



RAF	CEA	ctDNA	DPYD	FAP	HER2	KRAS	MSI	MSS	NRAS	NTRK	Shc	Tyrosinase
Lynch Syndrome												
K3CA	TMB	Tumor Location/Sidedness				UGT1A1						

## Hereditary Nonpolyposis Colorectal Cancer (HNPCC)

### Who should be tested for Lynch Syndrome (HNPCC)?

All colorectal cancer (bowel cancer) patients with microsatellite instability (MSI-High) should be tested for Lynch Syndrome. CRC patients with a family history of colorectal or other Lynch Syndrome associated cancers should be tested. All biological family members (siblings, children, cousins) of CRC patients with Lynch Syndrome should themselves be tested. An early Lynch Syndrome diagnosis can prevent colorectal cancer in family members. CRC patients diagnosed at less than 50 years old should undergo genetic counseling and evaluation for Lynch and other hereditary colorectal cancer syndromes.

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### What is Lynch Syndrome?

Lynch Syndrome, also called Hereditary Nonpolyposis Colorectal Cancer (HNPCC), is an inherited syndrome of high colorectal cancer risk. Lynch Syndrome is also associated with a high risk of other cancers, including endometrial (uterine) cancer, stomach (gastric) cancer, and ovarian cancer. It is caused by mutations in one of the mismatch repair genes. These genes are known as MLH1, MSH2, MSH3, MSH6, EPCAM, and PMS2. MLH1 and MSH2 mutations are the most common cause of Lynch Syndrome.

During growth, or healing of organ and tissue damage, your cells divide to make more cells. As each cell splits, the DNA divides and makes a copy of itself for the new cells. Mistakes in the copying process are called DNA mismatch. In patients with Lynch Syndrome, the ability to repair these common mistakes is impaired or deficient.

### How is Lynch Syndrome tested? How are the results reported?

When testing for Lynch Syndrome, your medical team is looking specifically at your genes, not your tumor's genes. Initial testing on tumor (tumour) tissue (immunohistochemistry, IHC) may be performed to screen for abnormalities in the proteins encoded by MMR genes. Genetic testing for Lynch-causing mutations in the MMR genes is performed on a blood sample or on cells collected from your mouth or saliva.

Testing for Lynch Syndrome is often accompanied by consultation with a genetic counselor, a health care provider with cancer genetics training. Genetic counselors provide risk assessment, education, and support for patients and families that may be affected by a genetic syndrome.

If you have Lynch Syndrome, your report will say "positive", "pathogenic mutation detected", or "variant detected, likely pathogenic" and will give the specific mutation found. Pathogenic describes something that causes a disease.

If you do not have Lynch Syndrome, your results will be reported as "negative" or "no pathogenic mutation detected".

### What do my Lynch Syndrome results mean for me? How do they impact my treatment?

If you do not have an MMR gene mutation that causes Lynch Syndrome, your prognosis will be determined from other information about your tumor. Your treatment options include traditional chemotherapy and targeted therapy and/or immuno-therapy based on the results of your other biomarker testing.

If you have a pathogenic mutation in one of your MMR genes, you have Lynch Syndrome.

- Lynch Syndrome causes 2-4% of colorectal cancers.
- Immunotherapy treatment (for example, pembrolizumab, ipilimumab, nivolumab) is effective against Lynch Syndrome colorectal cancers.
- Fluorouracil-based adjuvant chemotherapy may be less effective in Lynch associated stage II CRC.

If you have Lynch Syndrome, you have an increased risk of several different types of cancer including colorectal, endometrial (uterine), stomach (gastric), and ovarian, and, less frequently, biliary tract, urinary tract, and some skin cancers. The level of risk depends on which mutation you have. For example, MLH1 and MSH2 mutations lead to a lifetime cancer risk of 70-80%, while MSH6 and PMS2 mutations are associated with a 25-60% lifetime risk of cancer.

You will need lifelong screening for Lynch Syndrome associated cancers. Talk to your medical team about the timing and frequency of cancer screening tests and the possibility of preventive (prophylactic) procedures.

Because Lynch Syndrome is inherited, it is critical that your biological family members know about your Lynch Syndrome diagnosis and have their own genetic testing. If you have consulted with a genetic counselor in your Lynch Syndrome testing process, they can help you with information for your family members.



Biomarker testing can give you and your medical team valuable knowledge about your cancer and help guide your treatment choices. For more information about colorectal cancer biomarkers, please visit [knowyourbiomarker.org](https://www.knowyourbiomarker.org) and talk to your medical team.