

About 5 to 10 percent of all colorectal cancers are caused by a heritable mutation

Most cancer occurs by chance. In some families we see more cancer than we would expect by chance alone. In families that carry a genetic change or mutation that is associated with causing cancer, the cancer risk is much higher than that of the general population. Genetic testing helps to determine which of these families have cancer that is related to an inherited gene mutation.

Sporadic Cancer – Cancer which occurs by chance. People with sporadic cancer typically do not have relatives with the same type of cancer.

Familial Cancer – Cancer likely caused by a combination of genetic and environmental risk factors. People with familial cancer may have one or more relatives with the same type of cancer or related types of cancers; however, there does not appear to be a specific pattern of inheritance (e.g., the cancer risk is not clearly passed from parent to child).

Hereditary Cancer – Cancer occurs when an altered gene (genetic change or mutation) is passed down in the family from parent to child. People with hereditary cancer are more likely to have relatives with the same type or a related type of cancer. They may develop more than one cancer and their cancer often occurs at an earlier than average age.

Types of Common Hereditary Colon Cancer

1. **Lynch Syndrome**, also known as Hereditary Non-Polyposis Colorectal Cancer (HNPCC) is the most common hereditary cause of colorectal cancer and accounts for 2-3% of all colorectal cancers. The majority of Lynch syndrome is due to mutations in the MLH1, MSH2, MSH6, PMS2, or EPCAM (also known as TACSTD1) genes. These mutations are associated with an increased lifetime risk for colorectal cancer (CRC) and other malignancies within the tumor spectrum including at least endometrial, ovarian, gastric, small bowel, urothelial, hepatobiliary tract, sebaceous and pancreatic cancers. These mutations can be inherited from a person’s mother or father.

Lynch Syndrome affects 28,000 individuals annually. Cancer risks associated with Lynch Syndrome are largely derived from family studies. Mutations in MLH1 and MSH2 account for 70-90% of families with Lynch Syndrome.

Cancer Risks for Lynch Syndrome Mutation Carriers

| Lynch Syndrome | Mutation Carrier Risk | General Population Risk |
|-------------------------------|-----------------------|-------------------------|
| Colorectal | Up to 82% | 2% |
| Endometrial (uterine) | Up to 71% | 1.5% |
| Stomach | Up to 13% | < 1% |
| Ovarian | Up to 12% | < 1% |
| Second cancer within 10 years | 30% | 3.5% |
| Second cancer within 15 years | 50% | 5% |

2. **Familial Adenomatous Polyposis (FAP) or Attenuated FAP (AFAP)** which accounts for <1% of colorectal malignancies is an inherited condition that is caused by a mutation in the APC gene. Patients who have a mutation in the APC gene can have:

- Many precancerous polyps or adenomas; possibly hundreds or thousands in the colon and rectum.
- A milder form of FAP may present with a smaller number of colorectal polyps or adenomas.
- A greatly increased risk of colorectal cancer.
- An increased risk for other associated cancers.

An APC mutation can be inherited either from a person’s mother or father.

Cancer Risks for FAP or AFAP; APC Mutation Carriers

| FAP and AFAP | Gene Mutation Carrier Risk | General Population Risk |
|---------------------------|----------------------------|-------------------------|
| Colorectal cancer in FAP | Approximately 100% | 2% |
| Colorectal cancer in AFAP | 80-100% | 2% |
| Small bowel cancer | 5-12% | N/A |

3. **MYH-Associated Polyposis (MAP)** is a syndrome that was discovered fairly recently and is rare. Because of the numerous colorectal polyps or adenomas that occur in MAP, the colorectal cancer risk is known to be significantly increased.

Additionally, it is possible that risks of other cancers, such as small bowel, may be increased as well. Individuals with MAP often do not have a family history of colon cancer or colon polyps in family members, although siblings may be affected.

MAP is caused by mutations in the MYH gene and individuals with MAP have mutations in both of their MYH genes, one from each parent.

Screening Guidelines

If you are age 50 and older, you are at average risk if you have the following:

- No symptoms.
- No personal or family history of colorectal cancer or precancerous polyps (benign growths in the inside surface of the colon or rectum).
- No personal history of inflammatory bowel disease (ulcerative colitis or Crohn’s colitis).
- People with an increased risk for colorectal cancer may benefit from earlier, more frequent screenings.

You are at increased risk if you have one of the following:

- Personal history of colorectal cancer or precancerous polyps.
- Family history of a first-degree relative (such as a parent or sibling) who had cancer or a precancerous polyp in the colon or rectum before the age of 50, or multiple family members with colorectal cancer or polyps.
- Personal history of long-standing (more than eight years) inflammatory bowel disease.
- Family history of familial adenomatous polyposis (FAP). If left untreated, these individuals almost always go on to develop colon cancer by age 40.

- Family history of Lynch syndrome (formerly known as hereditary nonpolyposis colorectal cancer), a condition caused by mutations in specific genes.
- A patient may also have an increased risk for colorectal cancer if they've had therapy for another type of cancer. In that case, more frequent screenings may be recommended.

Otogenetics Colorectal Cancer Screening Panels

- **Colorectal Cancer Panel – 12 genes** APC, BMPR1A, CDH1, EPCAM, MLH1, MSH2, MSH6, MUTYH, PMS2, PTEN, SMAD4, STK11
- **Lynch Syndrome - 5 genes** EPCAM, MLH1, MSH2, MSH6, PMS2
- **Comprehensive Inherited Cancer Panel – 39 genes Linked to breast, ovarian, colon, pancreatic, and other major cancers** APC, ATM, BARD1, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A, CHEK2, ELAC2, EPCAM, FANCC, HRAS1, MEN1, METMLH1, MRE11A, MSH2, MSH6, MUTYH, NBN, NF1, NTRK1, PALB2, PALLD, PMS2, PTCH, PTEN, RAD50, RAD51, RAD51C, RAD51D, RET, SMAD4, STK11, TP53, VHL

What Do My Test Results Mean?

Testing does not tell you if you currently have cancer. Your test results tell you about your inherited *risk* of having cancers.

A negative test result means that you do not have a gene mutation in the genes that were evaluated.

Although the gene test can detect the majority of mutations:

- You could have a gene mutation that the test wasn't targeted to detect.
- Or if your family carries a high-risk gene mutation that researchers haven't yet identified then the test would not be able to detect this gene mutation and you could be a carrier.

A negative test result does not eliminate the chance of developing non-hereditary cancer. You may still have the same cancer risk as that of the general population.

A positive test result means that you have a gene mutation that is associated with colorectal cancer. A positive test result **does not** mean that you have cancer or that you will certainly have cancer. A positive test result tells you that you have a much higher risk of developing CRC cancer compared with someone who does not have the mutation. A positive test result helps you to better understand your personal risk of developing colorectal and associated cancers. You can then make choices on what to do to reduce your risk and about what follow up care is right for you.

Hereditary Colon Cancer Mutations Can Be Passed On In A Family

- If you have a mutation in one of these genes, your parents, your children, and your brothers and sisters have a chance that they have the same mutation.
- Other relatives may be at risk to carry the same mutation. Testing is the only way to accurately identify mutation carriers.
- It is important to share test results with family members.
- Individuals may differ in their viewpoints and reactions to genetic testing.

Colorectal Cancer Risk Management

Options for reducing cancer risk are available whether or not you have already had a diagnosis of cancer and/or polyps (adenomas). Your healthcare providers will discuss your testing options and medical management options for reducing risk such as **Increased Surveillance, Surgical Management, and Chemoprevention**. Please discuss your options with your healthcare providers to determine how you will manage your cancer risks.

For more information and patient advocacy groups, please visit our Patient Portal at

www.otogenetics.com/patientportal.com

Otogenetics Corporation

4553 Winters Chapel Road, Suite 100,
Atlanta GA 30360



Understanding Colorectal Cancer Screening



www.otogenetics.com

Discovery Diagnosis Better Health Outcomes