Pancreatic Cancer Research

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• Overview of anatomy and function of the pancreas.
• Nature of pancreatic cancer
• Inter-relationship between pancreatic disorders
• How we study pancreatic cancer and develop treatments and early diagnosis methods
• The road to defeating this disease
Overview
Anatomy and Function
of the Pancreas
Bile and Pancreatic Ducts and the Duodenum

Exocrine Endocrine and Pancreas Secretion
Duct Structure

Histology of the Exocrine Pancreas

Ductule

Acinus
Pancreatic Islet

Secretory Products

Insulin
Glucagon
Somatostatin
Pancreatic polypeptide
Amylin

Islet of Langerhans

Pancreatic Islet

Glucagon
Insulin
Classes of Enzymes in Pancreatic Juice

- **Proteases**: 90%
- **Amylase**: 7%
- **Lipases**: 2%
- **Nucleases**: <1%

G. Scheele, et al., Gastroenterology 1981; 80:461

Site of Zymogen Activation

- **Trypsinogen**
- **Enterokinase**
- **Zymogens**
- **Trypsin**
- **Active enzymes**

Digestion
Inter-relationship between pancreatic disorders

Nature of pancreatic cancer
RON is up regulated in PDAC

Expression of MSP1 is elevated in PDAC
Apte MV, Wilson JS, Lugea A, Pandol SJ. 
Gastroenterology. 2013;144:1210-9
Inter-relationship between pancreatic disorders
How we study pancreatic cancer and develop treatments and early diagnosis methods

Human studies
Consortium for the Study of Chronic Pancreatitis, Diabetes and Pancreatic Cancer Clinical Centers (CSCPDPC CCs)

Research Objectives

Identify and acquire cohorts of well characterized patients and associated bio-specimens (blood, pancreatic and duodenal juice, stools and when feasible pancreatic tissue) to pursue clinical research in types of patients shown in the following slide.

(1) Patients with pancreatitis to encourage translational research focusing upon elucidating the pathogenesis that will provide the basis for understanding the natural history and developing means of diagnosis, treatment and clinical management and its sequelae: chronic pain, pancreatic insufficiency, diabetes and pancreatic cancer.

(2) Patients with pancreatic cancer and pancreatogenic Diabetes Mellitus (T3cDM) to encourage translational research focusing on their mechanistic inter-relationships in order to develop better means for prevention, diagnosis, and treatment of these disorders.
The Pancreatic Cancer Detection Consortium (U01)

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.

Statins, Pancreatitis and Pancreatic Cancer Findings Lead to a Clinical Trial

- **Simvastatin is associated with reduced risk of acute pancreatitis: findings from a regional integrated healthcare system.** Wu BU, Pandol SJ, Liu IL. *Gut* 2015;64:133-138.


How we study pancreatic cancer and develop treatments and early diagnosis methods

Using animal models of pancreatic cancer

Effect of a High Fat High Calorie (HFHC) Diet on Weight Gain in Mice


©2013 by American Association for Cancer Research
Effects of HCHF Diet on Insulin, Glucose, IGF-1, Leptin, Cholesterol and Triglyceride Levels


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Effect of Kras and HFHC Diet on Progression of Pancreatic Cancer Lesions in Mouse


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Cytokine and chemokine levels were measured in the pancreas of wild-type (WT) and conditional KrasG12D (Kras)

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No Effective Treatment for Pancreatic Cancer

- **Abraxane**: Drug of choice used with Gemcitabine to slow tumor growth.

- Abraxane / Gemcitabine increases survival by *only 1.8 months.*
Why Failure of Drugs to Treat Pancreatic Cancer?

- High metastasis level
- Pancreatic cancer cell resistance to treatments

How Metavert™ Works and is Unique

Metavert™

- Blocks Epigenetic protein involved in metastasis
- Blocks Enzyme pathway connected to proliferation and resistance to cell death

Metastasis & resistance to treatments

Tumor growth

Avenzoar Pharmaceuticals
Solution: *Metavert™* Drug Treatment

- *Metavert™* is a drug that has shown significant slower tumor growth with much less toxicity in *pre-clinical* trials.

- *Metavert™* prevents metastasis and reduces resistance to chemo/radio therapy.

- *Metavert™* can be combined with the treatments available because it affects a unique target.

- *Metavert™* *does not* affect normal cells compared to standard chemotherapy drugs.

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*Metavert™*

Pre-Clinical Trial Results

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Avenzoar Pharmaceuticals
**Metavert™ Decreases Cancer Cell Survival**

![Graph showing cancer cell survival against Metavert dosage](image)

- **Bx-PC3 (Aggressive cancer cell)**
- **MIA PaCa-2 (Very aggressive cancer cell)**

**Metavert™ Dosage**

**Avenzoar Pharmaceuticals**

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**Metavert™ Works in Synergy with Standard Treatments**

**Radiation**

- Metavert + Irradiation
- Irradiation
- Metavert
- Control

**Chemotherapy**

- Metavert + Gemcitabine
- Gemcitabine
- Metavert
- Control

**Avenzoar Pharmaceuticals**
**Metavert™** Prevents Cancer Cell Metastasis

*Control*  *Metavert (150nM)*  *Metavert (300nM)*  *Metavert (600nM)*

Avenzoar Pharmaceuticals

**Metavert™ Significantly Improves Survival of KPC* Mice with Advanced Pancreatic Cancer**

42% of Metavert treated mice are alive after all control mice died

* K-ras & p53 mutant mice

Avenzoar Pharmaceuticals
The road to defeating this disease

- Team efforts for scientific skills and leadership in setting a sustained effort.
- Public (government and non-profits) and private leadership in identifying and supporting the team efforts.
- Focus on development of early diagnostic tests, prevention strategies and new treatments.