Quest Advanced Oncology

Hereditary Cancer Genetic Test Results

This report is intended to facilitate a discussion between providers and their patients.

INFORMATION FOR INDIVIDUALS WITH ONE OR TWO PATHOGENIC OR LIKELY PATHOGENIC VARIANT(S) IN THE *NTHL1* GENE

What this result means

Individuals who have **two** (one in each copy of *NTHL1)* pathogenic or likely pathogenic variants (sometimes called mutations) in the *NTHL1* gene have *NTHL1* tumor syndrome. Individuals with *NTHL1* tumor syndrome have a higher-than-average chance to develop adenomatous colorectal polyps, colorectal cancer, breast cancer, and endometrial cancer. The chance to develop cancer is increased but not everyone with a pathogenic or likely pathogenic variant will develop cancer. Cancer risks for people with **one** pathogenic or likely pathogenic in *NTHL1* are unknown.

Cancer risk

Information about cancer risks related to pathogenic variants in *NTHL1* is still emerging and is likely to change over time. Patients should be encouraged to check in with their doctor or genetic counselor on a yearly basis so that any new information about this gene, such as associated risks and cancer screening recommendations, can be shared.

Options for managing cancer risk

There are options for cancer prevention and early detection. The following are general guidelines for individuals who have pathogenic variants in both copies of their *NTHL1* gene. These guidelines are evolving and are not specific to any one individual. Each individual's gender, age, medical history, family history, quality of life goals, reproductive desires, general health status, and other medical information should be taken into account when developing a medical management plan.

	Considerations for cancer prevention/early detection	Age to begin	Frequency
Two *NTHL1* Pathogenic Variants (one in each copy of *NTHL1*)			
Colorectal Cancer	Colonoscopy	25-30 years	Every 2-3 years or every 1-2 years if polyps are found
	Surgical evaluation	Individualized based on polyp-burden and clinical presentation	—
One *NTHL1* Pathogenic Variant			
Colorectal Cancer	Unknown		

Source: National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology. Genetic/Familial High-Risk Assessment: Colorectal. V1.2020. **www.NCCN.org**

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What this result means for family members

For individuals with two pathogenic or likely pathogenic variants in *NTHL1* (one in each copy of *NTHL1*)
Parents will likely each have one of the two *NTHL1* variants. Siblings have a 50% chance to have one of the variants and a 25% chance to have both of the variants and a diagnosis of *NTHL1*-associated colorectal adenomatous polyposis. Children will all have one of the *NTHL1* variants.

For individuals with one pathogenic or likely pathogenic variant in *NTHL1*
Parents, brothers, sisters and children may each have a 50% chance to have the same variant. Children of parents who both have an *NTHL1* variant are at risk for *NTHL1*-associated colorectal adenomatous polyposis.

Other blood relatives also have an increased risk for the variant(s). It is important to share these test results with family members to allow each of them to decide if they want to be tested. Some family members may only need testing for these *NTHL1* variants, while other relatives may need a more comprehensive test with multiple genes. A genetic counselor or other healthcare provider can help determine the most appropriate testing options.

Reproductive information

Individuals interested in family planning should speak to their doctor and/or genetic counselor to discuss reproductive options. This may include discussion of prenatal diagnosis or pre-implantation genetic testing.

Risk assessment and counseling: an important first step

A genetic counselor or other qualified healthcare professional can help explain test results and what they mean for a patient and family members. A team of specialized Quest genetic counselors or clinical geneticists is available to speak with healthcare providers about test results by calling 1.866.GENE.INFO. Patients can access a directory of independent genetic counselors at **FindAGeneticCounselor.com**.

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Creating a plan: a checklist for patients

- ☐ Get a copy of your genetic test results.
- ☐ Talk with your healthcare provider about what this result means and the things you can do to manage your risk.
- ☐ Ask your healthcare provider if additional genetic testing may benefit you.
- ☐ Share your test results with your family members and give them a copy. Their healthcare provider will need this information in order to provide them with the most accurate risk assessment.
- ☐ Talk with your healthcare provider regularly so that you know about any important changes in genetic testing and cancer screening options. Be sure to let him/her know of any changes in your family history, including family members' genetic test results.
- ☐ Consider talking to a genetic counselor about your results.

Research opportunities

Prospective Registry of MultiPlex Testing (PROMPT) PromptStudy.info

GenomeConnect: The ClinGen Patient Portal GenomeConnect.org

Additional resources

Hereditary Colon Cancer Takes Guts hcctakesguts.org

Colorectal Cancer Alliance ccalliance.org

National Colorectal Cancer Roundtable nccrt.org

Quest Hereditary Cancer Testing Solutions QuestHereditaryCancer.com

Genetic Information Nondiscrimination Act (GINA) GINAhelp.org

National Society of Genetic Counselors FindAGeneticCounselor.com

This information is not a substitute for medical advice, diagnosis, or treatment. The diagnosis or treatment of any disease or condition may be based on personal history, family history, symptoms, a physical examination, laboratory test results, and other information considered important by a healthcare provider. Always talk with a healthcare provider about the meaning of genetic test results and before stopping, starting or changing any medication or treatment.

The classification and interpretation of the variant(s) identified reflect the current state of Quest Diagnostics' understanding at the time of this report. Variant classification and interpretation are subject to professional judgment, and may change for a variety of reasons, including but not limited to, updates in classification guidelines and availability of additional scientific and clinical information. This test result should be used in conjunction with the healthcare provider's clinical evaluation. Inquiry regarding potential changes to the classification of the variant is strongly recommended prior to making any clinical decision. For questions regarding variant classification updates, please call Quest Diagnostics at 1.866.GENE.INFO (1.866.436.3463) to speak to a genetic counselor or laboratory director, or visit **QuestDiagnostics.com/VariantIQ**.