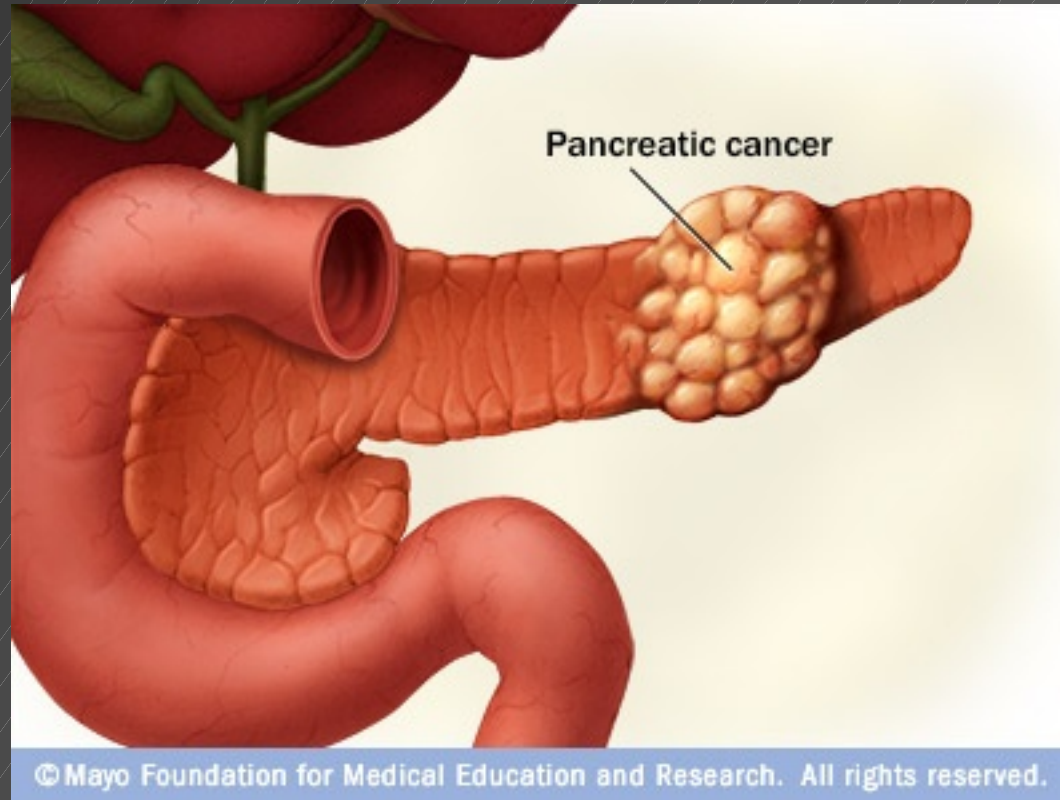


# GENETICS OF PANCREATIC



Jonathan Altamirano

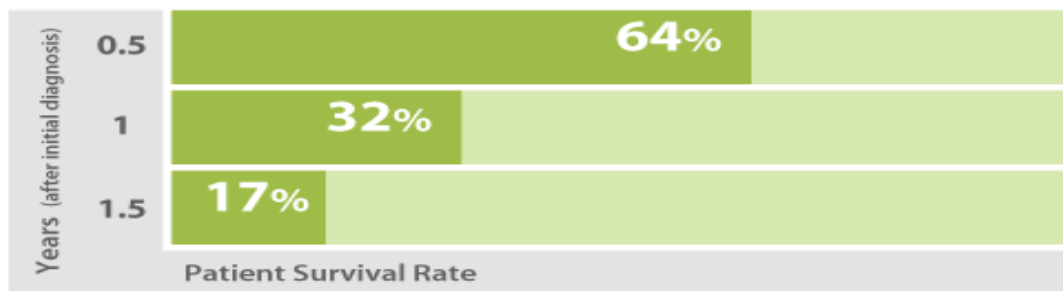
Biochem 118

03/15/12

# Pancreatic Cancer

- ⦿ Uncontrolled cell growth in pancreas
- ⦿ 4<sup>th</sup> leading cause of cancer related death
- ⦿ 5% survival rate past 5 years
  - Due to advanced stage at diagnosis
  - 20% people diagnose at appropriate time
- ⦿ Genetic and Environmental
  - 5-10% patients have family history

Advanced-Stage Pancreatic Cancer Survival Rate  
Patients Diagnosed Between 2004-2008  
Cancer Treatment Centers of America



# Environmental Risk Factors

- ⦿ Smoking: OR=1.74
  - Decreases to 1.2 after stopping
- ⦿ Type 2 Diabetes: OR= 1.8
  - Onset: 2.9
  - After duration: 1.4
- ⦿ Increased BMI: OR=1.55
- ⦿ Heavy Drinking=1.46



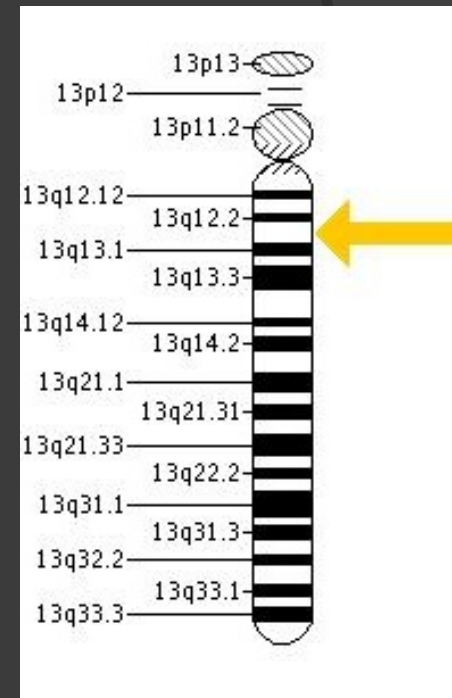
# Family History as Risk Factor

- ◎ 1<sup>st</sup> degree relative with cancer: OR=3.2
  - Sibling: 3.6
  - Parent: 2.6
- ◎ Number of Relatives with Pancreatic Cancer
  - 1: 1.76
  - 2 or more: 4.26
- ◎ 36.7% with family history develop before 50



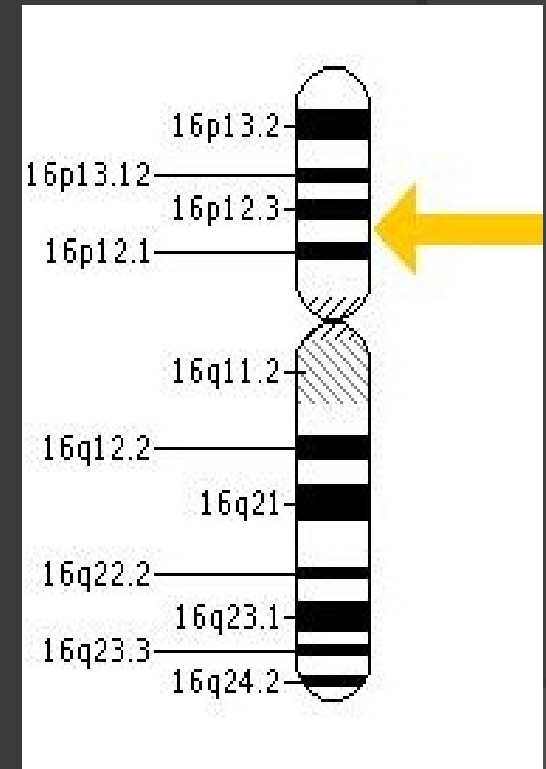
# BRCA2

- Location: 13q12.3
- Tumor Suppressing Protein
- Works with RAD51 and PALB2 to repair DNA
- Involved in Breast/Ovarian Cancer
- Mutation carriers= x3.5 chance
- 16% patients with 3+ relatives with germ-line mutations
- 12% patients with deleterious mutations
- Most mutated gene in hereditary pancreatic cancer



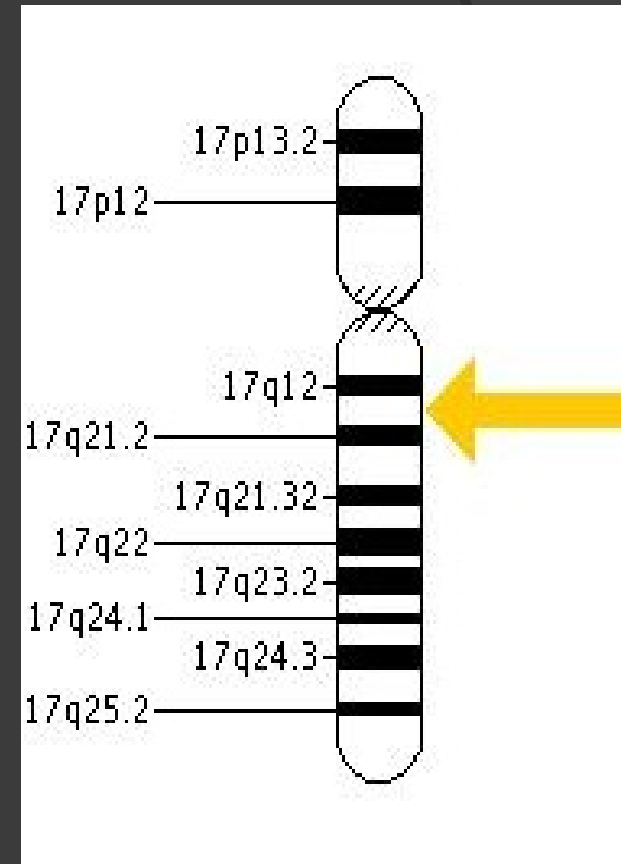
# PALB2

- Location: 16p12.2
- Partnered with BRCA2 to suppress tumors
  - Acts as anchor and stabilizer
- Involved in breast cancer
- Identified by multiple studies as a pancreatic cancer susceptibility gene
- Truncating mutation of PALB2, only found in cancer patients
- Second-most mutated gene in hereditary pancreatic cancer



# BRCA1

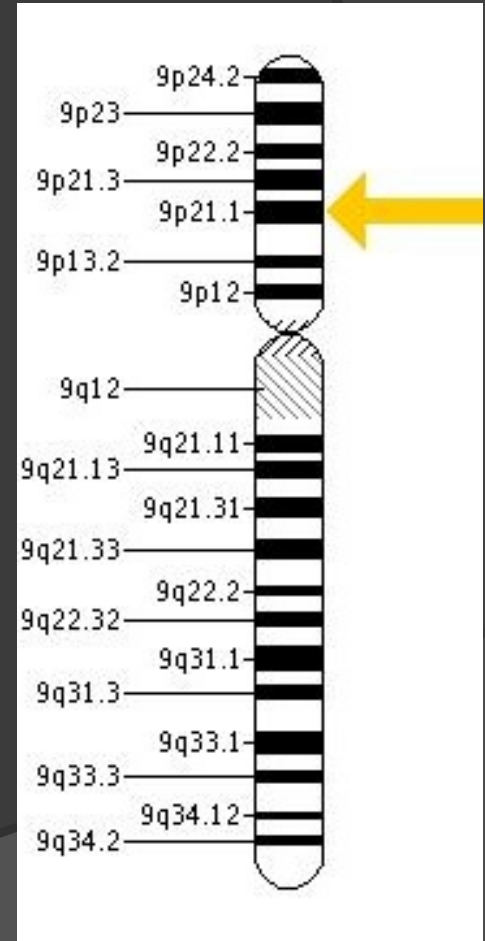
- Location: 17q21
- Works with RAD51 and BARD1 to mend DNA
- Involved in breast cancer
- Mutation carriers have seen x2.6 risk of pancreatic cancer
  - Debated: contrasting data





# p16

- ⦿ Also known as CDKN2A
- ⦿ Location:9p21
- ⦿ Interacts with CDK4 and CDK6 as a negative regulator of cell proliferation (Cell Cycle Arrest)
- ⦿ Germline defects increase risk of pancreatic cancer
- ⦿ Individuals with mutation: 38-fold increased risk
- ⦿ Other cancer risks: lung, breast, sarcoma





# Risk of Additional Cancers

- ⦿ Prostate Cancer: OR=1.45
- ⦿ Lymphoma: OR=2.83
- ⦿ Liver Cancer
- ⦿ Colon Cancer
- ⦿ Breast Cancer
- ⦿ Ovarian Cancer
- ⦿ Bile Duct Cancer

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