Hereditary Prostate Cancer
Information for Patients

What is hereditary prostate cancer?
Excluding skin cancer, prostate cancer is the most common cancer in American men. Despite the fact that many cases do not develop into a significant health problem, prostate cancer remains a leading cause of death according to the CDC. Prostate cancer occurs when the cells in the prostate begin to grow abnormally into a malignant tumor. 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 genetic change (mutation) that causes their cells to be more likely to become cancerous. The mutation can be passed through generations in a family. 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.

How is hereditary prostate cancer inherited?
Our genes, or DNA, tell the cells in our body how to work correctly. Cancer-risk genes are genes with roles that can impact whether a cell will begin to grow uncontrollably into cancer. We have two copies of every gene, one from our mother and the other from our father. Hereditary prostate cancer is most commonly inherited in an autosomal dominant way. For dominant conditions, having only one copy of a gene mutation is enough to cause symptoms. In the case of HPC, having one mutation leads to an increased risk for cancer. If a person has a mutation in one gene for HPC, there is a 50% risk that each of their children will inherit this mutation. Siblings, parents, and potentially other relatives could also have the mutation. Importantly, not everyone who has a mutation in a cancer-risk gene will develop cancer, but their chances are higher.

While rare, it is possible for a person to have a mutation for a dominant condition that is absent from both of their parents. In this situation, the mutation arose early before they were conceived or born. This is called de novo inheritance. Even after de novo inheritance, if a person has a mutation in one gene for hereditary prostate cancer, each of their children will have a 50% risk to inherit the mutation.

In rare cases, HPC can be inherited in an autosomal recessive way. For recessive conditions, both copies of a person’s gene must have a mutation before they will have an increased risk for cancer. Typically, an individual with a recessive condition will have inherited one mutation from their mom and one from their dad. Because the mom and dad have another copy of the gene without the mutation, they will usually not show symptoms. For these parents, there is a 25% risk with each pregnancy that the child will inherit both the mom’s and the dad’s mutations, and therefore, will have the recessive condition.

What are hereditary prostate cancer 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. Mutations in these two genes are also associated with a significant risk for breast and ovarian cancer, as well as prostate and pancreatic cancer. A mutation in BRCA2 also confers a higher risk for breast cancer in men, and melanoma for both men and women. Men with BRCA2 mutations who are diagnosed with prostate cancer tend to have more aggressive tumors and an earlier age of diagnosis than other men.
What will genetic testing tell me?

There are three possible results from genetic testing:

**NEGATIVE:**
A negative result indicates that a genetic mutation was not identified. A negative result may indicate that there is not a cancer-risk gene mutation in you or your family. However, it can also mean that the gene increasing risk in you or your family was not included on the ordered test, or that it may not be currently known. Your doctor can use a negative result to continue your treatment and screening based on your clinical and family history, or they may consider another type of genetic testing.

**VARIANT OF UNCERTAIN CLINICAL SIGNIFICANCE (VUS):**
The third possible test result is called a Variant of Uncertain Clinical Significance. A gene variant is a genetic difference that could be disease-causing (mutation) or could be a normal finding (benign). More research is needed to determine whether the variant is important or not, and it should be treated as a negative result until more information is available. Your doctor may follow up with the laboratory in the future to see if more has been learned. If you are interested in participating in research, many studies are listed at www.clinicaltrials.gov.

**POSITIVE:**
A positive result means that a genetic mutation causing an increased risk for prostate cancer was identified. Your risk for other cancers or health conditions may also be increased, depending on the gene involved. Your doctor can use this information to customize your care, which could include increased screening, preventative surgery, medication, and other steps. A positive result is also important for your family. Your parents, siblings, and children could have as high as a 50% chance to also have the mutation. As a result, sharing your genetic testing results with your relatives is important for their health.

Are there cancer-risk genes for HPC that don’t cause a syndrome?

Yes. Mutations in a gene called HOXB13 are currently believed to only increase the risk for prostate cancer. Individuals with HOXB13 mutations may be more likely to have an aggressive form of cancer. HOXB13 mutations are passed through a family in a dominant way.

Who might need genetic testing for hereditary prostate cancer?

Hereditary prostate cancer testing is indicated if you or a close relative meet certain criteria. Your physician will make the final decision about testing based on your clinical and family history, but some “red flags” suspicious for HPC are listed below:

- Known cancer-risk gene mutation in the family
- Personal or family history of prostate cancer diagnosed before age 55 years
- Multiple first degree relatives or different generations of prostate cancer
- Family history of breast cancer and either ovarian or pancreatic cancer in a single individual
- Male breast cancer
- Ashkenazi Jewish ancestry
- A family history of 3 or more individuals with breast, pancreatic, prostate, melanoma, or other cancers, especially if early onset or if multiple cancers occurred in a single individual

What will genetic testing tell me?

There are three possible results from genetic testing:
Can my family members be tested?
Yes. Targeted testing (Familial Mutation Test) is available through Fulgent. The cost is much lower than the cost of a genetic panel testing.

How long does it take to receive the results?
Results are usually available in 3 to 4 weeks after the laboratory receives the sample.

Will insurance cover the cost of the testing?
Fulgent accepts all commercial insurance plans. Most insurance companies have specific criteria that they use to determine coverage for genetic testing. Whenever, possible, Fulgent will obtain the required prior authorizations. Prior to testing, Fulgent’s insurance specialists will contact you if your anticipated out of pocket cost exceeds $100.

If I have genetic testing, can my employer or health insurance company discriminate against me?
NO. The Genetic Information Nondiscrimination Act (GINA) was signed into law in 2008. It protects Americans from discrimination by an employer or a health insurance company based on genetic information. Importantly, GINA does not offer protections for disability, long term care, or life insurance. It also does not apply to members of the U.S. military or employees of the Federal government, Indian Health Service, or Veterans Health Administration.

Where can I learn more?
GARD (Genetic and Rare Diseases Information Center- NIH) | www.rarediseases.info.nih.gov/diseases/4520/familial-prostate-cancer
Bright Pink | www.brightpink.org
FORCE (Facing Our Risk of Cancer Empowered) | www.facingourrisk.org/index.php
Lynch Syndrome International | www.lynchcancers.com