GENETICS OF PANCREATIC CANCER

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Pancreatic Cancer

- Uncontrolled cell growth in pancreas
- 4\textsuperscript{th} 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

![Bar chart showing survival rates for advanced-stage pancreatic cancer patients diagnosed between 2004-2008 at Cancer Treatment Centers of America. The chart indicates survival rates of 64\% at 0.5 years, 32\% at 1 year, and 17\% at 1.5 years.](image)
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\textsuperscript{st} 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
Sources

- Klein, Alison. Genetic Susceptibility to Pancreatic Cancer. In Perspective 2012
- Brand, Randall & Lynch, Henry Genotype/Phenotype of Familial Pancreatic Cancer. 2006