MAYO CLINIC LABORATORIES

Test Definition: PRS8P

Hereditary Prostate Cancer Panel, Varies

Overview

Useful For

Evaluating patients with a personal or family history suggestive of a hereditary prostate cancer syndrome

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

Identifying genetic variants associated with increased risk for prostate 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*)

Genetics Test Information

This test utilizes next-generation sequencing to detect single nucleotide and copy number variants in 18 genes associated with prostate cancer risk: *ATM, BRCA1, BRCA2, BRIP1, CHEK2, EPCAM* (copy number variants only), *FANCA, HOXB13, MLH1, MSH2, MSH6, NBN, PALB2, PMS2, RAD51B, RAD51C, RAD51D,* and *TP53*. For more information see Method Description and Targeted Genes and Methodology Details for Hereditary Prostate Cancer Panel.

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

Testing Algorithm

For more information see Breast, Gynecological and Prostate Cancer Testing Algorithm.

Special Instructions

- Molecular Genetics: Inherited Cancer Syndromes Patient Information
- Informed Consent for Genetic Testing
- Informed Consent for Genetic Testing (Spanish)
- Targeted Genes and Methodology Details for Hereditary Prostate Cancer Panel
- Breast, Gynecological and Prostate Cancer Testing Algorithm

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. 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 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:
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 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

Hereditary prostate cancer accounts for approximately 5% to 10% of all prostate cancer cases and up to half of all early-onset prostate cancer cases.(1-3) Evaluation of the genes on this panel may be useful for families with a history of prostate cancer to determine cancer risk, surveillance recommendations, and targeted treatments (such as poly adenosine diphosphate-ribose polymerase [PARP] inhibitor therapy).(4,5)

The 2 most common hereditary prostate cancer syndromes are hereditary breast and ovarian cancer (HBOC) syndrome and Lynch syndrome.(3-5)

HBOC syndrome is caused by disease-causing variants in the *BRCA1* and *BRCA2* genes. Individuals with HBOC syndrome are also at increased risk for multiple cancer types, including prostate cancer.(5)

Lynch syndrome is caused by variants in the *MLH1*, *MSH2*, *MSH6*, and *PMS2* mismatch-repair genes and deletions of the *EPCAM* gene. A subset of these patients presents with prostate cancer.(3-5)

This panel includes other genes known to increase prostate cancer risk.(3-5) The risk of developing cancer associated with these syndromes varies. Some individuals with a disease-causing variant in one of these genes develop multiple primary cancers.(4)

The National Comprehensive Cancer Network and the American Cancer Society provide recommendations regarding the medical management of individuals with hereditary prostate cancer syndromes.(4,5)

Reference Values

An interpretive report will be provided.

Interpretation

All detected variants are evaluated according to American College of Medical Genetics and Genomics recommendations.(6) 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 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 detailed information regarding gene specific performance and technical limitations, see Method Description or contact a laboratory genetic counselor at

800-533-1710.

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.(6) 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.

Rarely, incidental or secondary findings may implicate another predisposition or presence of active disease. Incidental findings may include, but are not limited to, results related to the sex chromosomes. These findings will be carefully reviewed to determine whether they will be reported.

Clinical Reference

1. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2021. CA Cancer J Clin. 2021;71(1):7-33
2. Lange EM, Salinas CA, Zuhlke KA, et al. Early onset prostate cancer has a significant genetic component. Prostate. 2012;72(2):147-156
3. Pritchard CC, Mateo J, Walsh M, et al. Inherited DNA-repair gene mutations in men with metastatic prostate cancer. N Engl J Med. 2016;375(5):443-453. doi:10.1056/NEJMoa1603144
4. Schaeffer E, Srinivas S, Antonarakis ES, et al. NCCN guidelines insights: Prostate cancer, version 1.2021. J Natl Compr Canc Netw. 2021;19(2):134-143
5. 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
6. 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 deletion/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 are 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 Prostate Cancer Panel.(Unpublished Mayo method)

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

Genes analyzed: *ATM, BRCA1, BRCA2, BRIP1, CHEK2, EPCAM* (copy number variants only)*, FANCA, HOXB13, MLH1, MSH2, MSH6, NBN, PALB2, PMS2, RAD51B, RAD51C, RAD51D,* and *TP53*

PDF Report

Supplemental

Day(s) Performed

Varies

Report Available

14 to 21 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

81432

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
PRS8P	Hereditary Prostate Cancer Panel	100213-8

Result ID	Test Result Name	Result LOINC® Value
614803	Test Description	62364-5
614804	Specimen	31208-2
614805	Source	31208-2
614806	Result Summary	50397-9
614807	Result	82939-0
614808	Interpretation	69047-9
614809	Resources	99622-3
614810	Additional Information	48767-8
614811	Method	85069-3
614812	Genes Analyzed	48018-6
614813	Disclaimer	62364-5
614814	Released By	18771-6