TumorNext-*Lynch*

A TEST FOR PATIENTS WITH COLORECTAL OR UTERINE CANCER

Because knowing your risk can mean early detection and prevention
Germline vs. Tumor Testing

TumorNext-Lynch looks for mutations and other changes in your tumor (also referred to as somatic testing) and inherited (germline) mutations in your blood.

It is important to understand the key differences between germline and tumor genetic tests, since they can give you very different information about your health and your family.

**WHAT’S THE DIFFERENCE?**

<table>
<thead>
<tr>
<th>WHAT IS TESTED?</th>
<th>INHERITANCE</th>
<th>RISKS</th>
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<tbody>
<tr>
<td><strong>INHERITED (GERMLINE)</strong></td>
<td>Blood or saliva</td>
<td>Can be inherited and passed on to family members</td>
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<td></td>
<td>Genes that are identical in all cells of your body</td>
<td>Linked to an increased risk for other cancer(s)</td>
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<tr>
<td><strong>TUMOR (SOMATIC)</strong></td>
<td>Your tumor tissue for cancer-specific changes</td>
<td>Not inherited and only present in your tumor cells. Cannot be passed to family members</td>
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TumorNext-Lynch tests for both germline (inherited) mutations that cause Lynch syndrome, as well as mutations and other changes in your tumor that may be able to rule out Lynch syndrome. The results of this testing can help your healthcare provider know more about your cancer risks, so they can make a better plan for how to care for you and your family members.

**HOW CAN TUMORNEXT-LYNCH HELP?**

**GERMLINE (INHERITED)**
Learning if you have Lynch syndrome can help you understand your future cancer risks and if you need to undergo more cancer screening or consider preventive options. Your test results could also impact your family members, as they may also have an increased cancer risk.

**TUMOR (SOMATIC)**
Learning if you have certain genetic changes or mutations in your tumor can help to rule out a diagnosis of Lynch syndrome and can help your healthcare provider understand if you may or may not be a good candidate for certain treatments.

**WHO SHOULD HAVE TESTING WITH TUMORNEXT-LYNCH?**
Patients with a personal history of colorectal or uterine cancer who:

- Have tumor screening results that suggest a possible diagnosis of Lynch syndrome, like abnormal MSI or IHC* results
- Have a personal and family history of cancer suspicious for Lynch syndrome

*WHAT IS MSI/IHC?*
Immunohistochemistry (IHC) and microsatellite instability analysis (MSI) are two tests performed on tumor tissue to screen for Lynch syndrome and they may be done automatically at some hospitals for patients with certain types of cancer, like colorectal or uterine. The results of these tests can tell us if a tumor has certain traits that may make it more likely for the patient to have Lynch syndrome, but it can’t diagnose or confirm that someone has the condition. When people have abnormal MSI or IHC results, additional testing, such as TumorNext-Lynch, is needed to confirm or rule out Lynch syndrome.
Know the Basics: Inherited Mutations and Hereditary Cancer

TYPES OF CANCER

SPORADIC CANCER
Happens by chance in one or two related family members, typically at older ages

FAMILIAL CANCER
A clustering of cancer in a family that may be due to genes and/or other shared factors, such as environment and lifestyle

HEREDITARY CANCER
A clustering of cancer in a family due to inherited gene changes (mutations), which can be passed from parent to child

ABOUT HEREDITARY CANCER

Many people have a family history of cancer, but only 5-10% of cancer is hereditary.

People who have these gene mutations are born with them - they do not develop over time.

Learning if you have an inherited mutation can help you know more about your cancer risks.

People with a higher chance of developing cancer may need screening, like colonoscopies, that start at younger ages, and occur more often.
Understanding Disease Better Through Quality Testing

YOUR GENES CARRY A STORY THAT IS UNIQUE TO YOU AND MAKES YOU WHO YOU ARE. GENETIC TESTING CAN HELP YOU BETTER UNDERSTAND YOUR RISKS FOR CANCER.

Lynch syndrome is caused by inherited mutations in either MLH1, MSH2, MSH6, PMS2, or EPCAM. It is the most common cause of hereditary colorectal and uterine cancer and occurs in an estimated 1/279-1/440 Americans. People with Lynch syndrome have an increased risk for multiple types of cancer including colorectal, uterine, ovarian, and others. The graph below highlights some of the cancer risks for a person with Lynch syndrome compared to someone in the general population who does not have this condition.

**Lynch Syndrome Lifetime Cancer Risks (%)**

*Recent publications suggest lower risks for MSH6 and PMS2 mutation carriers*
What are the Benefits of TumorNext-\textit{Lynch}?

**BENEFITS OF TUMOR TESTING:**

Provides more information that can help clarify whether or not you have Lynch syndrome, so that your healthcare provider knows how to best care for you and your family.

**BENEFITS OF BOTH TUMOR AND GERMLINE TESTING:**

Your healthcare provider may be able to discuss additional personalized treatment options based on your genetic test results.

**BENEFITS OF GERMLINE GENETIC TESTING:**

Your healthcare provider can adjust your cancer screening plan (such as age of initial screening, type, and frequency) based on your genetic test results.

- An example of cancer screening is a colonoscopy

Your healthcare provider may discuss possible cancer prevention options, such as preventive surgery to reduce the risk for certain cancers.

- An example is prophylactic hysterectomy and oophorectomy (removing the uterus, ovaries and Fallopian tubes before a cancer occurs).
Has genetic mutation
No mutation

FOR YOUR FAMILY MEMBERS:

If you test positive for an inherited genetic mutation, your close family members (like your parents, brothers, sisters, children) have a 50/50 random chance of also having the same mutation.

• Men and women have the same chance to inherit a mutation, but their chance to develop cancer may be different.
• Typically genetic testing is recommended for adults, but it is important to discuss genetic testing for children under age 18 with your healthcare provider to determine if it may be helpful.
Possible Genetic Test Results

**CONSISTENT WITH A DIAGNOSIS OF LYNCH SYNDROME**

- You are at an increased risk for cancers such as colorectal and uterine. Your healthcare provider will discuss the best management recommendations for you.

- Genetic testing for certain family members may be recommended.

**RULES OUT A DIAGNOSIS OF LYNCH SYNDROME**

- You were not found to have an inherited gene mutation that causes Lynch syndrome.

- If you had previously abnormal Lynch syndrome screening results (MSI/IHC), the testing explained these results and found that you most likely do not have Lynch syndrome.

**PERSONALIZED TREATMENT OPTIONS**

- Based on certain traits of your tumor, you may be a candidate for personalized treatment options, such as immunotherapy. Talk to your doctor about which treatment options may be right for you.

**INCONCLUSIVE RESULTS THAT CANNOT CONFIRM OR RULE OUT A DIAGNOSIS OF LYNCH SYNDROME**

- Cancer risk(s) and treatment recommendations are based on personal and family history

*It is possible to have a combination of positive and VUS results, since multiple genes are tested.*
Resources For You

Ambry’s Patient Education Website
ambrygen.com/patient

American Cancer Society
cancer.org

American Society of Clinical Oncology
cancer.net

Cancercare
cancercare.org

Genetic Information Nondiscrimination Act
ginahelp.org

National Cancer Institute
cancer.gov

FIND A GENETIC COUNSELOR

National Society of Genetic Counselors
nsgc.org

Canadian Association of Genetic Counsellors
cagc-accg.ca
Frequently Asked Questions

1 HOW IS GENETIC TESTING PERFORMED AND HOW LONG DOES IT TAKE?

Germline testing is done using a blood or saliva sample, which is collected using a special kit that is shipped overnight to Ambry (all coordinated by your healthcare provider). A sample of your ovarian tumor will also be needed for the tumor testing, and Ambry will request that this be sent by the pathology department at your hospital. Testing looks for mutations that cause an increased risk for cancer. The time to complete the testing may depend on how quickly Ambry receives your tumor sample. After we receive the required samples, it will take 21-28 days for the results to be sent to your healthcare provider.

2 WHAT WILL HAPPEN WHEN MY RESULTS ARE READY?

Your healthcare provider will receive your results; they will not be sent directly to you. Every healthcare provider may have a different method and time frame to contact you to discuss your results, so it is important to discuss this process with them. Based on your test results, your healthcare provider will discuss any next steps.

3 WILL MY GENETIC TEST RESULTS AFFECT MY INSURANCE COVERAGE?

In the U.S., the Genetic Information Nondiscrimination Act (2008) prohibits discrimination by health insurance companies and employers, based on genetic information. Depending on where you live in the world, you may have different (or fewer) laws in this area. Visit ginahelp.org to learn more.
4 **SHOULD I TELL MY FAMILY MEMBERS ABOUT MY GENETIC TEST RESULTS?**

It is important to share your results with your family members as they may provide additional information about their cancer risks and management options. Your healthcare provider may be able to guide you on finding the best way to inform family members.

5 **WILL GENETIC TESTING BE COVERED BY MY INSURANCE?**

Many insurance plans cover germline genetic testing and Ambry is contracted with the majority of U.S. health plans. Your out-of-pocket cost may vary based on your individual plan; therefore, we offer personalized verification of insurance coverage and financial options for your genetic testing. A team of dedicated specialists is available to help you get access to the genetic testing you need and answer any questions you have about our payment options. Call or email our Billing department at +1 949.900.5795 or billing@ambrygen.com with any questions.

6 **WHAT IS AN EXPLANATION OF BENEFITS (EOB)?**

Your insurance company sends you an EOB to explain any services paid on your behalf. You can contact us directly to speak with a Billing specialist with any questions or concerns about your EOB. Some genetic tests take weeks to process in order to receive the best results. In addition, insurance companies can take several weeks or even a couple of months to process claims.

**STILL HAVE QUESTIONS?**

Talk to your doctor or visit our website: ambrygen.com
Finding Answers.