The Genetics of Pancreatic Cancer

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What are genes?

Genes carry information within each cell of the human body. Researchers estimate that there are 30,000 different genes in each cell. Genes are packaged onto chromosomes. There are 23 pairs of chromosomes in each cell. One chromosome of each pair is inherited from the person's father and one from the person's mother.

Genes control how a cell functions, including how quickly it grows, how often it divides, and how long it lives. To control these functions, genes produce proteins that perform specific tasks and act as messengers for the cell. Therefore, it is essential that each gene have the correct instructions or "code" for making its protein so that the protein can perform the proper function for the cell.

What role do genes play in pancreatic cancer?

Many cancers begin when one or more genes in a cell are mutated (changed), creating an abnormal protein or no protein at all. The information provided by an abnormal protein is different from that of a normal protein, which can cause cells to multiply uncontrollably and become cancerous.

A person may either be born with a genetic mutation in all of their cells (germline mutation) or acquire a genetic mutation in a single cell during his or her lifetime. An acquired mutation is passed on to all cells that develop from that single cell (called a somatic mutation). Somatic mutations can sometimes be caused by environmental factors, such as cigarette smoke. Most pancreatic cancers (about 90%) are considered sporadic, meaning that the damage to the genes occurs by chance after a person is born and there is no risk of passing on the gene to a person's children. Inherited pancreatic cancers are less common (about 10%) and occur when gene mutations are passed within a family, from one generation to the next.

What are the chances a mutated gene is inherited?

Every cell usually has two copies of each gene: one inherited from a person's mother and one inherited from a person's father. Most types of hereditary pancreatic cancer follow an autosomal dominant inheritance pattern, in which a mutation needs to happen in only one copy of the gene for the person to have an increased risk of getting the disease. This means that a parent with a gene mutation may pass on a copy of the normal gene or a copy of the gene with a mutation. Therefore, a child who has a parent with a mutation has a 50% chance of inheriting that mutation. A brother, sister, or parent of a person who has a gene mutation also has a 50% chance of having the same mutation.

What is a person's average risk for pancreatic cancer?

A person with an average risk of pancreatic cancer has less than a 1% chance of developing pancreatic cancer sometime during his or her life.

How can a person know if he or she has inherited a genetic mutation that increases his or her risk of pancreatic cancer?

Only genetic testing [2] can determine whether a person has a genetic mutation. Most experts strongly recommend that people considering genetic testing first talk with a genetic counselor [3]. Genetic counselors are trained to explain the risks and benefits of genetic testing.

How does a person know if pancreatic cancer runs in the family?

Pancreatic cancer runs in a family when two or more first-degree relatives (parents, brothers, sisters, children) are diagnosed with pancreatic cancer. This is sometimes called familial pancreatic cancer. Families with three or more close relatives (first-degree relatives, grandparents, aunts, uncles, nieces, nephews, grandchildren, cousins) diagnosed with pancreatic cancer, and with one relative diagnosed before age 50, are also considered to have familial pancreatic cancer.

What is a person's risk if pancreatic cancer runs in the family?

If a person has a first-degree relative with pancreatic cancer, his or her risk of developing the disease is much higher than the average person's risk. The National Institutes of Health (NIH) estimates that the risk of developing pancreatic cancer is increased four to five times for a person with one first-degree relative with pancreatic cancer, six to seven times for a person with two first-degree relatives, and 32 times for a person with three first-degree relatives with the disease.

Which inherited genetic mutations raise the risk of pancreatic cancer?

There are several genetic conditions associated with an increased risk of pancreatic cancer. The most common hereditary syndromes linked with

increased pancreatic cancer risk are described below.

Hereditary pancreatitis (HP) [4]**.** HP is a condition that is associated with recurrent pancreatitis (inflammation or swelling of the pancreas) and pancreatic cancer. It can begin in childhood and become worse over time.

Peutz-Jeghers syndrome (PJS) [5]**.** PJS is caused by a specific genetic mutation and is associated with multiple polyps in the digestive tract that become noncancerous tumors, increased pigmentation (dark spots on the skin) on the face and hands, and an increased risk of colorectal [6], pancreatic, breast [7], uterine [8], ovarian [9], and lung [10] cancers.

Familial malignant melanoma [11] **and pancreatic cancer (FAMM-PC).** FAMM-PC is associated with a specific genetic mutation. Families with FAMM-PC have an increased risk of melanoma [12] and pancreatic cancer.

Hereditary breast and ovarian cancer (HBOC) syndrome [13]**.** HBOC is associated with mutations in the *BRCA1* and/or *BRCA2* (BRCA stands for BReast CAncer). Women with HBOC have an increased risk of breast cancer [7] and ovarian cancer [9]. Men with HBOC have an increased risk of breast cancer [14] and prostate cancer [15]. People with HBOC also have an increased risk of pancreatic cancer, specifically people who have a mutation on the *BRCA2* gene but a *BRCA1* mutation may also cause a small increased risk.

Lynch Syndrome [16]**.** Lynch syndrome is caused by mutations in several different genes and increases the risk of colorectal cancer [6], as well as cancers of the stomach [17], small intestine [18], liver [19], bile duct [20], urinary tract [21], the brain and central nervous system [22], pancreas, and possibly breast [7].

Other forms of familial pancreatic cancer. Research to find other genes associated with familial pancreatic cancer is ongoing. Families in which more than one person has developed pancreatic cancer who do not have any other signs of a specific hereditary cancer syndrome may consider participating in clinical trials to help researchers learn more about pancreatic cancer genes. A genetic counselor can help you and your family find such studies.

Are there other genetic conditions associated with an increased risk of pancreatic cancer?

The hereditary cancer syndromes described below may also increase a person's risk of pancreatic cancer. If you are concerned about your family history, talk with your doctor or genetic counselor to learn more. As research continues, doctors may learn more about the causes of inherited pancreatic cancer.

Li-Fraumeni syndrome (LFS) [23]**.** LFS is a rare condition associated with a specific genetic mutation. People with LFS have a higher risk of developing osteosarcoma [24], soft tissue sarcoma [25], leukemia, breast cancer [7], brain cancer [22], and adrenal cortical tumors [26]. People with LFS have developed pancreatic cancer, but the risk of developing the disease is not known.

Familial adenomatous polyposis (FAP) [27]**.** People with FAP often develop polyps (a growth in the colon or rectum) that are noncancerous at first, but eventually develop into cancer if not treated. FAP is caused by a specific genetic mutation that increases the risk of developing colorectal cancer [6] and other types of cancer, such as stomach [17], small intestine [18], pancreas, thyroid [28], and hepatoblastoma (liver cancer that usually occurs in early childhood).

What is your risk level?

In addition to family history, other environmental and lifestyle factors may increase your risk of pancreatic cancer. Discussing your family history and personal risk factors with a doctor can help you better understand your risk. People with a higher than average risk may benefit from genetic counseling. There is no standard procedure for screening either the general population or people with an increased risk of pancreatic cancer. However, researchers are studying high resolution computed tomography (CT or CAT) scanning [29], endoscopic ultrasound [30], and endoscopic retrograde pancreatocholangiography (also called endoscopic retrograde cholangiopancreatography or ERCP) as possible screening methods. Learn more about possible screening methods for pancreatic cancer [31].

A risk factor [32] is anything that increases a person's risk of developing cancer. Having a particular genetic mutation linked to pancreatic cancer does not mean that a person will develop cancer. Controllable risk factors, such as eating a balanced diet, maintaining a healthy weight, exercising, limiting alcoholic beverages, and avoiding tobacco products also play a role. Smoking is the biggest controllable risk factor for pancreatic cancer. Although, some people who develop pancreatic cancer have few known risk factors. Research continues to help doctors better understand the risk between genetic mutations and pancreatic cancer. Talk with a doctor for more information about risk factors and prevention for pancreatic cancer.

More Information

Guide to Pancreatic Cancer [33]

Sharing Genetic Test Results With Your Family [34]

Direct-to-Consumer Genetic Testing [35]

Additional Resources

Listing of Pancreatic Cancer Family Registries [36]

Links:
[1] http://www.cancer.net/about-us
[2] http://www.cancer.net/node/24895
[3] http://www.cancer.net/node/24907
[4] http://www.cancer.net/node/18926
[5] http://www.cancer.net/node/19535
[6] http://www.cancer.net/node/18701
[7] http://www.cancer.net/node/18618
[8] http://www.cancer.net/node/19308
[9] http://www.cancer.net/node/19481
[10] http://www.cancer.net/node/19148
[11] http://www.cancer.net/node/18853
[12] http://www.cancer.net/node/19251
[13] http://www.cancer.net/node/18922
[14] http://www.cancer.net/node/18590
[15] http://www.cancer.net/node/19562
[16] http://www.cancer.net/node/19223
[17] http://www.cancer.net/node/19645
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[35] http://www.cancer.net/node/24382
[36] http://pancreatica.org/about-pancreatic-cancer/registries/