD40 agonists alter tumor stroma and show efficacy against pancreatic carcinoma in mice and humans

http://www.ncbi.nlm.nih.gov/pubmed/21436454

ScienceNOW article: Good news about a very bad cancer (features Drs. Fleming, Bar-Sagi, and Brody)

http://news.sciencemag.org/sciencenow/2011/03/good-news-about-a-very-bad-cance.html

A study out of the University of Pennsylvania also gained some media attention last month. Dr. Bob Vonderheide and colleagues report that activation of CD40, in combination of gemcitabine, showed promise as a treatment for pancreatic cancer. Rather than impacting the tumor directly, the group found that activation of CD40 and cell killing took place in the stromal cells surrounding the tumor.

A novel method for quantification of gemcitabine and its metabolites in tumour tissue by LC-MS/MS

http://www.ncbi.nlm.nih.gov/pubmed/21431415

Ken Olive, PhD (2011 Tempur-Pedic® Retailers –Pancreatic Cancer Action Network – AACR Career Development Award) and Dave Tuveson, MD, PhD (Scientific Advisory Board chair; 2003 Pancreatic Cancer Action Network – AACR – Career Development Award) are co-authors on this *Cancer Chemotherapy and Pharmacology* paper. Research conducted at Cambridge explored novel methods to quantify concentrations of gemcitabine and its metabolites, 2',2'-difluorodeoxyuridine (dFdU) and 2',2'-difluorodeoxycytidine-5'-triphosphate (dFdCTP), in tumor tissue, as compared to (19)F NMR spectroscopy. The authors developed a sensitive LC-MS/MS method capable of quantifying gemcitabine, dFdU and dFdCTP in pancreatic tumor tissue, requiring only 10mg of tissue.

A sluggish march toward cure for pancreatic cancer

http://www.hemonctoday.com/article.aspx?rid=81331

This *HemOnc Today* article discusses the progress (and lack thereof) in pancreatic cancer treatment options. Work by Diane Simeone, MD (2010 The Randy Pausch Family – Pancreatic Cancer Action Network – AACR Innovative Grant) is featured, and Eileen O'Reilly, MD (Medical Advisory Board) is involved in a discussion regarding VEGF as a treatment target in pancreatic cancer.

Highlight articles: "2011 ASCO Gastrointestinal Cancers Symposium"
http://www.joplink.net/prev/201103/index.html
This *Journal of the Pancreas* issue includes a section highlighting research presented at the GI ASCO meeting in San Francisco, January 20-22, 2011. Several articles pertain to pancreatic cancer.

Future directions in the treatment of neuroendocrine tumors
http://www.ncbi.nlm.nih.gov/pubmed/21263089
The Consensus report of the National Cancer Institute Neuroendocrine Tumor clinical trials planning meeting is presented in the *Journal of Clinical Oncology*. Since the diagnosed incidence of NETs has been rising, the NET Task Force of the National Cancer Institute GI Steering Committee convened a clinical trials planning meeting to identify key unmet needs, develop appropriate study end points, standardize clinical trial inclusion criteria, and formulate priorities for future NET studies for the US cooperative group program. One key recommendation was to evaluate pancreatic NETs independently from NETs of other sites.

Targeted therapies: Hope for pancreatic neuroendocrine tumors
http://www.ncbi.nlm.nih.gov/pubmed/21451489
A *Nature Reviews Clinical Oncology* article also reviews the current treatment options for pancreatic neuroendocrine tumors.

MK-1775, a potent Wee1 inhibitor, synergizes with gemcitabine to achieve tumor regressions
http://www.ncbi.nlm.nih.gov/pubmed/21389100
A team of researchers at Johns Hopkins, including Anirban Maitra, MD (2004 Pancreatic Cancer Action Network – AACR Career Development Award), explored the effects of Wee1 inhibition on pancreatic cancer xenografts. The effects of MK-1775 was explored alone or in combination with gemcitabine, in xenografts from human pancreatic cancer samples that were p53-null or p53-intact. The combination of MK-1775 and gemcitabine abrogated cell cycle arrest and facilitated tumor death specifically in samples which lacked p53.

Pooled survival and response data from phase III randomized controlled trials for gemcitabine
http://www.ncbi.nlm.nih.gov/pubmed/21436672
Arshad, *et al* pooled results from published randomized phase III trials of gemcitabine-based regimens in the treatment of advanced pancreatic cancer. The authors conclude that the length of survival for patients with advanced pancreatic cancer remains disappointing, and further trials of novel agents to complement or replace gemcitabine are indicated.

Synergistic effect between erlotinib and MEK inhibitors in KRAS wild-type pancreatic cancer cells
http://www.ncbi.nlm.nih.gov/pubmed/21385921
T-Gen researchers underwent a high-throughput RNAi screen to identify candidate genes whose down-regulation could enhance the effects of EGFR inhibition (via erlotinib) in human pancreatic cancer cells. One of the six confirmed hits, MAPK1, was further evaluated. Treatment of pancreatic cancer cells with erlotinib in combination with one of two MAP kinase kinase (MEK) inhibitors, RDEA119 and AZD6244, both showed significant synergistic effects. Examination of the MAPK signaling pathway by Western

blotting indicated effective inhibition of the EGFR signaling by the drug combination in KRAS wildtype cells, but not in KRAS mutant cells.

Aurora B kinase inhibitor AZD1152: determinants of action and ability to enhance chemotherapeutics
http://www.ncbi.nlm.nih.gov/pubmed/21304529
AZD1152-hydroxyquinazoline pyrazol anilide, and its prodrug AZD1152, were tested in pancreatic and colon cancer mouse models in combination with chemotherapies. This Italian study reports that AZD1152 is effective in combination with gemcitabine and oxaliplatin in pancreatic and colon cancer, respectively.

Connexin-26 is a key factor mediating gemcitabine bystander effect
http://www.ncbi.nlm.nih.gov/pubmed/21388975
The participation of gap junctional intercellular communication (GJIC) was investigated as a possible mechanism for mediating gemcitabine cytotoxicity in pancreatic tumors. Over-expression of connexin-26 triggered increased GJIC and enhanced the gemcitabine cytotoxic bystander effect.

Genexol inhibits primary tumour growth and metastases in gemcitabine-resistant PDA
http://www.ncbi.nlm.nih.gov/pubmed/21309930
Genexol-PM, a modified form of paclitaxel, was found to be an effective treatment for gemcitabine-resistant pancreatic ductal adenocarcinoma, as indicated in an orthotopic xenograft mouse model. Genexol has shown promise in clinical trials of other malignancies.

A randomized phase II of gemcitabine and sorafenib versus sorafenib alone
http://www.ncbi.nlm.nih.gov/pubmed/21424698
This paper describes a clinical trial at the Norris Cancer Center at USC. In this phase II trial, metastatic pancreatic cancer patients were stratified to receive sorafenib (small molecule inhibitor of VEGF, PDGFR, and Raf) or sorafenib plus gemcitabine. The outcome of the trial showed that neither sorafenib alone, nor in combination with gemcitabine, showed effectiveness in metastatic pancreatic cancer.

A randomized phase II study of PX-12, an inhibitor of thioredoxin
http://www.ncbi.nlm.nih.gov/pubmed/20461382
T-Gen coordinated a randomized phase II study of PX-12, a novel small molecule inhibitor of the proto-oncogene thioredoxin (Trx-1) in patients with advanced cancer of the pancreas, following progression after a gemcitabine-containing treatment combination. The study was terminated early because the patients had low baseline Trx-1 levels and PX-12 did not exhibit anti-tumor activity.

First-line treatment of pancreatic cancer patients with 5-fluorouracil/folinic acid plus gemcitabine
http://www.ncbi.nlm.nih.gov/pubmed/21400239
A German multicenter phase II trial by the CONKO group looked at the efficacy and safety of combining 5-FU/folinic acid plus gemcitabine (GFF) in patients with advanced pancreatic cancer. The GFF combination appeared to be well tolerated and effective.

Pharmacologic ascorbate synergizes with gemcitabine in pre-clinical models of pancreatic cancer
http://www.ncbi.nlm.nih.gov/pubmed/21402145
This paper by Espey, *et al* explored combining ascorbate to enhance the effects of gemcitabine in pancreatic cancer. The group found that pharmacologically achievable concentrations of ascorbate could synergize with gemcitabine treatment in pancreatic cancer cell lines, regardless of gemcitabine-sensitivity and epithelial-mesenchymal status. Further, pancreatic cancer xenograft models recapitulated these results of ascorbate enhancing the effectiveness of gemcitabine. These data support testing of pharmacologic ascorbate in adjunctive treatments for cancers prone to high failure rates with conventional therapeutic regimens, such as pancreatic cancer.

Adjuvant therapy for pancreatic cancer: a logical strategy in search of progress
http://www.ncbi.nlm.nih.gov/pubmed/21384245
This editorial in the *Annals of Surgical Oncology* calls on the journal's readership to take a leadership role in the standardization of the management of patients with localized pancreatic cancer.

Optimizing adjuvant therapy for resected pancreatic cancer
http://www.cancer.gov/ncicancerbulletin/030811/page7
The March 8, 2011 edition of the *NCI Cancer Bulletin*'s included a pancreatic cancer study as its Featured Clinical Trial. The trial is a Phase III Randomized Study of Adjuvant Gemcitabine Hydrochloride with Versus without Erlotinib Hydrochloride Followed by the Same Chemotherapy Regimen with Versus without Chemoradiotherapy with Either Capecitabine or Fluorouracil in Patients with Resected Head of Pancreas Adenocarcinoma (RTOG-0848). Aims of this trial are to determine whether erlotinib plus gemcitabine is better than gemcitabine alone, and whether chemoradiation is superior to chemotherapy alone to prevent recurrence after pancreatic cancer surgery.

Induction chemotherapy with gemcitabine, oxaliplatin, and 5-fluorouracil/leucovorin
http://www.ncbi.nlm.nih.gov/pubmed/21420250
A Taiwan Cooperative Oncology Group Phase II Study looked at triplet induction chemotherapy (gemcitabine, oxaliplatin, and 5-fluorouracil/leucovorin) followed by concomitant chemoradiotherapy in patients with locally advanced pancreatic cancer. The results suggest that three months of triplet induction chemotherapy followed by gemcitabine-based chemoradiotherapy is feasible, moderately active, and associated with encouraging survival in patients with locally advanced pancreatic cancer.

Biliary metal stents are superior to plastic stents for preoperative biliary decompression
http://www.ncbi.nlm.nih.gov/pubmed/21373939
This paper describes a retrospective study of patients at University of Alabama with obstructive jaundice secondary to pancreatic head cancer. The authors compared the outcome of patients who underwent their index endoscopic retrograde cholangiopancreatography (ERCP) with a plastic or self-expandable metal stent (SEMS) for biliary decompressions. Results suggested that preoperative SEMS were superior to plastic stents.

Overcoming drug resistance in pancreatic cancer

http://www.ncbi.nlm.nih.gov/pubmed/21391891

This review summarizes recent advances in the mechanisms of drug resistance in pancreatic cancer and potential strategies to overcome this. Increasing drug delivery efficiency and decreasing drug resistance is the current aim in pancreatic cancer treatment, and will also benefit the treatment of other cancers.

SURVIVORSHIP

Annual report to the nation on the status of cancer, 1975-2007

http://www.ncbi.nlm.nih.gov/pubmed/21454908

This annual report represents a collaborative study involving the American Cancer Society, the Centers for Disease Control and Prevention (CDC), the National Cancer Institute, and the North American Association of Central Cancer Registries (NAACCR). During the time period measured, overall cancer incidence and mortality rates dropped. However, for both men and women, both incidence and mortality rates of pancreatic cancer increased. Tumors of the brain and other nervous system are featured in this report.

Diabetes mellitus, fasting glucose, and risk of cause-specific death

http://www.ncbi.nlm.nih.gov/pubmed/21366474

This *New England Journal of Medicine* report examined the extent to which diabetes or hyperglycemia is related to risk of death from cancer or other nonvascular conditions. Diabetes (vs. no diabetes) was moderately associated with death from cancers of the liver, pancreas, ovary, colorectum, lung, bladder, and breast.

Patient willingness to undergo pharmacodynamic, pharmacokinetic tests in early phase oncology trials

http://www.ncbi.nlm.nih.gov/pubmed/21246533

Researchers at T-Gen and the Virginia G. Piper Cancer Center conducted a prospective study examining the willingness of patients to undergo pharmacodynamic and pharmacokinetic assays as well as frequent imaging studies. Overall, they found that willingness to participate in study-required tests was very high. Patients were most willing to undergo the least invasive testing, and willingness decreased with increased frequency of testing. These data can help inform future design of patient-friendly biomarker-driven cancer clinical trials.

Nearly 12 million in U.S. are cancer survivors, per CDC and NCI

http://www.msnbc.msn.com/id/42010069/ns/health-cancer/

The Center for Disease Control and National Cancer Institute report that there were 11.7 million cancer survivors in the United States in 2007, up from 9.8 million in 2001 and 3 million in 1971. Of the survivors, 22 percent had been diagnosed with breast cancer, 19 percent prostate, and 10 percent colon.