

Hereditary Prostate Cancer

Excluding skin cancer, prostate cancer is the most common cancer in American men. Although many cases do not develop into a significant health problem, prostate cancer remains a leading cause of death according to the CDC. Approximately 40-50% of cases of prostate cancer are believed to have an inherited cause. Hereditary prostate cancer (HPC) occurs when a person has a pathogenic (disease-causing) variant that increases the risk of cells turning cancerous. Men with HPC have a higher risk of developing prostate than other men, and can be at risk for other cancers or health problems, as well.



WHAT CAUSES HPC?

HPC is most commonly inherited in an autosomal dominant way. For dominant conditions, having only one copy of a gene variant is enough to cause symptoms. Less commonly, HPC can be inherited in an autosomal recessive way. For recessive conditions, both copies of a person's gene must have a variant to increase the risk for cancer. Importantly, not everyone who has a pathogenic-variant in a cancer-risk gene will develop cancer, but their chances are higher.

WHAT ARE HPC SYNDROMES?

Hereditary prostate cancer syndromes are conditions that impact other areas of an individual's body in addition to increasing their risk for prostate cancer. A syndrome can be inherited in a dominant, de novo, or recessive manner. Two examples of hereditary prostate cancer syndromes are listed below:

Hereditary Breast and Ovarian Cancer (HBOC) - Two genes, named BRCA1 and BRCA2, are common causes of hereditary breast cancer. variants in these two genes are also associated with a significant risk for breast and ovarian cancer, as well as prostate and pancreatic cancer. A variant in BRCA2 also confers a higher risk for breast cancer in men, and melanoma for both men and women. Men with BRCA2 variants who are diagnosed with prostate cancer tend to have more aggressive tumors and an earlier age of diagnosis than other men.

Lynch syndrome - Also known as Hereditary Non-Polyposis Colorectal Cancer (HNPCC), Lynch syndrome is caused by a pathogenic variant in a gene whose job is to repair the DNA damage that normally occurs as cells grow and divide. Men with Lynch syndrome have a two to five-fold increased risk for prostate cancer compared to men without Lynch syndrome. Because of the high risk for cancer, people with Lynch syndrome require increased screening earlier than those without the condition.

WHO IS THIS TEST FOR?

These panels may be appropriate for anyone with a personal or family history of prostate cancer. Testing is strongly recommended if you or a member of your family has been diagnosed with prostate cancer before the age of 55, or if there have been multiple cases of cancer in a single individual. It is also recommended for people of Ashkenazi Jewish ancestry.

BENEFITS OF GENETIC TESTING

- Establish or confirm a diagnosis
- Identify risk for other cancers and health conditions
- Assist in modifying lifestyle changes, including diet and exercise
- Result in more personalized treatment, which may include routine screening tests, pharmacological treatments, and prophylactic surgeries
- Inform family members of their own risk factors

TEST OPTIONS

Visit Fulgent website for most up-to-date list

Prostate Cancer Focus Panel

13 genes: *ATM, BRCA1, BRCA2, CHEK2, EPCAM, HOXB13, MLH1, MSH2, MSH6, NBN, PALB2, PMS2, TP53*

Prostate Cancer Comprehensive Panel

20 genes: *ABRAXAS1, ATM, ATR, BRCA1, BRCA2, BRIP1, CHEK2, EPCAM, GEN1, HOXB13, MLH1, MRE11, MSH2, MSH6, NBN, PALB2, PMS2, RAD51C, RAD51D, TP53*

TEST SPECIFICATIONS

Sample Requirements (kits available upon request):

- Blood, two 4-mL EDTA tubes lavender top (preferred)
- Extracted DNA, 3 µg in TE buffer
- Buccal swab or saliva

Coverage* ~99% at 50x

Turnaround Time** 2-3 weeks

* Full gene sequencing and deletion/duplication, including detection of MSH2 inversion for select panels, BRCA2 Alu variant, and PMS2 (including exons 1-5 and 12-15), as well as sequencing of noncoding regions for selected genes. Please contact us for more details.

**Rush order available upon request

WHERE CAN I LEARN MORE?

GARD (Genetic and Rare Diseases Information Center- NIH) -

rarediseases.info.nih.gov/diseases/4520/familial-prostate-cancer

FORCE (Facing Our Risk of Cancer Empowered) - facingourrisk.org/index.php

CCARE Lynch Syndrome - fightlynch.org

A Patient's Guide to Genetic Testing

What does a genetic test check for?

Genetic testing checks the order of one's DNA sequence (coded by the letters A, T, G, C) in specific genes linked to genetic conditions. Letters that were added, missing, or changed, are known as variants and can sometimes be harmful to one's health, increasing the risk for a genetic condition.

What are the potential results?

There are three possible results from genetic testing:

- +
Positive
 A pathogenic/likely pathogenic variant is detected in one's DNA. This type of variant is known to increase one's risk of a genetic condition. Identifying the specific gene involved can help confirm a diagnosis, inform screening and management, and reveal risk factors for an individual and/or their family.
- **Negative**
 No variation known to be associated with a genetic condition was detected in one's DNA. While a result may not show an increased risk for the condition(s) tested for, one can still be at risk for disease, especially if there is a family history.
- ?
Variant of Uncertain Significance (VUS)
 A variant was detected in one's DNA, however, not enough information is known about this variant to determine whether or not it is known cause the condition(s) tested for. More research is needed to better understand this variant.

What about family members?

Children, siblings, and parents of individuals who have a variant(s) identified in genetic testing could carry the same variant(s) and benefit from testing. Regardless of whether or not a variant was identified, individuals can still be at an increased risk for a genetic condition, especially with a family history.

Do genetic test results affect health insurance or employment?

No, the Genetic Information Nondiscrimination Act (GINA) was signed into law in 2008.

It protects individuals from discrimination by an employer or a health insurance company based on genetic testing results and genetic information. GINA does not protect against life and disability insurance discrimination. For more information on GINA, go to www.ginahelp.org.

Where can I learn more?

Medline Plus/Genetics Home Reference - medlineplus.gov/genetics/understanding

National Society of Genetic Counselors - nsgc.org

Fulgent Genetics - fulgentgenetics.com/products/carrierscreening/learning.html