The Genetics of Colorectal 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 colorectal 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 colorectal cancers (about 95%) 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 colorectal cancers are less common (about 5%) and occur when gene mutations are passed within a family from one generation to the next.

What are the chances a damaged 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 colorectal cancer usually follows 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 colorectal cancer?

A person with an average risk of colorectal cancer has about a 5% chance of developing colorectal cancer. Men have a slightly higher risk of developing colorectal cancer than women.

How can a person know if he or she has inherited a genetic mutation that increases his or her risk of colorectal 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 colorectal cancer runs in the family?

Colorectal cancer may run in the family if first-degree relatives (parents, brothers, sisters, children) or many other family members (grandparents, aunts, uncles, nieces, nephews, grandchildren, cousins) have had colorectal cancer. This is especially true when family members are diagnosed with colorectal cancer before age 50.

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

If a person's first-degree relatives developed colorectal cancer younger than age 50, his or her risk of colorectal cancer is nearly double the average risk of colorectal cancer. The risk increases if other close relatives have colorectal cancer.

Which inherited genetic mutations raise the risk of colorectal cancer?

There are several genetic conditions associated with an increased risk of colorectal cancer. Some of the most common hereditary colorectal cancer syndromes are described below.

Lynch syndrome [4]**.** Lynch syndrome is caused by mutations in several different genes and increases the risk of colorectal cancer, as well as cancers of the stomach [5], small intestine [6], liver [7], bile duct [8], urinary tract [9], the brain and central nervous system [10], and possibly breast [11].

- Muir-Torre syndrome [12] is a type of HNPCC associated with skin changes in adulthood that are usually not cancerous.
- Turcot syndrome [13] is a type of both HNPCC and familial adenomatous polyposis (see below) that is associated with an increased risk of colorectal cancer and brain tumors [14], specifically glioblastoma for people with HNPCC.

Familial adenomatous polyposis (FAP) [15]**and attenuated family adenomatous polyposis (AFAP)** **[16].** People with FAP or AFAP often develop polyps (a growth in the colon or rectum) that are noncancerous at first, but eventually develop into cancer if not treated. FAP and AFAP are caused by a specific genetic mutation that increases the risk of developing colorectal cancer and other types of cancer, such as stomach [5], small intestine [6], pancreas [17], thyroid [18], and hepatoblastoma (liver cancer that usually occurs in early childhood).

- Gardner syndrome [19] is a type of FAP also associated with osteomas (bony tumors) of the jaw, extra teeth, and soft tissue tumors including lipomas (fatty tissue) and fibromas (fibrous tissue).
- Turcot syndrome [13] is a type of both HNPCC (see above) and FAP. Medulloblastoma, a type of brain tumor, is more common for people who have a genetic mutation associated with FAP.

MYH-associated polyposis (MAP) [20]**.** MAP is caused by a specific genetic mutation that is associated with multiple colon polyps that increase the risk of colorectal cancer.

Peutz-Jeghers syndrome (PJS) [21]**.** 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 breast [11], uterine [22], ovarian [23], and lung [24] cancers.

Juvenile polyposis syndrome (JPS) [25]**.** JPS is caused by mutations of two different genes. People with JPS often have specific types of polyps in the colon or other parts of the digestive system that increase the risk of colorectal, stomach [5], small intestine [6], and pancreatic [17] cancers.

What is your risk level?

In addition to family history, other environmental and lifestyle factors may increase your risk of colorectal cancer. Discussing your family history and personal risk factors with a doctor helps you better understand your risk. People with a higher than average risk may benefit from genetic counseling and early detection strategies.

A risk factor [26] is anything that increases a person's risk of developing cancer. Having a particular genetic mutation linked to colorectal cancer cannot predict 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. Most people who develop colorectal cancer have few known risk factors. Research to better understand the link between genetic mutations and colorectal cancer is ongoing. Talk with a doctor for more information about risk factors, prevention, and screening for colorectal cancer.

More Information

Genetics [27]

Guide to Colorectal Cancer [28]

Chemoprevention [29]

Sharing Genetic Test Results With Your Family [30]

Direct-to-Consumer Genetic Testing [31]

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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/patient/Cancer+Types/Lynch+Syndrome

[5] http://www.cancer.net/node/19645
[6] http://www.cancer.net/node/19632
[7] http://www.cancer.net/node/19134
[8] http://www.cancer.net/node/18505
[9] http://www.cancer.net/node/18520
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