

# 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



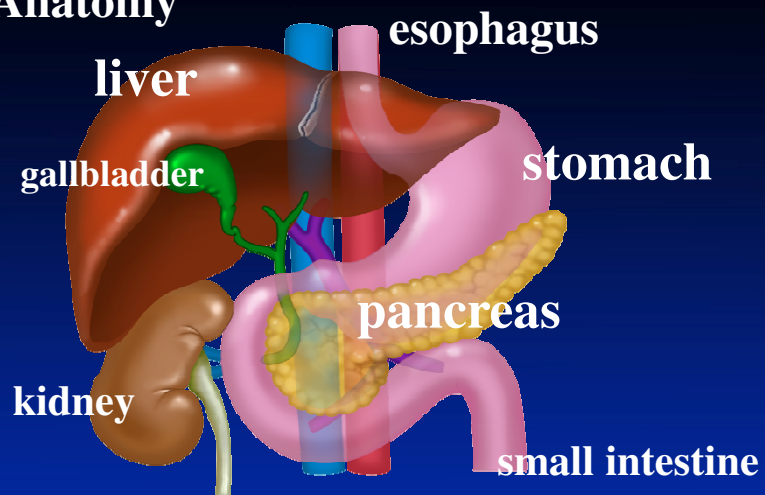
# Overview

## Anatomy and Function of the Pancreas



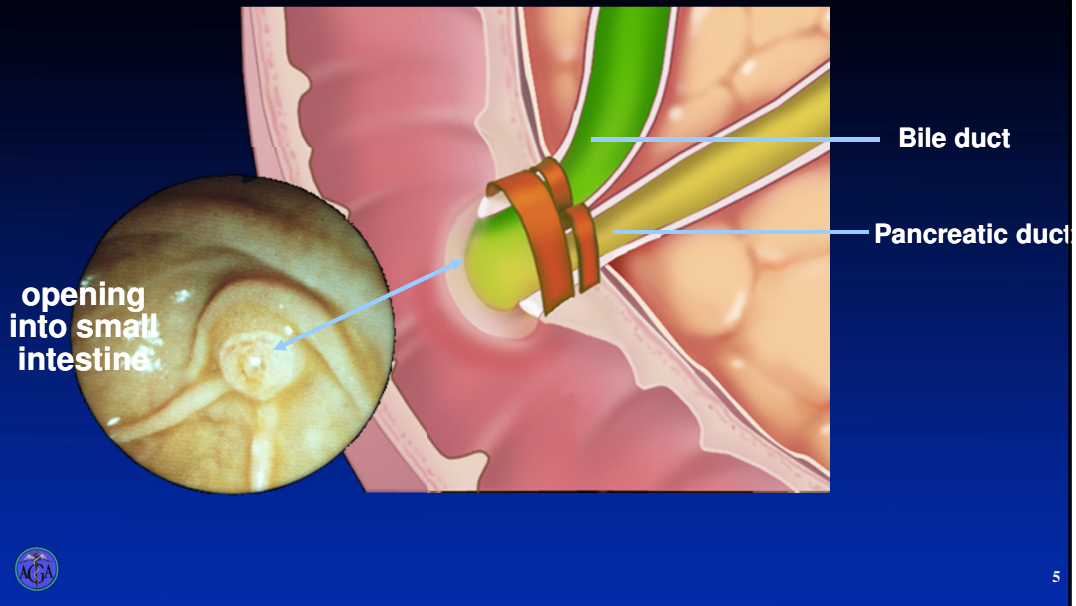
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### Organ Anatomy

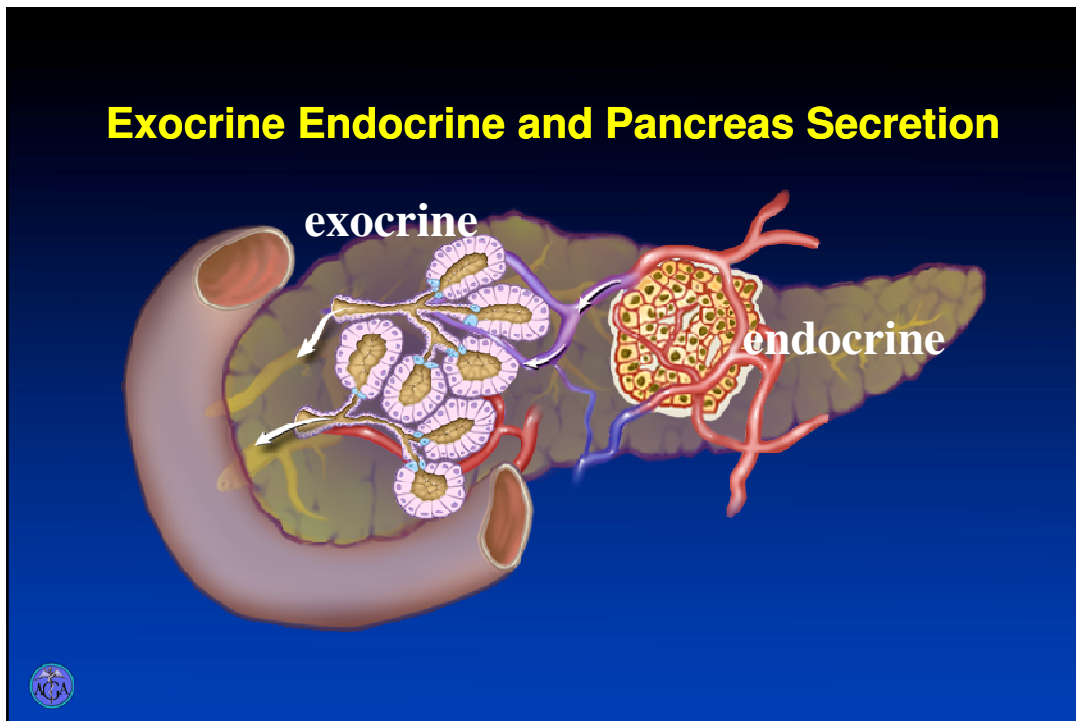


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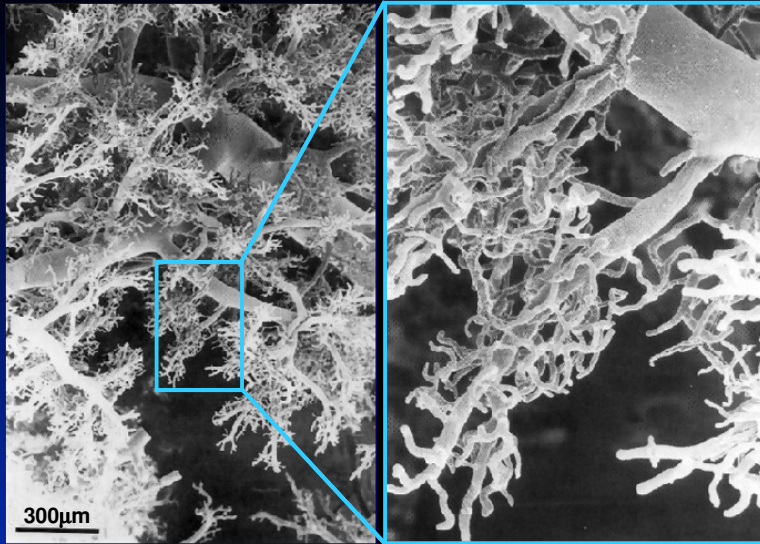
## Bile and Pancreatic Ducts and the Duodenum



## Exocrine Endocrine and Pancreas Secretion

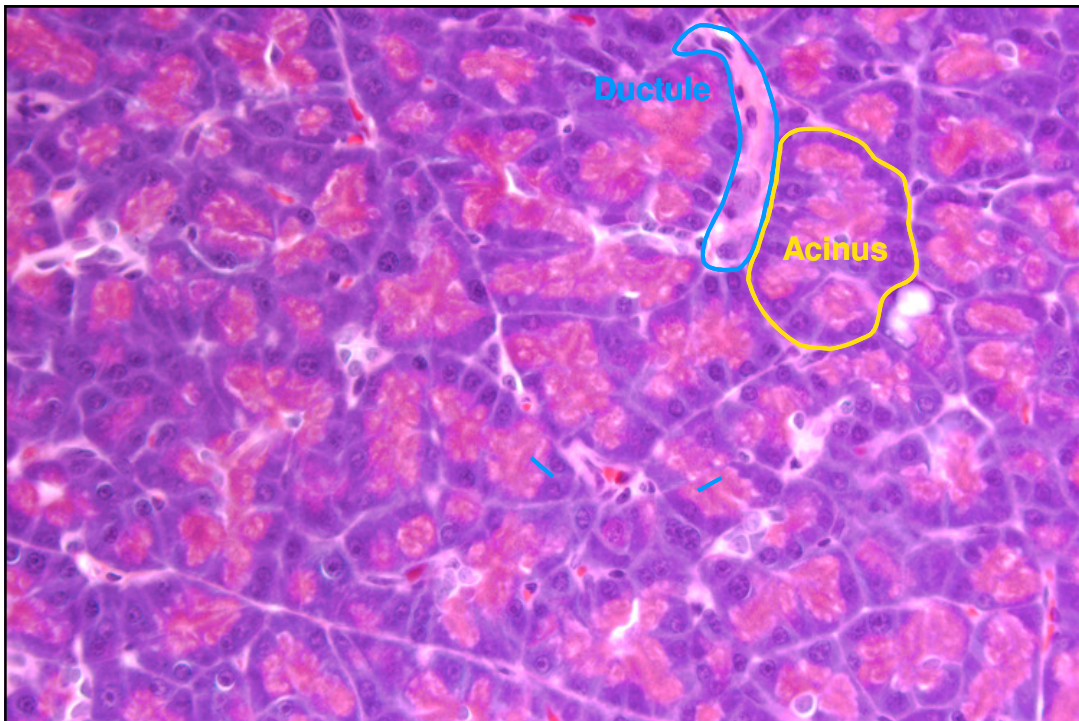


## Duct Structure



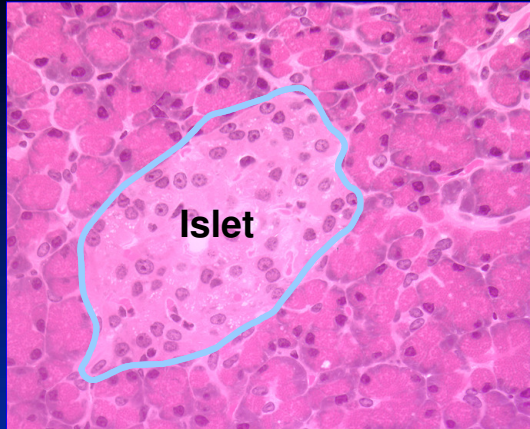
N. Ashizawa, et al., *Pancreas* 1991; 6:542

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**Pancreatic Islet**

**Secretory Products**

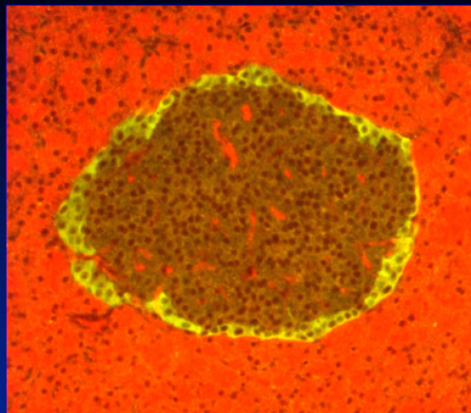


**Islet of Langerhans**

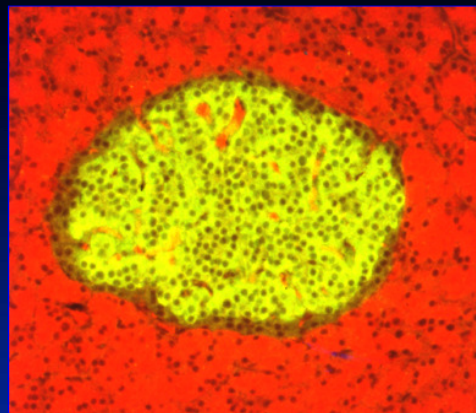
- Insulin**
- Glucagon**
- Somatostatin**
- Pancreatic polypeptide**
- Amylin**



**Pancreatic Islet**



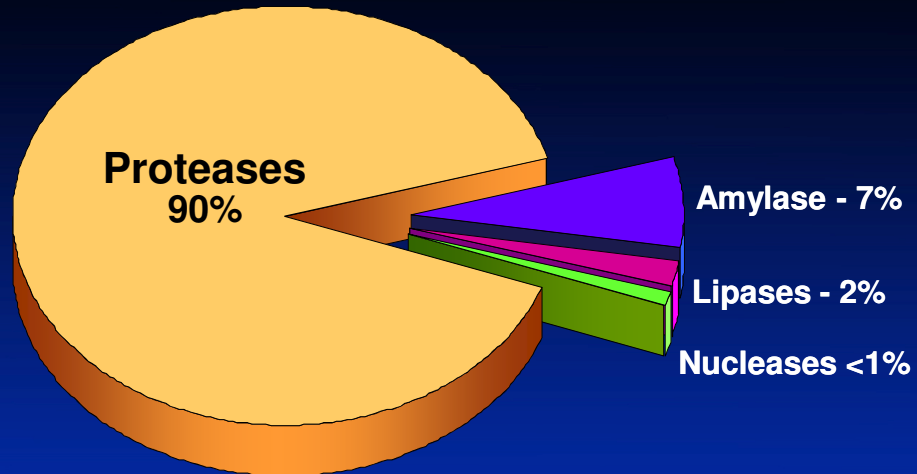
**Glucagon**



**Insulin**



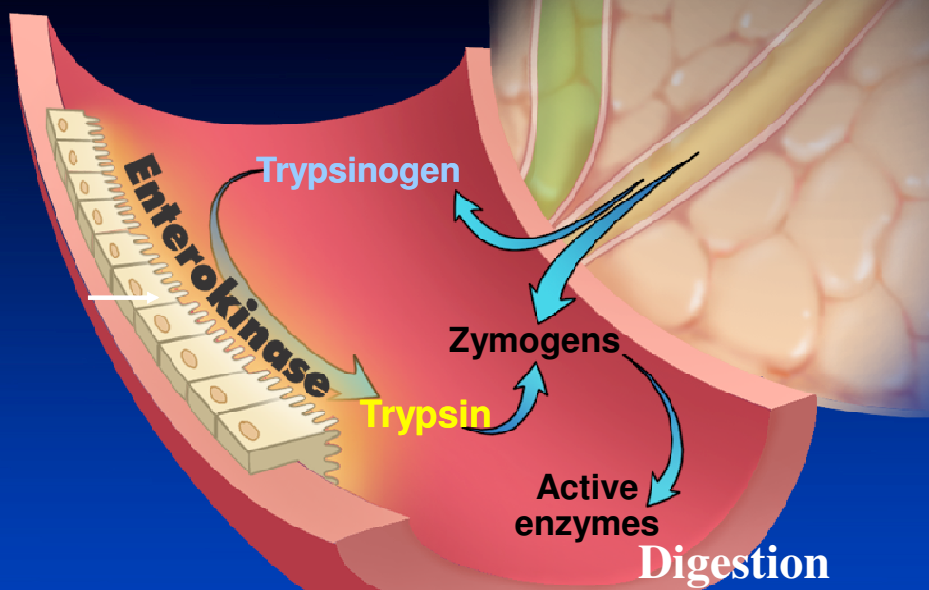
## Classes of Enzymes in Pancreatic Juice



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

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## Site of Zymogen Activation



## **Inter-relationship between pancreatic disorders**



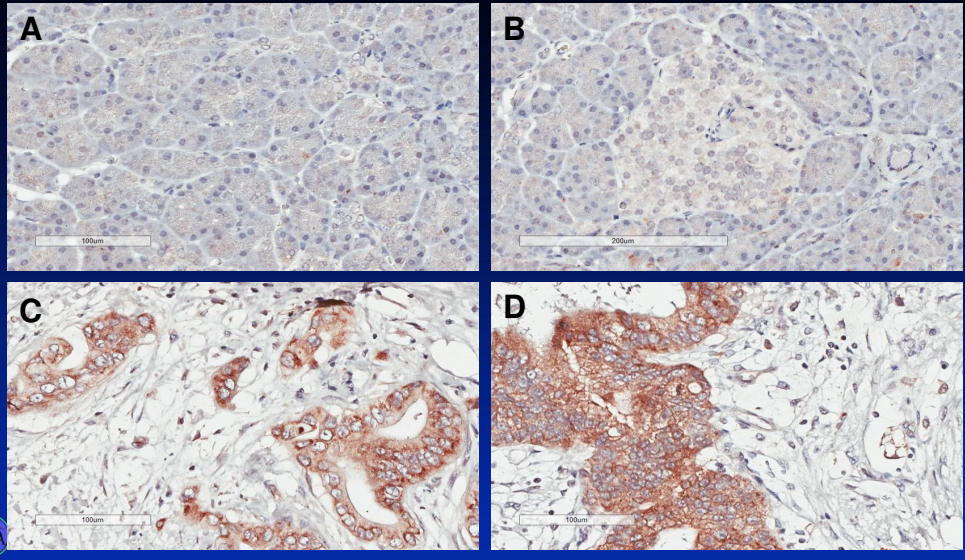
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## **Nature of pancreatic cancer**

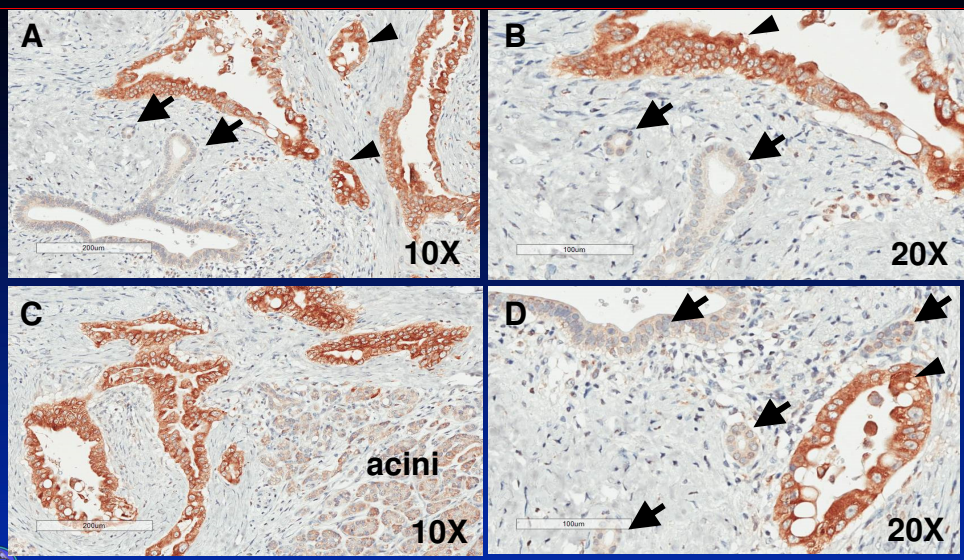


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# RON is up regulated in PDAC

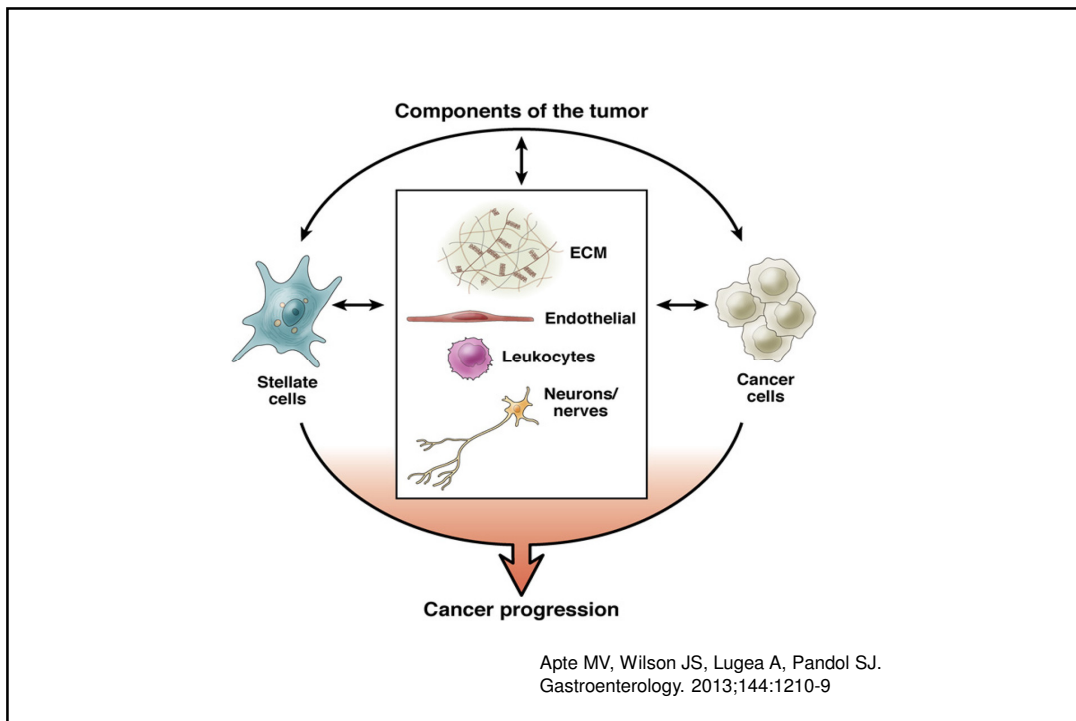
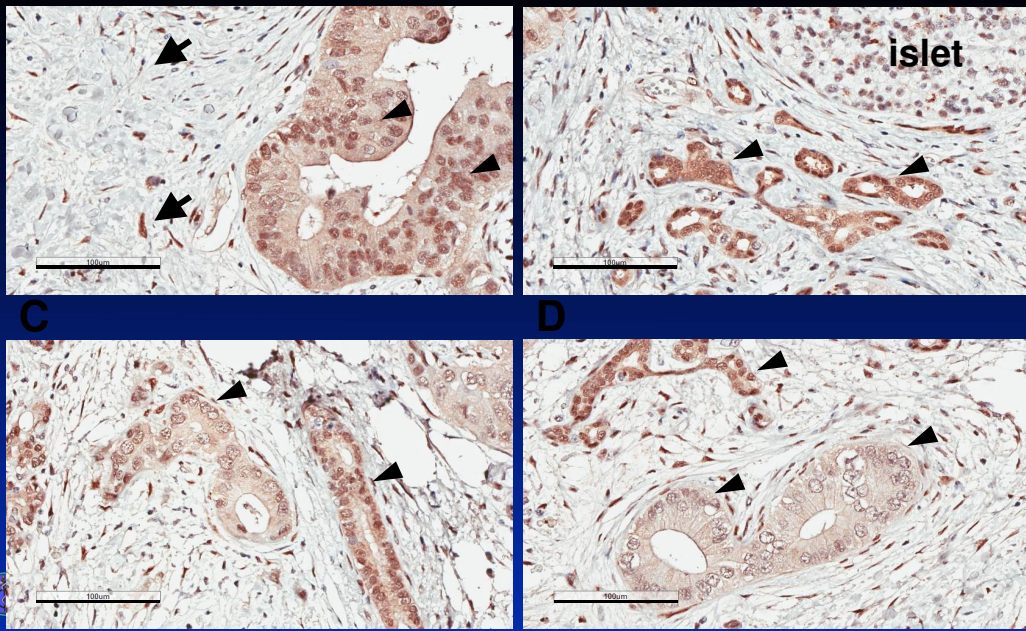


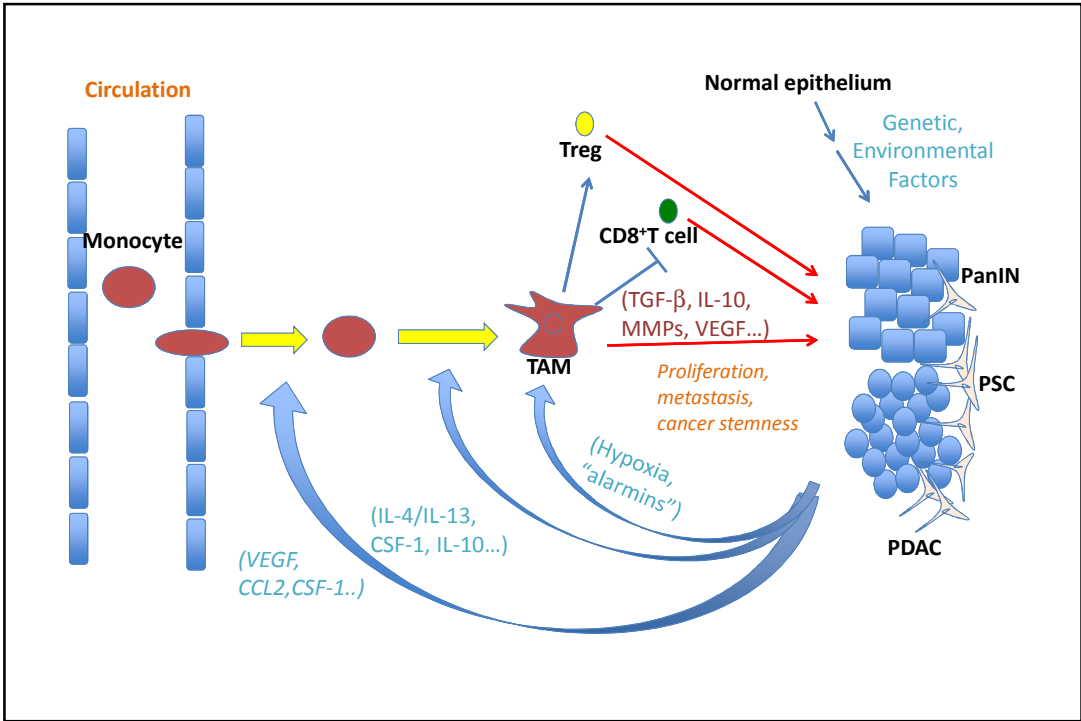
# Expression of MSP1 is elevated in PDAC





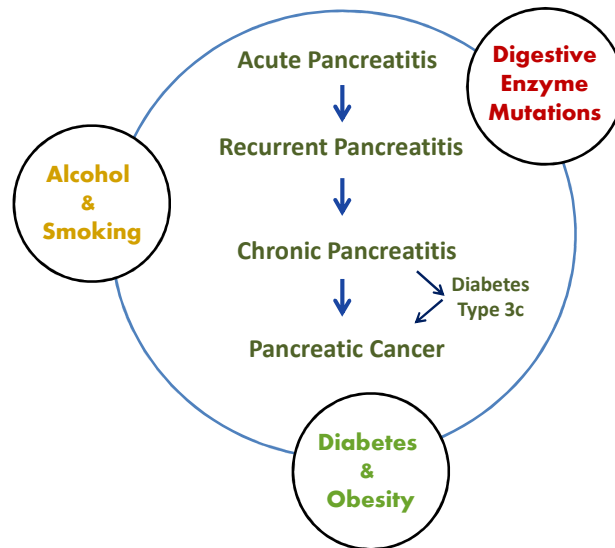
## YAP expression in PDAC cancer cells and stellate cells





Inter-relationship between pancreatic disorders

## Pancreatic Disease Continuum and Risk Factors



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 (CSCPDPCCs)**

**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.

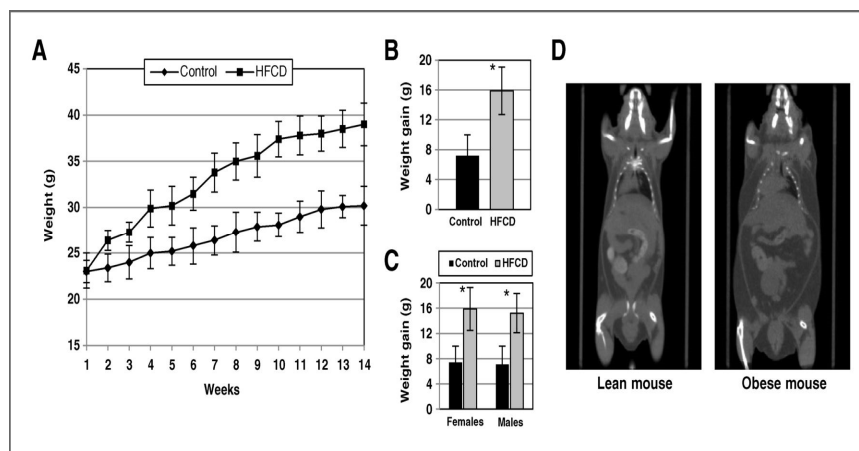
## Statins, Pancreatitis and Pancreatic Cancer Findings Lead to a Clinical Trial

- **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.
- **The association of statin use after cancer diagnosis with survival in pancreatic cancer patients: a SEER-medicare analysis.** Jeon CY, Pandol SJ, Wu B, Cook-Wiens G, Gottlieb RA, Merz CN, Merz NB, Goodman MT. *PLoS One* 2015;10:e0121783.
- **Impact of Statin Use on Survival in Patients Undergoing Resection for Early-Stage Pancreatic Cancer.** Wu BU, Chang J, Jeon CY, Pandol SJ, Huang B, Ngor EW, Difronzo AL, Cooper RM. *Am J Gastroenterol* 2015;110:1233-1239.

# 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

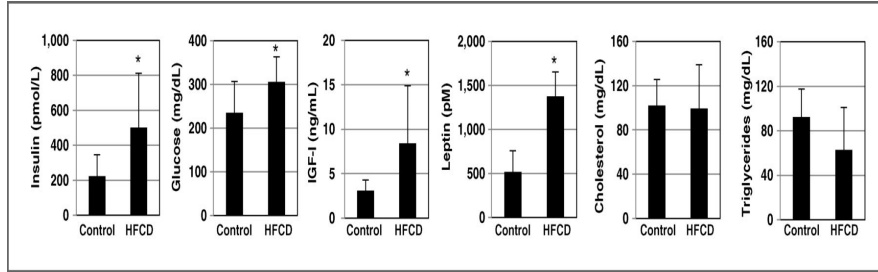


Dawson D W et al. *Cancer Prev Res* 2013;6:1064-1073

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ACR Cancer Prevention Research

## Effects of HCHF Diet on Insulin, Glucose, IGF-1, Leptin, Cholesterol and Triglyceride Levels

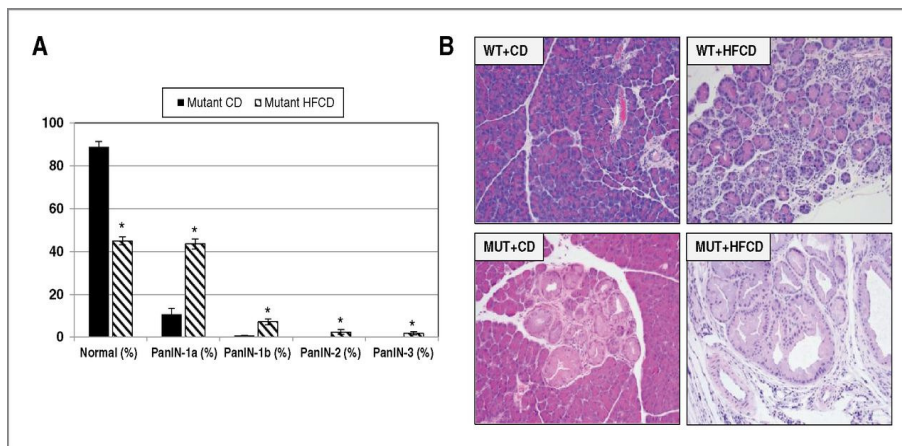


Dawson D W et al. *Cancer Prev Res* 2013;6:1064-1073

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AAO Cancer Prevention Research

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

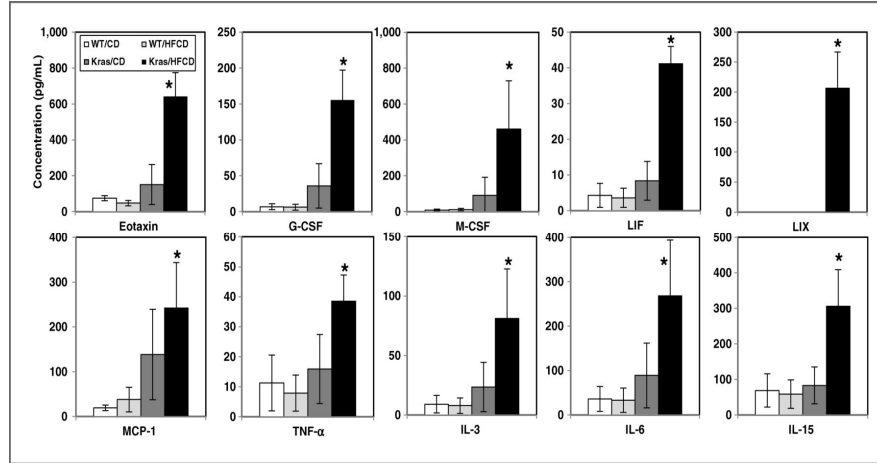


Dawson D W et al. *Cancer Prev Res* 2013;6:1064-1073

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



Dawson D W et al. *Cancer Prev Res* 2013;6:1064-1073

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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**.

Avenzoar Pharmaceuticals





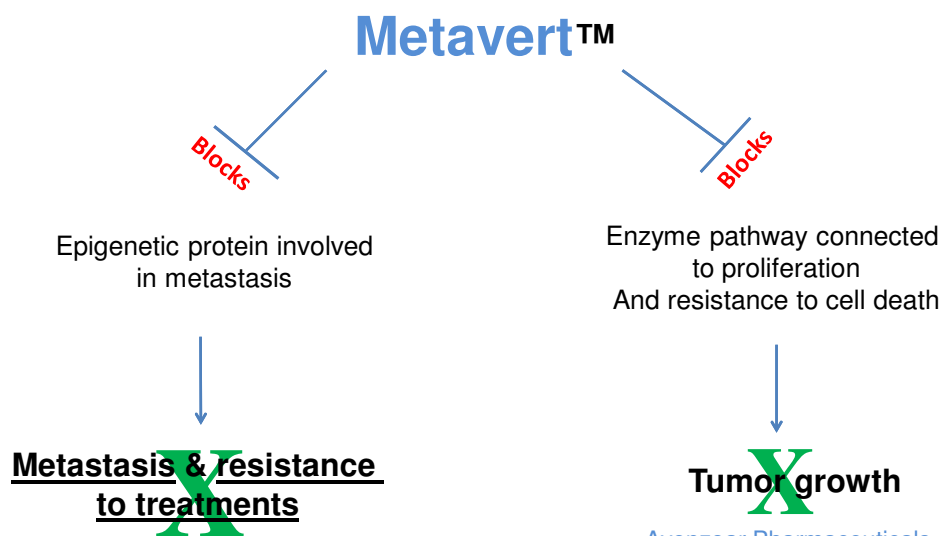
## Why Failure of Drugs to Treat Pancreatic Cancer?

- High metastasis level
- Pancreatic cancer cell resistance to treatments


Avenzoar Pharmaceuticals



## How *Metavert*<sup>TM</sup> Works and is Unique



## 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.

Avenzoar Pharmaceuticals

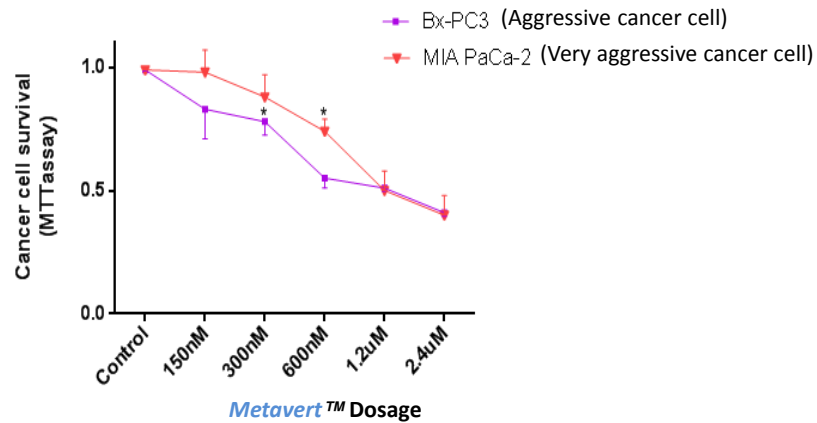


## **Metavert™** Pre-Clinical Trial Results

Avenzoar Pharmaceuticals



## Metavert™ Decreases Cancer Cell Survival

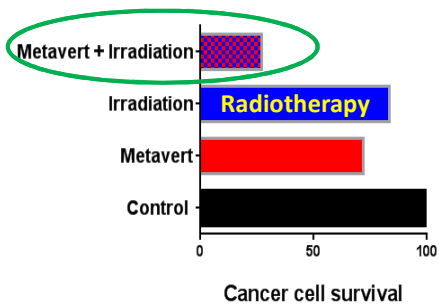


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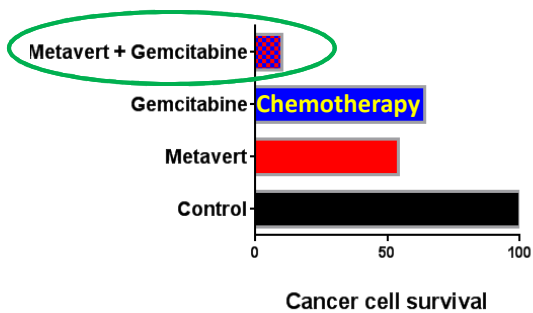


## Metavert™ Works in Synergy with Standard Treatments

### Radiation



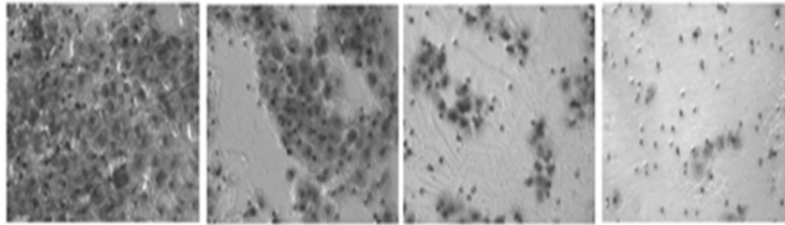
### Chemotherapy



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## Metavert™ Prevents Cancer Cell Metastasis



Control

Metavert  
(150nM)

Metavert  
(300nM)

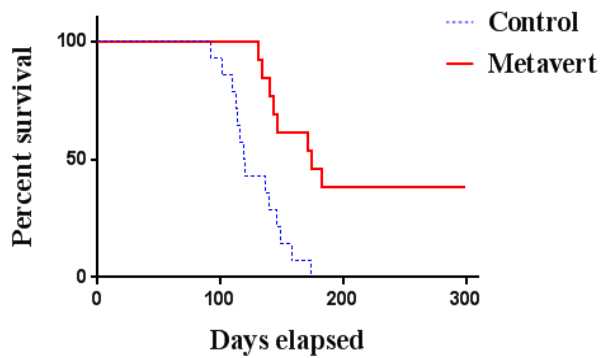
Metavert  
(600nM)

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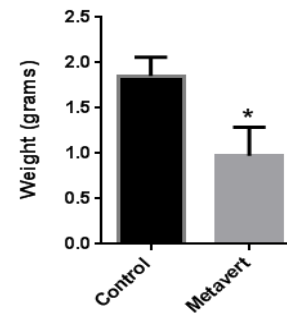


## Metavert™ Significantly Improves Survival of KPC\* Mice with Advanced Pancreatic Cancer

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



Tumor weight



\* 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.