

Overview

Useful For

- Evaluating patients with a personal or family history suggestive of a hereditary gastrointestinal cancer or hereditary polyposis syndrome
- Establishing a diagnosis of a hereditary gastrointestinal cancer syndrome or hereditary polyposis syndrome allowing for targeted cancer surveillance based on associated risks
- Identifying genetic variants associated with increased risk for gastrointestinal cancer and polyposis, allowing for predictive testing and appropriate screening of at-risk family members

Genetics Test Information

This test utilizes next-generation sequencing to detect single nucleotide and copy number variants in 26 genes associated with hereditary colorectal cancer, gastric cancer, or polyposis risk: *APC* (including promoters 1A and 1B), *ATM*, *AXIN2*, *BMPR1A*, *CDH1*, *CHEK2*, *CTNNA1*, *EPCAM* (copy number variants only), *GREM1* (upstream enhancer region duplication only), *KIT*, *MLH1*, *MLH3*, *MSH2*, *MSH3*, *MSH6*, *MUTYH*, *NTHL1*, *PDGFRA*, *PMS2*, *POLD1*, *POLE*, *PTEN* (including promoter), *RNF43*, *SMAD4*, *STK11*, *TP53*. For more information, see Method Description and [Targeted Genes and Methodology Details for Hereditary Gastrointestinal Cancer Panel](#).

Identification of a disease-causing variant may assist with diagnosis, prognosis, clinical management, familial screening, and genetic counseling for hereditary gastrointestinal cancer syndromes and hereditary polyposis syndromes.

[Prior Authorization](#) is available for this assay.

Testing Algorithm

First-tier testing may be considered/recommended. For more information see [Lynch Syndrome Testing Algorithm](#).

Special Instructions

- [Molecular Genetics: Inherited Cancer Syndromes Patient Information](#)
- [Informed Consent for Genetic Testing](#)
- [Hereditary Gastrointestinal Cancer Panel Prior Authorization Ordering Instructions](#)
- [Lynch Syndrome Testing Algorithm](#)
- [Informed Consent for Genetic Testing \(Spanish\)](#)
- [Targeted Genes and Methodology Details for Hereditary Gastrointestinal Cancer Panel](#)

Method Name

Sequence Capture and Next-Generation Sequencing (NGS), Polymerase Chain Reaction (PCR), Sanger Sequencing and/or Multiplex Ligation-Dependent Probe Amplification (MLPA)

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

Customization of this panel and single gene analysis for any gene present on this panel are available. For more information see CGPH / Custom Gene Panel, Hereditary, Next-Generation Sequencing, Varies.

Targeted testing for familial variants (also called site-specific or known mutations testing) is available for the genes on this panel. For more information see FMTT / Familial Variant, Targeted Testing, Varies. To obtain more information about this testing option, call 800-533-1710.

Necessary Information

[Prior Authorization](#) is available, **but not required**, for this test. If proceeding with the prior authorization process, submit the required form with the specimen.

Specimen Required

Patient Preparation: A previous bone marrow transplant from an allogenic donor will interfere with testing. For instructions for testing patients who have received a bone marrow transplant, call 800-533-1710.

Specimen Type: Whole blood

Container/Tube:

Preferred: Lavender top (EDTA) or yellow top (ACD)

Acceptable: Green top (Sodium heparin)

Specimen Volume: 3 mL

Collection Instructions:

1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot.**

Specimen Stability Information: Ambient 4 days/Refrigerated 4 days/Frozen 4 days

Additional Information:

1. Specimens are preferred to be received within 4 days of collection. Extraction will be attempted for samples received after 4 days, and DNA yield will be evaluated to determine if testing may proceed.
2. To ensure minimum volume and concentration of DNA is met, the preferred volume of blood must be submitted. Testing may be canceled if DNA requirements are inadequate.

Specimen Type: Saliva

Patient Preparation: Patient **should not** eat, drink, smoke, or chew gum 30 minutes prior to collection.

Supplies: Saliva Swab Collection Kit (T786)

Specimen Volume: 1 Swab

Collection Instructions: Collect and send specimen per kit instructions.

Specimen Stability Information: Ambient (preferred) 30 days, Refrigerated 30 days

Additional information: Due to lower quantity/quality of DNA yielded from saliva, some aspects of the test may not

perform as well as DNA extracted from a whole blood sample. When applicable, specific gene regions that were unable to be interrogated will be noted in the report. Alternatively, additional specimen may be required to complete testing.

Forms

- 1. **New York Clients-Informed consent is required.** Document on the request form or electronic order that a copy is on file.
[-Informed Consent for Genetic Testing](#) (T576)
[-Informed Consent for Genetic Testing \(Spanish\)](#) (T826)
- 2. [Molecular Genetics: Inherited Cancer Syndromes Patient Information Sheet](#) (T519)
- 3. [Hereditary Gastrointestinal Cancer Panel Prior Authorization Ordering Instructions](#)
- 4. If not ordering electronically, complete, print, and send a [Oncology Test Request](#) (T729) with the specimen.

Specimen Minimum Volume

Whole blood: 1 mL; Saliva: See Specimen Required

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Clinical & Interpretive

Clinical Information

Colorectal cancer occurs in approximately 4% to 6% of individuals in the general population.(1) In some cases, individuals with a personal or family history of colorectal cancer, gastric cancer, or polyposis may be at increased risk of cancer due to a hereditary cancer syndrome.(2,3) Evaluation of the genes on this panel may be useful for families with a history of colorectal cancer, gastric cancer, polyposis, or gastrointestinal cancers to determine cancer risk, surveillance recommendations, and targeted treatments.(2-4)

The most common hereditary colon cancer syndrome is Lynch syndrome, accounting for about 2% to 4% of all colon cancer cases.(2) Lynch syndrome is associated with germline variants in the mismatch repair genes, *MLH1*, *MSH2*, *MSH6*, *PMS2*, or deletions of the *EPCAM* gene.(2,3) It is predominantly characterized by significantly increased risks for colorectal and endometrial cancer.(2,3) The lifetime risk for colorectal cancer is highly variable and dependent on the gene involved.(2,3) Other malignancies within the tumor spectrum include gastric cancer, ovarian cancer, hepatobiliary and upper tract urothelial carcinomas, and small bowel cancer.(2,3)

Although rare, individuals and families with polyposis may also be at risk for a hereditary polyposis syndrome, such as familial adenomatous polyposis (FAP).(2) FAP is caused by variants in the *APC* gene and characterized by numerous adenomatous polyps.(2) The presence of extracolonic manifestations is variable and includes gastric and duodenal polyps, ampullary polyps, osteomas, dental abnormalities (unerupted teeth), congenital hypertrophy of the retinal pigment epithelium (CHRPE), benign cutaneous lesions, desmoid tumors, hepatoblastoma, and extracolonic cancers.(2)

Other genes are also known to cause hereditary colorectal cancer, gastric cancer, polyposis, and gastrointestinal cancers.(2) The risk for developing cancer associated with these syndromes varies.(2) Some individuals with a disease-causing variant in one of these genes develop multiple primary cancers.(2)

The National Comprehensive Cancer Network and the American Cancer Society provide recommendations regarding the medical management of individuals with hereditary gastrointestinal cancer syndromes.(2,4)

Reference Values

An interpretive report will be provided.

Interpretation

All detected variants are evaluated according to American College of Medical Genetics and Genomics recommendations.(5) Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

Cautions

Clinical Correlations:

Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.

If testing was performed because of a clinically significant family history, it is often useful to first test an affected family member. Detection of a reportable variant in an affected family member would allow for more informative testing of at-risk individuals.

To discuss the availability of additional testing options or for assistance in the interpretation of these results, contact the Mayo Clinic Laboratories genetic counselors at 800-533-1710.

Technical Limitations:

Next-generation sequencing may not detect all types of genomic variants. In rare cases, false-negative or false-positive results may occur. The depth of coverage may be variable for some target regions; assay performance below the minimum acceptable criteria or for failed regions will be noted. Given these limitations, negative results do not rule out the diagnosis of a genetic disorder. If a specific clinical disorder is suspected, evaluation by alternative methods can be considered.

There may be regions of genes that cannot be effectively evaluated by sequencing or deletion and duplication analysis as a result of technical limitations of the assay, including regions of homology, high guanine-cytosine (GC) content, and repetitive sequences. Confirmation of select reportable variants will be performed by alternate methodologies based on internal laboratory criteria.

This test is validated to detect 95% of deletions up to 75 base pairs (bp) and insertions up to 47 bp. Deletions-insertions (delins) of 40 or more bp, including mobile element insertions, may be less reliably detected than smaller delins.

Deletion/Duplication Analysis:

This analysis targets single and multi-exon deletions/duplications; however, in some instances single exon resolution cannot be achieved due to isolated reduction in sequence coverage or inherent genomic complexity. Balanced structural

rearrangements (such as translocations and inversions) may not be detected.

This test is not designed to detect low levels of mosaicism or differentiate between somatic and germline variants. If there is a possibility that any detected variant is somatic, additional testing may be necessary to clarify the significance of results.

Genes may be added or removed based on updated clinical relevance. For the most up to date list of genes included in this test as well as detailed information regarding gene specific performance and technical limitations, see Method Description or contact a laboratory genetic counselor.

If the patient has had an allogeneic hematopoietic stem cell transplant or a recent blood transfusion, results may be inaccurate due to the presence of donor DNA. Call Mayo Clinic Laboratories for instructions for testing patients who have received a bone marrow transplant.

Reclassification of Variants Policy:

Currently, it is not standard practice for the laboratory to systematically review previously classified variants on a regular basis. The laboratory encourages healthcare providers to contact the laboratory at any time to learn how the classification of a particular variant may have changed over time.

Variant Evaluation:

Evaluation and categorization of variants are performed using published American College of Medical Genetics and Genomics and the Association for Molecular Pathology recommendations as a guideline.⁽⁵⁾ Other gene-specific guidelines may also be considered. Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance. Variants classified as benign or likely benign are not reported.

Multiple in silico evaluation tools may be used to assist in the interpretation of these results. The accuracy of predictions made by in silico evaluation tools is highly dependent upon the data available for a given gene, and periodic updates to these tools may cause predictions to change over time. Results from in silico evaluation tools should be interpreted with caution and professional clinical judgment.

Clinical Reference

1. Howlader N, Noone AM, Krapcho M, et al: SEER Cancer Statistics Review. 1975-2018. National Cancer Institute; Updated April 15, 2021. Accessed September 12, 2024. Available at: https://seer.cancer.gov/csr/1975_2018/
2. Gupta S, Provenzale D, Llor X, et al. NCCN Guidelines Insights: Genetic/familial high-risk assessment: colorectal, version 2.2019. J Natl Compr Canc Netw. 2019 1;17(9):1032-1041
3. Idos G, Valle L: Lynch syndrome. In: Adam MP, Everman DB, Mirzaa GM, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 2004. Updated February 4, 2021. Accessed September 12, 2022. Available at www.ncbi.nlm.nih.gov/books/NBK1211/
4. Smith RA, Andrews KS, Brooks D, et al. Cancer screening in the United States, 2019: A review of current American Cancer Society guidelines and current issues in cancer screening. CA Cancer J Clin. 2019;69(3):184-210
5. Richards S, Aziz N, Bale S, et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med. 2015;17(5):405-424

Performance

Method Description

Next-generation sequencing (NGS) and/or Sanger sequencing are performed to test for the presence of variants in coding regions and intron/exon boundaries of the genes analyzed, as well as some other regions that have known disease-causing variants. The human genome reference GRCh37/hg19 build was used for sequence read alignment. At least 99% of the bases are covered at a read depth over 30X. Sensitivity is estimated at above 99% for single nucleotide variants, above 94% for deletions-insertions (delins) less than 40 base pairs (bp), above 95% for deletions up to 75 bp and insertions up to 47 bp. NGS, multiplex ligation-dependent probe amplification (MLPA), and/or a polymerase chain reaction (PCR)-based quantitative method is performed to test for the presence of deletions and duplications in the genes analyzed. PCR and gel electrophoresis is performed to test for the presence of the 10 megabase inversion of coding exons 1-7 of the *MSH2* gene.

There may be regions of genes that cannot be effectively evaluated by sequencing or deletion and duplication analysis as a result of technical limitations of the assay, including regions of homology, high guanine-cytosine (GC) content, and repetitive sequences. For details regarding the targeted genes analyzed and specific gene regions not routinely covered, see [Targeted Genes and Methodology Details for Hereditary Gastrointestinal Cancer Panel](#). (Unpublished Mayo method)

Confirmation of select reportable variants may be performed by alternate methodologies based on internal laboratory criteria.

Genes analyzed: *APC* (including promoters 1A and 1B), *ATM*, *AXIN2*, *BMPR1A*, *CDH1*, *CHEK2*, *CTNNA1*, *EPCAM* (copy number variants only), *GREM1* (upstream enhancer region duplication only), *KIT*, *MLH1*, *MLH3*, *MSH2*, *MSH3*, *MSH6*, *MUTYH*, *NTHL1*, *PDGFRA*, *PMS2*, *POLD1*, *POLE*, *PTEN* (including promoter), *RNF43*, *SMAD4*, *STK11*, and *TP53*

PDF Report

Supplemental

Day(s) Performed

Varies

Report Available

21 to 28 days

Specimen Retention Time

Whole blood: 2 weeks (if available); Saliva: 1month; Extracted DNA: 3 months

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes

Fees

- Authorized users can sign in to [Test Prices](#) for detailed fee information.
- Clients without access to Test Prices can contact [Customer Service](#) 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact [Customer Service](#).

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

81435

Prior Auhtorization

Insurance preauthorization is available for this testing; forms are available.

Patient financial assistance may be available to those who qualify. Patients who receive a bill from Mayo Clinic Laboratories will receive information on eligibility and how to apply.

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
CRCGP	Hereditary GI Cancer Panel	107546-4

Result ID	Test Result Name	Result LOINC® Value
614695	Test Description	62364-5
614696	Specimen	31208-2
614697	Source	31208-2
614698	Result Summary	50397-9
614699	Result	82939-0
614700	Interpretation	69047-9
614701	Resources	99622-3
614702	Additional Information	48767-8
614703	Method	85069-3
614704	Genes Analyzed	48018-6
614705	Disclaimer	62364-5
614706	Released By	18771-6