Test Definition: XCP

Hereditary Expanded Cancer Panel, Varies

Overview

Useful For

Evaluating hereditary cancer in patients with a personal or family history suggestive of a hereditary cancer syndrome using a panel of 87 genes

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 87 genes associated with a variety of hereditary cancer syndromes: *AIP*, *ALK*, *APC* (including promoters 1A and 1B), *ATM*, *AXIN2*, *BAP1*, *BARD1*, *BLM*, *BMPR1A*, *BRCA1*, *BRCA2*, *BRIP1*, *BUB1B*, *CDC73*, *CDH1*, *CDK4*, *CDKN1B*, *CDKN2A*, *CHEK2*, *CTNNA1*, *DICER1*, *DIS3L2*, *EGFR*, *ELP1*, *EPCAM* (copy number variants only), *EXT1*, *EXT2*, *FANCA*, *FH*, *FLCN*, *GPC3*, *GREM1* (upstream enhancer region duplication only), *HOXB13*, *KIT*, *LZTR1*, *MAX*, *MC1R*, *MEN1*, *MET*, *MITF* (c.952G>A p.E318K variant only), *MLH1*, *MLH3*, *MSH2*, *MSH3*, *MSH6*, *MUTYH*, *NBN*, *NF1*, *NF2*, *NTHL1*, *PALB2*, *PDGFRA*, *PHOX2B*, *PMS2*, *POLD1*, *POLE*, *POT1*, *PRKAR1A*, *PTCH1*, *PTEN* (including promoter), *RAD51B*, *RAD51C*, *RAD51D*, *RB1*, *RECQL4*, *REST*, *RET*, *RNF43*, *SDHA*, *SDHAF2*, *SDHB*, *SDHC*, *SDHD*, *SMAD4*, *SMARCA4*, *SMARCB1*, *SMARCE1*, *STK11*, *SUFU*, *TMEM127*, *TP53*, *TRIP13*, *TSC1*, *TSC2*, *VHL*, *WRN*, *WT1*. See Method Description and Gene Selection Table for additional details.

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

Special Instructions

- Molecular Genetics: Inherited Cancer Syndromes Patient Information
- Informed Consent for Genetic Testing
- Informed Consent for Genetic Testing (Spanish)

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.

Testing minors for adult-onset predisposition syndromes is discouraged by the American Academy of Pediatrics, the American College of Medical Genetics and Genomics, and the National Society of Genetic Counselors.

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 specimens 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 requested volume 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:
DNA Saliva Kit High Yield (T1007)
Saliva Swab Collection Kit (T786)
Container/Tube:
Preferred: High-yield DNA saliva kit
Acceptable: Saliva swab
Specimen Volume: 1 Tube if using T1007 or 2 swabs if using T786
Collection Instructions: Collect and send specimen per kit instructions.
Specimen Stability Information: Ambient (preferred) 30 days/Refrigerated 30 days
Additional Information: Saliva specimens are acceptable but not recommended. 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. The following documents are available:
-Informed Consent for Genetic Testing (T576)
-Informed Consent for Genetic Testing (Spanish) (T826)
2. Molecular Genetics: Inherited Cancer Syndromes Patient Information (T519)
3. If not ordering electronically, complete, print, and send a Oncology Test Request (T729) with the specimen.

Specimen Minimum Volume

Whole Blood1 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

Hereditary cancer syndromes explain about 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, targeted cancer treatments, and determining risk for family members.(3)

This panel evaluates 87 genes associated with an increased risk for the following cancers: breast, colon, gastric, ovarian, pancreatic, prostate, renal, skin, thyroid, and endometrial cancers, as well as paragangliomas, pheochromocytomas, and Wilms tumor.

The risk for developing cancer associated with these syndromes varies. Several of the of the genes on this panel have established cancer risk and National Comprehensive Cancer Network (NCCN) or expert group guidelines and recommendations for management.(4-9)

Indications for testing include but are not limited to:
-Individuals with multiple primary cancers
-Individuals with cancer diagnosed at young age
-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 recommendations.(10) 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.

Deletion/duplication events that extend past the genes included on the panel may occur. In these instances, genes included in the ordered test are provided on the report and interpreted, and genomic breakpoints are reported if they are confirmed. However, copy number variants for genes not listed in the Method Description are typically not reported or interpreted for haploinsufficiency/triplosensitivity. CMACB / Chromosomal Microarray, Congenital, Blood; WESPR / Panel to Whole Exome Sequencing Reflex Test, Varies; or WGSDX / Whole Genome Sequencing for Hereditary Disorders, Varies is recommended for a full interpretation of deletions/duplications predicted to extend past the genes included on the panel.

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 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.(10) 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 March 18, 2025. Available at: https://seer.cancer.gov/csr/1975_2018/
2. Nagy R, Sweet K, Eng C. Highly penetrant hereditary cancer syndromes. Oncogene. 2004;23(38):6445-6470
3. Samadder NJ, Riegert-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;7(2):230-237
4. Daly MB, Pal T, Berry MP, 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;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;17(9):1032-1041
6. 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;17(4):367-402
7. Haddad RI, Nasr C, Bischoff L, et al. NCCN Guidelines Insights: Thyroid carcinoma, Version 2.2018. J Natl Compr Canc Netw. 2018;16(12):1429-1440
8. 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;57(2):75-89

9. 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
10. 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, 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 Gene Selection Table.(Unpublished Mayo method)

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

Genes analyzed: *AIP, ALK, APC* (including promoters 1A & 1B)*, ATM, AXIN2, BAP1, BARD1, BLM, BMPR1A, BRCA1, BRCA2, BRIP1, BUB1B, CDC73, CDH1, CDK4, CDKN1B, CDKN2A, CHEK2, CTNNA1, DICER1, DIS3L2, EGFR, ELP1, EPCAM* (copy number variants only)*, EXT1, EXT2, FANCA, FH, FLCN, GPC3, GREM1* (upstream enhancer region duplication only)*, HOXB13, KIT, LZTR1, MAX, MC1R, MEN1, MET, MITF* (c.952G>A p.E318K variant only)*, MLH1, MLH3, MSH2, MSH3, MSH6, MUTYH, NBN, NF1, NF2, NTHL1, PALB2, PDGFRA, PHOX2B, PMS2, POLD1, POLE, POT1, PRKAR1A, PTCH1, PTEN* (including promoter)*, RAD51B, RAD51C, RAD51D, RB1, RECQL4, REST, RET, RNF43, SDHA, SDHAF2, SDHB, SDHC, SDHD, SMAD4, SMARCA4, SMARCB1, SMARCE1, STK11, SUFU, TMEM127, TP53, TRIP13, TSC1, TSC2, VHL, WRN,* and *WT1*

PDF Report

No

Day(s) Performed

Varies

Report Available

21 to 28 days

Specimen Retention Time

Whole blood: 2 weeks (if available); Saliva: 1 month; 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

81403
81292
81295
81298
81162
81201
81307
81317
81321
81351
81404 x 4
81405 x 6
81406 x 7
81407 x2
81408 x 2
81479
81479 (if appropriate for government payers)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
XCP	Hereditary Expanded Cancer Panel	97656-3

Result ID	Test Result Name	Result LOINC® Value
614899	Test Description	62364-5
614900	Specimen	31208-2

614901	Source	31208-2
614902	Result Summary	50397-9
614903	Result	82939-0
614904	Interpretation	69047-9
614905	Resources	99622-3
614906	Additional Information	48767-8
614907	Method	85069-3
614908	Genes Analyzed	48018-6
614909	Disclaimer	62364-5
614910	Released By	18771-6