The Genetics of Prostate Cancer

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What are genes?

Genes carry information in the form of DNA 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 prostate 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). Most prostate cancers (about 75%) are considered sporadic, meaning that the damage to the genes occurs by chance after a person is born. Prostate cancer that runs in a family, called familial prostate cancer, is less common (about 20%) and occurs because of a combination of shared genes and shared environmental or lifestyle factors. Hereditary (inherited) prostate cancer is rare (about 5%) and occurs 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. Hereditary prostate cancer appears to 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 man's average risk for prostate cancer?

A man with an average risk for prostate cancer has about a 15% chance of developing prostate cancer by age 80. The risk of prostate cancer is higher for black men than for white men. The exact reasons for this difference are not known and probably involve both biologic and socioeconomic factors.

How can a man know if he has inherited a genetic mutation that increases his risk of prostate cancer?

Only genetic testing [2] can determine whether a man has a genetic mutation, but there are no genetic tests available to specifically determine a man's chance of developing prostate cancer. Most experts strongly recommend that people concerned about a family history of prostate cancer first talk with a genetic counselor [3]. Genetic counselors are trained to determine the possibility of hereditary cancer risk for a family. However, more research is needed to better understand the genes associated with prostate cancer before genetic testing can be used to determine a man's risk of developing the disease.

How does a man know if prostate cancer runs in his family?

A man may have an increased risk of developing prostate cancer if two or more close relatives have prostate cancer. Familial prostate cancer is when two or more first-degree relatives (father, brother, son) are diagnosed with prostate cancer. Hereditary prostate cancer is when a family has any of the following characteristics:

- Three or more first-degree relatives with prostate cancer
- Prostate cancer in three generations on the same side of the family
- Two or more close relatives (father, brother, son, grandfather, uncle, nephew) on the same side of the family diagnosed with prostate cancer before age 55

Not all doctors agree with the same definitions for familial and hereditary prostate cancer, but the terms are used to help researchers and doctors learn more about patients and their family histories. Having a family history of prostate cancer does not mean that a man will develop prostate cancer.

What is a man's risk if prostate cancer runs in his family?

If a man has a first-degree relative with prostate cancer, his risk of developing prostate cancer is two to three times higher than the average risk. The risk increases as more relatives are diagnosed with prostate cancer. Researchers are constantly learning more about how specific changes in the DNA of cancer cells can cause normal prostate cells to become cancerous. This information may help doctors understand how prostate cancer can run in families.

Which inherited genetic mutations raise the risk of prostate cancer?

Currently, there is not one gene that definitively causes prostate cancer, although some genes or gene mutations have been shown to be more common for men with prostate cancer. Research to identify genes associated with an increased risk of prostate cancer is ongoing, and men with a strong family history of prostate cancer may want to consider participating in such research.

One gene known to increase the risk of prostate cancer, by as much as three times the average risk, is located on chromosome 17. What this gene does when it is not mutated is not known, but men who inherit the mutated version of the gene have a 44% higher prostate-specific antigen (PSA) level. PSA is a protein that is found in higher-than-normal levels in men with various conditions of the prostate, including prostate cancer and noncancerous conditions.

Other genes that may cause an increased risk of developing prostate cancer include *HPC1*, *HPC2*, *HPCX*, and *CAPB*. Research on these genes is new and it is not clear that they definitely cause prostate cancer. Therefore, genetic tests for these genes are not yet available to screen men who have a family history of prostate cancer.

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

The following genetic condition may increase a man's risk of prostate cancer:

Hereditary breast and ovarian cancer (HBOC) syndrome [4]**.** HBOC is associated with mutations in the *BRCA1* and/or *BRCA2* (BRCA stands for BReast CAncer). HBOC is most commonly associated with an increased risk of breast [5] and ovarian cancer [6] in women. However, men with HBOC also have an increased risk of breast cancer [7] and prostate cancer. Mutations in *BRCA1* and *BRCA2* are thought to cause only a small percentage of familial prostate cancers. Genetic testing may only be appropriate for families with prostate cancer that may also have HBOC.

What is your risk level?

In addition to family history, other environmental and lifestyle factors may increase your risk of prostate cancer. Discussing your family history and personal risk factors with a doctor can help you better understand your risk. If a man has a higher than average risk, he may consider genetic counseling and prostate cancer screening.

A risk factor [8] is anything that increases a person's risk of developing cancer. Having a particular genetic mutation linked to prostate cancer cannot predict that a man 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. Research to better understand the link between genetic mutations and prostate cancer is ongoing. Talk with a doctor for more information about risk factors, prevention, and screening for prostate cancer.

More Information

Genetics [9]

Guide to Prostate Cancer [10]

Sharing Genetic Test Results With Your Family [11]

Direct-to-Consumer Genetic Testing [12]

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/18922
[5] http://www.cancer.net/node/18618
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