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My46 Trait Profile

Lynch syndrome

Other Names: Hereditary Non Polyposis Colon Cancer (HNPCC)

Lynch syndrome is a cancer syndrome where individuals have an increased chance of developing colon cancer, uterine cancer, and other types of cancers. It is caused by mutations in any one of many different genes.

Characteristics of Lynch syndrome

Most cancer occurs as a result of normal aging, lifestyle, and exposures. However, approximately 5% of colon cancer is caused by an inherited risk factor (genetic change or mutation) that increases the chances of developing colon, uterine, and some other cancers. The characteristics of Lynch syndrome can include early-onset cancer, multiple generations affected with cancer, and family members developing more than one separate cancer (e.g., colon cancer and uterine cancer). Lynch syndrome is the most common inherited colon cancer syndrome. It is estimated that as many as 1 in 370 to 1 in 440 people have Lynch syndrome. The chance of developing colon cancer for a person with Lynch syndrome can be as high as 80% over their lifetime. The average age of colon cancer diagnosis is 44 years old. The chance of developing uterine cancer for women with Lynch syndrome is approximately 60% over their lifetime. Other cancers associated with Lynch syndrome include ovarian, stomach, small bowel, pancreas, brain, breast and skin cancer.

Diagnosis/Testing

Most individuals with Lynch syndrome have a change or mutation in one of the following genes: MLH1, MSH2, MSH6, PMS2, and EPCAM. These genes (except for the EPCAM gene) are considered mismatch repair genes because they make proteins that are responsible for correcting mistakes in the genetic code that occur during cell division. Mutations in these genes do not allow for these errors to be corrected and as a result, cells may grow uncontrollably. This uncontrolled growth is what can cause the cancers in affected individuals.

Management/Surveillance

With appropriate management and surveillance, cancers can be prevented or detected at earlier stages, when there is a greater chance for successful treatment. Individuals with Lynch syndrome are recommended to have a colonoscopy (i.e., a procedure to examine the inside of the colon and rectum) every 1-2 years starting at the age of 20. The National Cancer Network (NCCN) recommends that females with Lynch syndrome have risk-reducing surgeries such as hysterectomies (removal of the uterus) and bilateral salpingo-oophorectomies (removal of the fallopian tubes and ovaries) once completing childbearing or between the ages of 35-40 years old. Screening for ovarian and uterine cancer may also be recommended and can include transvaginal ultrasound, CA-125 (blood tests), and uterine biopsies.

Mode of inheritance

Lynch syndrome is inherited in an autosomal dominant pattern. This means inheriting one gene mutation is enough for an individual to be at increased risk of developing Lynch syndrome-related cancers.

Risk to family members

Each child or sibling of an individual with Lynch syndrome has a 50% chance of inheriting a gene mutation. The

mutation is most often inherited from a parent. Sometimes, it is clear from the family history of cancer whether a mutation was inherited from the father or mother. When it is not clear, genetic testing can help identify the origin of the mutation, so extended family members can be informed.

When both parents have a mutation in the same mismatch repair gene (i.e. MLH1, MSH2, MSH6, PMS2), it is possible for their children to inherit two copies of the gene with mutations. This causes a condition called Constitutional Mismatch Repair deficiency (also known as Biallelic Mismatch Repair Deficiency), which is associated with a very high risk of developing brain or colon cancer at a young age.

Special considerations

None

Resources

KinTalk at UCSF
http://kintalk.org
Lynch Syndrome International
http://www.lynchcancers.com
Genetics Home Reference: Lynch syndrome
http://ghr.nlm.nih.gov/condition/lynch-syndrome
Cancer.Net: Lynch Syndrome
http://www.cancer.net/cancer-types/lynch-syndrome

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