Genetic Counseling and Testing for Pancreatic Cancer

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What is genetic counseling?

- Two main foci:
  - Medical
    - Helping individuals/families to understand genetic risk
  - Psychosocial
    - Helping individuals/ families adjust to diagnoses

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Who Should See a Genetic Counselor?

- One of your family members has tested positive for a gene mutation
- You were diagnosed with pancreatic cancer younger than 60 years old
- You were diagnosed with pancreatic cancer at any age and one of your family members has been diagnosed with any of the following (especially younger than 50):
  - Pancreatic cancer
  - Breast cancer
  - Ovarian cancer
  - Colon cancer
- You have not been diagnosed with cancer, but you have a relative who fits one of these categories and is not available to test

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What happens in a genetic counseling session?

- Gather your medical history
- Gather and assess your family history
- Review basic genetics, inheritance and the genetic condition that you may be tested for
- Identify your chance to have a genetic change and what that could mean for you and your family members
- Discuss genetic testing options
- Give you support resources and make referrals

Medical History

- Age at cancer diagnosis
- Specific type of cancer
- Treatment (completed, planned, ongoing)
- Surgical history
- Cancer screening methods
- Women
  - Reproductive history
  - Breast biopsy history
  - Age at menarche/menopause

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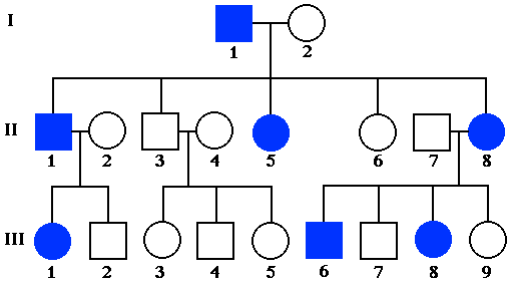
Importance of Family History

- Family history taken in the form of a pedigree
  - Pedigree is a graphical representation of a family's medical history
- Why do we take a family history?
  - To identify patterns that help us recognize what genetic condition (if any) your family may have



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Family History Questions

- Information your Genetic Counselor may ask about your relatives
  - Current age/age at death; cause of death
  - Age at diagnosis
  - Type and location of primary cancer/laterality
  - Second cancer-metastatic disease vs. new primary
  - Environmental exposures
  - Other medical conditions associated with cancers (ulcerative colitis, pancreatitis etc)
  - Ancestry (German, Irish, Native American etc.)
    - Presence of other physical findings associated with cancer syndromes (benign polyps/tumors, macrocephaly, abnormal skin pigmentation etc.)

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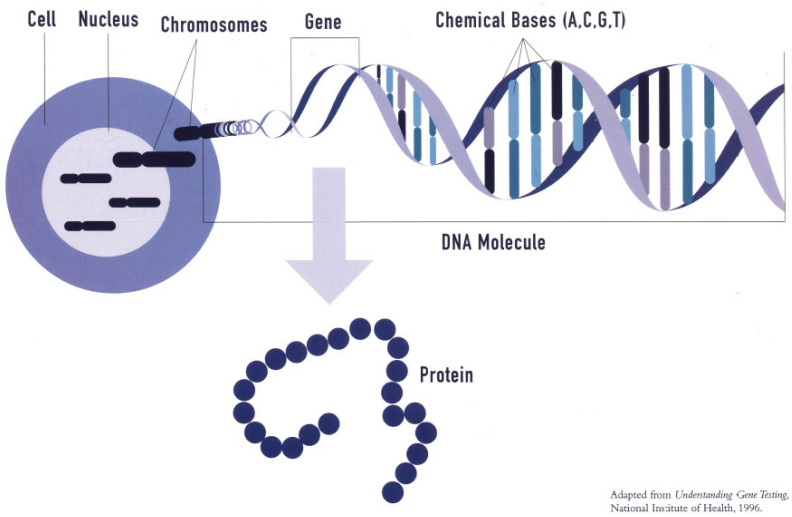
DNA, Genes, Chromosomes



Adapted from *Understanding Gene Testing*, National Institute of Health, 1996.

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Pancreatic Cancer

- Pancreatic cancer affects about 1 in 65 (1.5%) individuals
- Two major types
  - 95% are exocrine (adenocarcinomas)
  - 5% are endocrine (neuroendocrine/islet cell tumors)

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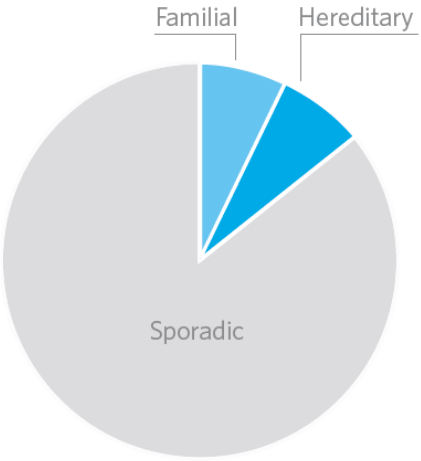
Pancreatic Cancer



- Sporadic- occur at older ages with little to no family history.
- Hereditary- genetic cause has been found.
- Familial- no identifiable genetic cause. Most likely a combination of genes, environment and lifestyle.

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BRCA1 and BRCA2

- Mutations in the *BRCA2* gene
  - May account for about 10% of hereditary pancreatic cancer
  - Cause between ~10-20% lifetime chance to have pancreatic cancer
  - Cause an increase risk of breast, ovarian, and prostate cancer

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Lynch Syndrome

- Also known as Hereditary Non-polyposis Colorectal Cancer (HNPCC)
- May cause as much as 4% of hereditary pancreatic cancer
- *MLH1* and *MSH2* mutations can cause up to a 6% lifetime chance of pancreatic cancer
- Increases the chance of colon, uterine, ovarian, stomach and other cancers

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Puetz-Jeghers Syndrome

- Rare hereditary cancer predisposition syndrome (*STK11*)
- Causes between 10-35% lifetime chance to have pancreatic cancer
- Causes an increased chance to have breast, colon, stomach, small intestine, gynecologic cancers, testicular and lung cancers.
- Causes freckle-like spots around and inside mouth/lips

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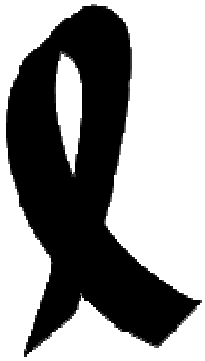
Familial Atypical Multiple Mole Melanoma (FAMMM)

- Rare hereditary cancer predisposition
- Caused by mutations in the *CDKN2A(p16*) and *CDK4* genes.
- CDKN2A mutations cause up to a 17% lifetime chance to have pancreatic cancer
- Cause in increased chance of atypical moles and melanoma.



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Other Genes

- *PALB2*= Partner And Localizer of *BRCA2*
  - Causes about 3% of hereditary pancreatic cancers
- *PRSS1* (and others)
  - Causes hereditary pancreatitis. Chronic inflammation of pancreas increases chance to develop pancreatic cancer
- *ATM*
  - About 0.5-1% of the Western population has a mutation in *ATM*
  - Causes 2-3% of hereditary pancreatic cancers

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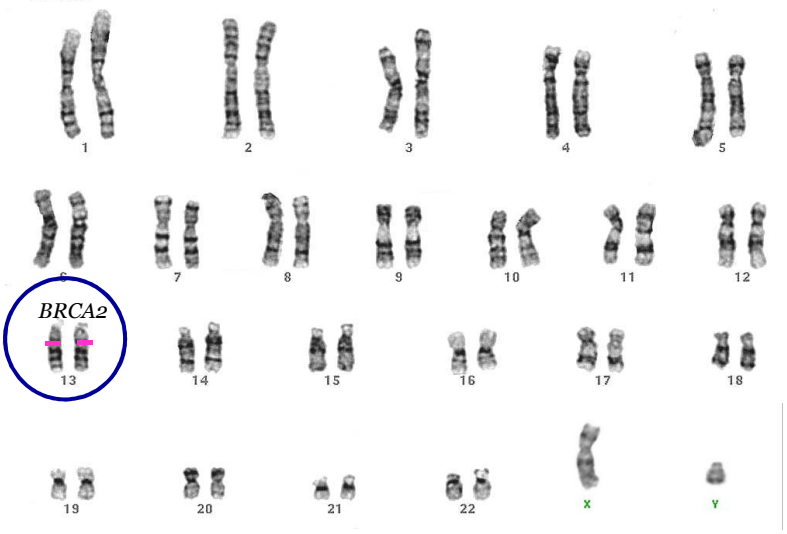
Autosomal Dominant Inheritance



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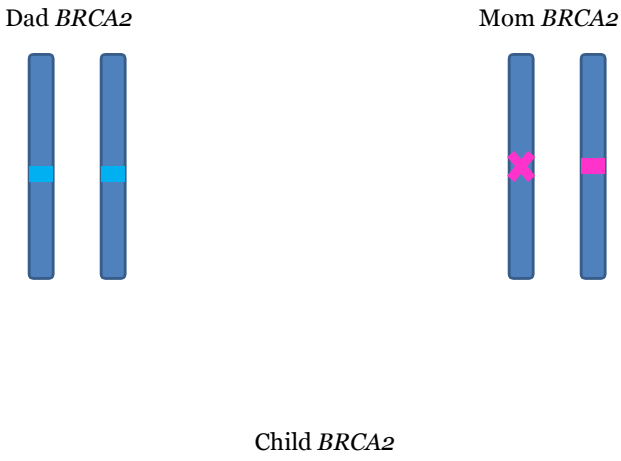

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Risk Assessment

- Risk assessment is based on:
  - Your personal and family medical history
  - Known mutation in a family member
  - Autosomal dominant inheritance
  - Statistical analysis of pedigree (Bayesian statistics, BRCAPRO, etc.)

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Genetic Testing

- Test for one syndrome (i.e. Lynch) or many at the same time
- *APC, ATM, BRCA1, BRCA2, CDKN2A, EPCAM, MLH1, MSH2, MSH6, PALB2, PMS2, STK11*, and *TP53.*
- Results in 2-4 weeks

DNA Testing.

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Types of Possible Test Results

- Positive= Mutation found
  - i.e. *BRCA2* S1870X (6137C>A)
  - Give recommendations for cancer screening/risk reduction
  - Identify other family members who would benefit from testing
- Negative= No mutation found
  - Estimate future cancer risks and make screening recommendations based on your personal/family history
- Variant= Genetic change found
  - There is a change in your DNA but we don't know what it means
  - Recommend screening based on current information about that exact change and your family history

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Pancreatic Cancer Screening

- Research is on-going to determine the best methods and intervals
- Not recommended unless
  - the family meets the definition of familial pancreatic cancer
  - an individual has a gene mutation and a family history of pancreatic cancer

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Pancreatic Cancer Screening Methods

- Magnetic resonance cholangiopancreatography (MRI-MRCP)
  - MRI done to look specifically for abnormalities in the pancreas and surrounding structures
- Endoscopic ultrasound (EUS)
  - Thin tube inserted through the mouth into the small intestine and then uses ultrasound to produce images of the pancreas.
- CA19-9
  - Blood test that can indicate pancreatic cancer

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Genetic Information Non-Discrimination Act

GINA
GENETIC INFORMATION NONDISCRIMINATION ACT

- Prohibits discrimination by health insurance companies and employers based on "genetic information"
  - Genetic information= genetic test results, relative's test results (up to and including 4th degree), and/or information about family history of any disease or disorder
- Group *and* individual health insurance plans
  - Can't use genetic information to set eligibility, premium or contribution amounts
  - Can't be considered a pre-existing condition
  - May not request or require a person to have a genetic test

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Genetic Information Non-Discrimination Act

GINA
GENETIC INFORMATION NONDISCRIMINATION ACT

- Employers cannot use genetic information to:
  - Hire, fire, promote, or for job assignments
  - They also can't request, require or buy genetic information
- Does NOT cover:
  - Manifest disease
  - Life, disability, or long-term care insurance
  - Members of the military
  - Employers with <15 people
  - People employed in law enforcement may be required to submit a DNA sample before taking part in crime scene investigation

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Patient Resources

PANCREATIC CANCER ACTION NETWORK

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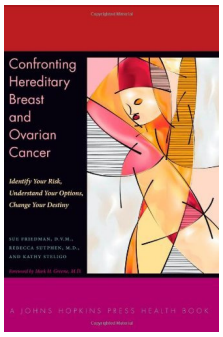

RAISING AWARENESS LSI LYNCH SYNDROME

FORCE Facing Our Risk of Cancer EMPOWERED

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WAGE
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