

Hereditary Pancreatic Cancer

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The lifetime risk of pancreatic cancer among men and women in the United States is ~1.4% and most cases of pancreatic cancers are sporadic (1). However, an estimated 10% of cases may be due to an underlying hereditary cause (2,3). Although our knowledge and the genetic testing options for hereditary pancreatic cancer have increased in recent years, the underlying genetic cause for clusters of pancreatic cancer in many families is still unclear.

Hereditary pancreatic cancer can be divided into several distinct categories: 1) known hereditary cancer syndromes mainly defined by risk for other cancers which include an increased risk of pancreatic cancer; 2) known hereditary disease which causes inflammation of the pancreas leading to an increased risk of pancreatic cancer; 3) familial pancreatic cancer (a clustering of pancreatic cancer in 2 or more first degree relatives) in which the underlying genetic cause is not yet known (4).

Genetic testing is available for the following:

Hereditary Cancer Syndromes

Syndromes and Genes	Lifetime Risk of Pancreatic Cancer	Other Cancers at Increased Risks
Hereditary Breast and Ovarian Cancer Syndrome (HBOC) Genes: <i>BRCA1</i> and <i>BRCA2</i>	4-8%	Breast, ovarian, prostate cancer and melanoma
Familial Atypical Multiple Mole Melanoma Syndrome (FAMMM) Gene: <i>CDKN2A</i>	10-19% Ref: 2,3,4,7	Melanoma
Familial Adenomatous Polyposis Syndrome (FAP) Gene: <i>APC</i>	2-4%	Colon polyps (100s to 1000s), colon cancer, osteomas, fibromas, CHRPE, desmoid tumors, small bowel and stomach cancer
Lynch Syndrome/Hereditary Non-Polyposis Colorectal Cancer (HNPCC) Genes: <i>MLH1</i> , <i>MSH2</i> , <i>MSH6</i> , <i>PMS2</i> , <i>EPCAM</i>	3-4% Ref: 3,12	Colon, uterine, ovarian, other gastrointestinal, urinary tract, sebaceous skin cancer

Peutz-Jeghers Syndrome (PJS) Gene: <i>STK11</i>	11-36% Ref 2,3	Gastrointestinal tract polyps, colorectal, breast, gynecological and stomach cancer. Other: dark blue to brown spots on the lips, hands, feet and in the mouth
Other syndromes Genes: <i>PALB2</i> and <i>ATM</i>	Not as well defined Ref: 9,10,11	Female breast cancer

Hereditary Diseases Associated with an Increased Risk of Pancreatic Cancer

Syndrome and Genes	Lifetime Risk of Pancreatic Cancer	Other Cancers at Increased Risks
Hereditary Pancreatitis (HP) Genes: <i>PRSS1</i> and <i>SPINK1</i>	25-40% Ref: 2,3	Recurrent episodes of severe pancreatitis (inflammation of the pancreas)
Cystic Fibrosis (CF) Gene: <i>CFTR</i>	Not as well defined Ref: 2	Chronic obstructive lung disease and pancreatic insufficiency

Referral for Genetic Counseling:

Consider being evaluated by a genetic counselor if you have a personal and/or family history that includes any of the following:

- Multiple cases of pancreatic cancer on the same side of the family
- A combination of related cancers on the same side of the family (e.g. pancreatic/breast/ovarian, pancreatic/melanoma, or pancreatic/colon/uterine/ovarian)
- Multiple related cancer diagnoses in one individual (e.g. pancreatic/melanoma, pancreatic/breast)
- Ashkenazi Jewish ancestry and pancreatic cancer
- Pancreatic cancer and multiple and/or early onset gastrointestinal polyps including greater than 15 gastrointestinal polyps or greater than 5 hamartomatous polyps

Screening for Individuals at Increased Risk: Routine population screening for pancreatic cancer is not useful due the limitations of the available screening and the fact that pancreatic cancer is rare (2,3). However, some data suggest that screening may prove valuable in individuals at high risk by detecting cancers at an earlier, treatable stage (2,3). The optimal screening method for pancreatic cancer is still unclear due to the risks and limitations of each of the available methods. However, consideration of screening, particularly in the setting of a research study, is recommended for individuals with a significantly increased risk to develop pancreatic cancer. We provide referrals for appropriate individuals to discuss pancreatic cancer screening and clinical trial options with our pancreatic experts.

Please contact the Smilow Cancer Genetics and Prevention Program at 203-200-4362 if you would like further information or to schedule an appointment.

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