

Overview

Useful For

[Evaluation for hereditary cancer in patients with a personal or family history suggestive of a hereditary cancer syndrome](#)

Establishing a diagnosis of a hereditary cancer syndrome allowing for targeted cancer surveillance based on associated risks

Identifying genetic variants associated with increased risk for cancer, allowing for predictive testing, and appropriate screening of at-risk family members

[Therapeutic eligibility with poly adenosine diphosphate-ribose polymerase \(PARP\) inhibitors based on certain gene alterations \(eg, *BRCA1*, *BRCA2*\) in selected tumor types](#)

Genetics Test Information

This test utilizes next-generation sequencing to detect single nucleotide and copy number variants in 36 genes associated with hereditary cancer syndromes: *APC* (including promoters 1A and 1B), *ATM*, *AXIN2*, *BARD1*, *BMPR1A*, *BRCA1*, *BRCA2*, *BRIP1*, *CDH1*, *CDK4*, *CDKN2A*, *CHEK2*, *DICER1*, *EPCAM* (copy number variants only), *GREM1* (upstream enhancer region duplication only), *HOXB13*, *MEN1*, *MLH1*, *MSH2*, *MSH3*, *MSH6*, *MUTYH*, *NBN*, *NF1*, *NTHL1*, *PALB2*, *PMS2*, *POLD1*, *POLE*, *PTEN* (including promoter), *RAD51C*, *RAD51D*, *RET*, *SMAD4*, *STK11*, *TP53*. For more information, see Method Description, [Targeted Genes and Methodology Details for Hereditary Common Cancer Panel](#)

Identification of a pathogenic variant may assist with diagnosis, prognosis, clinical management, familial screening, and genetic counseling for hereditary cancer syndromes.

Testing Algorithm

See [Lynch Syndrome Testing Algorithm](#)

Special Instructions

- [Molecular Genetics: Inherited Cancer Syndromes Patient Information](#)
- [Informed Consent for Genetic Testing](#)
- [Lynch Syndrome Testing Algorithm](#)
- [Informed Consent for Genetic Testing \(Spanish\)](#)
- [Targeted Genes and Methodology Details for Hereditary Common 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 is 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 Mutation, Targeted Testing, Varies.

Shipping Instructions

Specimen preferred to arrive within 96 hours of collection.

Specimen Required

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

Specimen Type: Whole blood

Container/Tube:

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

Acceptable: Any anticoagulant

Specimen Volume: 3 mL

Collection Instructions:

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

Specimen Stability Information: Ambient (preferred) 4 days/Refrigerated

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. [Targeted Genes and Methodology Details for Hereditary Common Cancer Panel](#)

4. If not ordering electronically, complete, print, and send a [Oncology Test Request](#) (T729) with the specimen.

Specimen Minimum Volume

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

[Hereditary cancer syndromes account for approximately 5% to 10% of cancer cases.\(1,2\) Determining if there is a genetic risk factor contributing to cancer in an individual or family can be useful for tailoring surveillance plans, consideration of prophylactic risk reducing interventions, consideration of targeted treatments, and determining risk for family members.\(3-9\)](#)

This panel evaluates for 36 genes known to be associated with an increased risk of common cancers, including breast cancer, colon cancer, gastric cancer, ovarian cancer, pancreatic cancer, polyposis, prostate cancer, skin cancer, thyroid cancer, and endometrial cancer. The risk for developing cancer as well as other features associated with these syndromes varies. Many of the genes on this panel have established cancer risk and National Comprehensive Cancer Network (NCCN) or expert group guidelines and recommendations for management.(3-8)

Indications for testing include but are not limited to:

- Individuals with multiple primary cancers
- Individuals with cancer diagnosed at young ages
- Individuals with a family history of multiple relatives with cancer
- Individuals whose family history of cancer may seem to overlap with more than one hereditary cancer syndrome

Reference Values

An interpretive report will be provided.

Interpretation

All detected variants are evaluated according to American College of Medical Genetics and Genomics (ACMG) recommendations.(1) 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, Mayo Clinic Laboratory genetic counselors at [800-533-1710](tel: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. Insertions/deletions (indels) of 40 or more bp, including mobile element insertions, may be less reliably detected than smaller indels.

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 to 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 see [Targeted Genes and Methodology Details for Hereditary Common Cancer Panel](#) . For 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 heterologous 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:

At this time, it is not standard practice for the laboratory to systematically review previously classified variants on a regular basis. The laboratory encourages health care 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 is performed using published American College of Medical Genetics and Genomics and the Association for Molecular Pathology recommendations as a guideline. 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 judgement.

Clinical Reference

1. 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 May;17(5):405-424
2. [Howlader N, Noone AM, Krapcho M, et al: SEER Cancer Statistics Review. 1975-2018. National Cancer Institute; Updated April 2021. Accessed July 6, 2021. Available at: \[https://seer.cancer.gov/csr/1975_2018/\]\(https://seer.cancer.gov/csr/1975_2018/\)](#)
3. Nagy R, Sweet K, Eng C: Highly penetrant hereditary cancer syndromes. *Oncogene.* 2004 Aug 23;23(38):6445-6470
4. Daly MB, Pal T, Berry M, et al: Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic, Version 2.2021, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw.* 2021 Jan 6;19(1):77-102
5. 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 Sep 1;17(9):1032-1041
6. Saslow D, Boetes C, Burke W, et al: American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. *CA Cancer J Clin.* 2007 Mar-Apr;57(2):75-89
7. [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 May;69\(3\):184-210](#)
8. Coit DG, Thompson JA, Albertini MR, et al. Cutaneous Melanoma, Version 2.2019, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw.* 2019 Apr 1;17(4):367-402
9. Haddad RI, Nasr C, Bischoff L, et al: NCCN Guidelines Insights: Thyroid Carcinoma, Version 2.2018. *J Natl Compr Canc Netw.* 2018 Dec;16(12):1429-1440
10. Samadder NJ, Rigert-Johnson D, Boardman L, et al: Comparison of Universal Genetic Testing vs Guideline-Directed Targeted Testing or Patients With Hereditary Cancer Syndrome. *JAMA Oncol.* 2021 Feb 1;7(2):230-237

Performance**Method Description**

Next-generation sequencing (NGS) and/or Sanger sequencing is 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 pathogenic 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 insertions/deletions (indels) 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 are performed to test for the presence of the 10 megabase inversion of coding exons 1-7 of the *MSH2* gene. For details regarding the targeted genes analyzed for this test, see [Targeted Genes and Methodology Details for Hereditary Common Cancer Panel](#).

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 specific gene regions not routinely covered, see [Targeted Genes and Methodology Details for Hereditary Common Cancer Panel](#)

Confirmation of select reportable variants may be performed by alternate methodologies based on internal laboratory criteria.(Unpublished Mayo method)

Genes analyzed: *APC* (including promoters 1A & 1B), *ATM*, *AXIN2*, *BARD1*, *BMPR1A*, *BRCA1*, *BRCA2*, *BRIP1*, *CDH1*, *CDK4*, *CDKN2A*, *CHEK2*, *DICER1*, *EPCAM* (copy number variants only), *GREM1* (upstream enhancer region duplication only), *HOXB13*, *MEN1*, *MLH1*, *MSH2*, *MSH3*, *MSH6*, *MUTYH*, *NBN*, *NF1*, *NTHL1*, *PALB2*, *PMS2*, *POLD1*, *POLE*, *PTEN* (including promoter), *RAD51C*, *RAD51D*, *RET*, *SMAD4*, *STK11*, *TP53*

PDF Report

Supplemental

Day(s) Performed

Varies

Report Available

3 to 4 weeks

Specimen Retention Time

Whole Blood: 2 weeks (if available); Extracted DNA: 3 months

Performing Laboratory Location

Rochester

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 Regional Manager. 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. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

81201
81408 x 2
81162
81406 x 4
81404
81403
81405 x 2
81292
81295
81298
81307

81319
81321
81351
81479

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
COMCP	Hereditary Common Cancer Panel	97656-3

Result ID	Test Result Name	Result LOINC® Value
614683	Test Description	62364-5
614684	Specimen	31208-2
614685	Source	31208-2
614686	Result Summary	50397-9
614687	Result	82939-0
614688	Interpretation	69047-9
614689	Resources	99622-3
614690	Additional Information	48767-8
614691	Method	85069-3
614692	Genes Analyzed	48018-6
614693	Disclaimer	62364-5
614694	Released By	18771-6