Somatic and Germline Genetic Testing for Patients with Advanced Prostate Cancer

What You Should Know

Advanced prostate cancer is different for everyone.

A treatment that works well for one person may not work for someone else. Fortunately, specific genetic tests are available that can help you and your doctor choose the right treatment for you.

Two main genetic tests are used for this purpose. **Somatic testing** looks for changes in the genes and proteins of your tumor cells. **Germline genetic testing** looks at your healthy cells for genetic information inherited from your parents. **If you have advanced prostate cancer, getting both types of tests will give you and your doctor the most complete understanding of your treatment options.**

These tests also provide important information about how your disease might progress, your eligibility for clinical trials of new treatments, and whether you and your family may be at increased risk for prostate cancer and certain other cancers. This helps everyone make informed choices to support the best possible health outcomes.

This Guide Covers:

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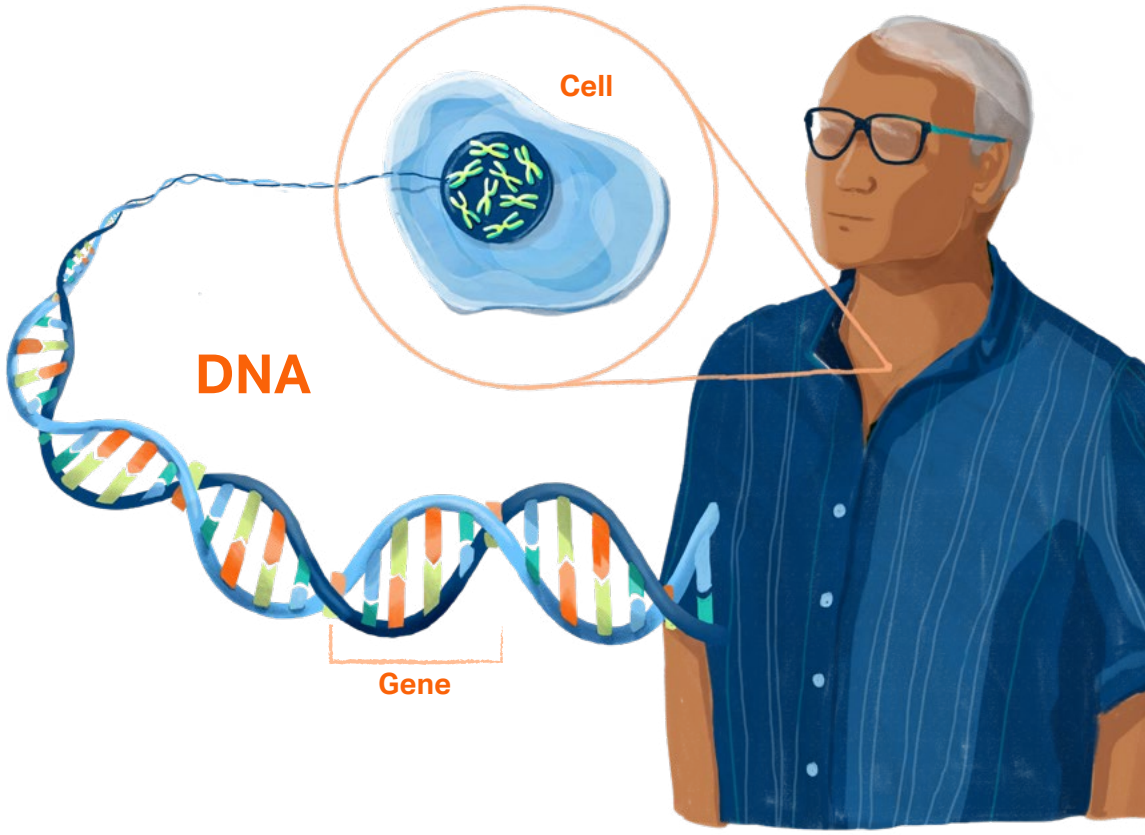
Let's start with the basics.

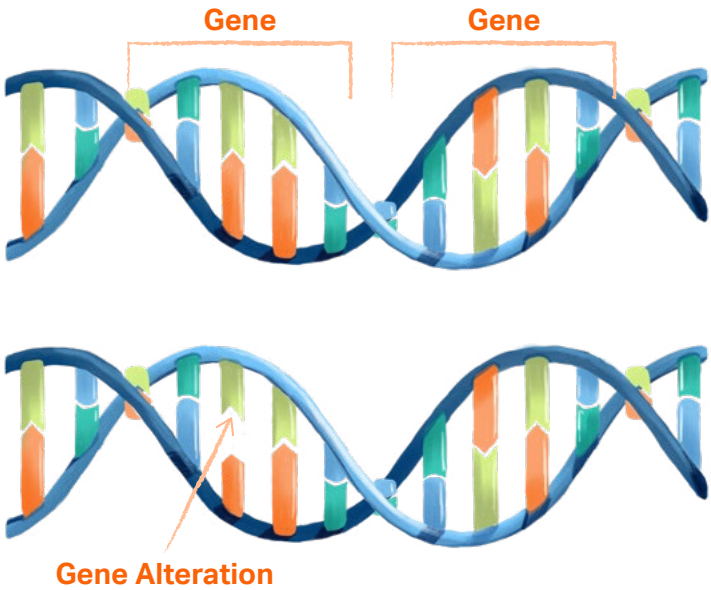
What is DNA?

DNA is the chemical code that tells your body how to look, grow, and work. Every cell in your body has a copy (except your red blood cells).

What is a gene?

DNA is made up of thousands of bundles called genes. Some genes control physical features, like eye and hair color. Others affect how your body works.





What is a gene alteration?

A gene alteration is a permanent change in the DNA of a gene. Gene alterations can be inherited from a parent, or can occur after birth.

There are millions of different gene alterations. Some do not affect how your body works. Others increase your risk of cancer or other diseases, make a disease more aggressive, or affect how well certain treatments work.

Note: Gene alterations used to be called "mutations," but this term is no longer preferred because many gene alterations do not cause or affect disease.

There are two types of genetic tests (Somatic & Germline) that are important to help guide your treatment choice.

What are somatic and germline genetic testing?

These tests look for gene alterations and related changes that provide important information about your prostate cancer. There are two types of tests:

Both somatic and germline genetic testing use broad (multigene) panels to look at many different genes at the same time. These genes include BRCA1, BRCA2, other homologous recombination repair (HRR) genes, mismatch repair (MMR) genes, and many others.

1 Somatic Testing

Somatic testing looks for specific changes in the DNA and proteins of your **tumor cells** that can drive tumor growth and treatment response. This test uses tumor tissue from a prostate biopsy or surgery. If tumor tissue is unavailable, a blood sample can be tested for circulating tumor DNA (ctDNA). Somatic testing is sometimes called genomic testing, tumor testing, or biomarker testing. These terms all mean the same thing.

2 Germline Genetic Testing

Germline genetic testing looks at your **healthy cells** for gene alterations you inherited from your parents. The test is done on a saliva or blood sample. Germline genetic testing is sometimes called hereditary testing or inherited cancer risk gene testing. These terms all mean the same thing.

How can somatic and germline genetic testing help me?

Treatment selection

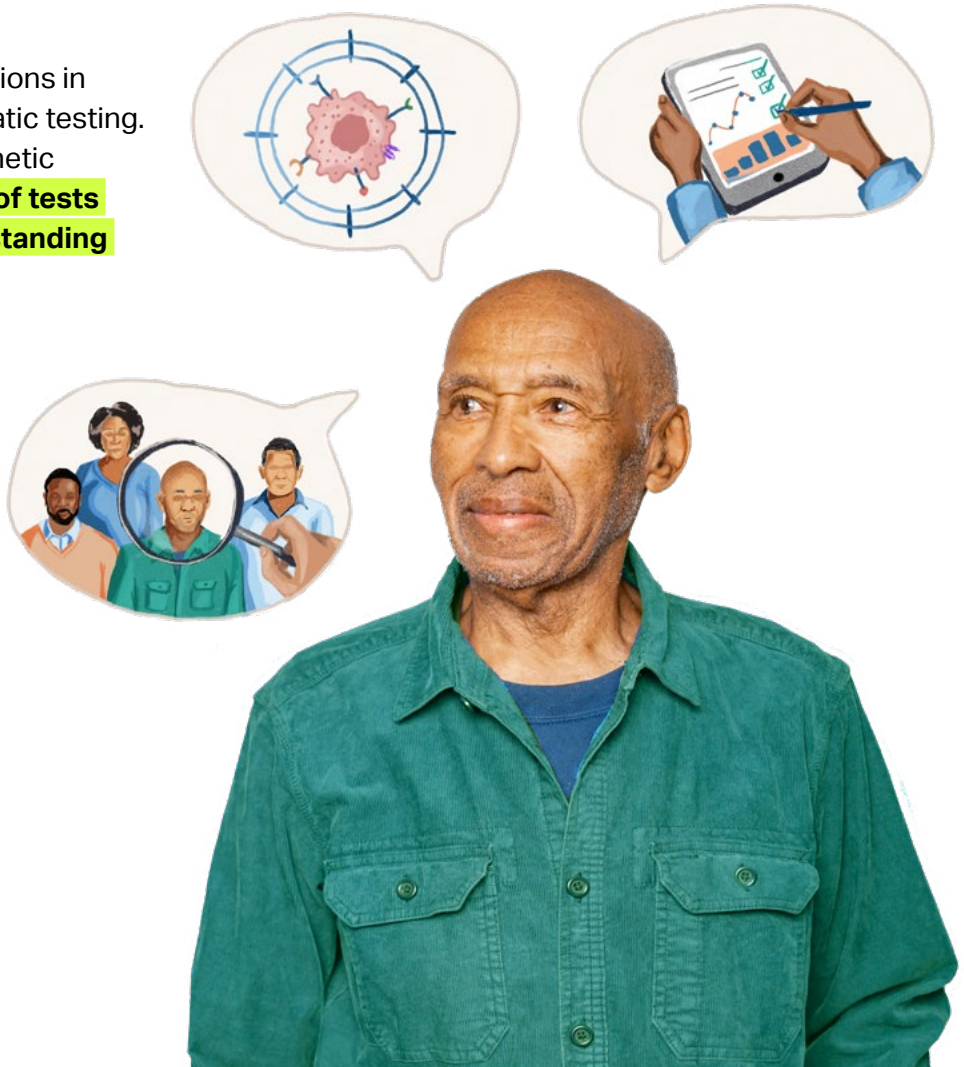
Advanced prostate cancer is different for everyone. A treatment that works well for one patient may not help another. Somatic and germline genetic testing can help show if certain treatments are likely to work for you.

For example, treatments called PARP inhibitors work best if you have gene alteration(s) affecting DNA repair. In contrast, immunotherapy may work well if your tumor cells have changes called microsatellite instability (MSI-H), mismatch repair deficiency (dMMR), or high tumor mutational burden (TMB-H).

Only some of the important gene alterations in prostate cancer are found through somatic testing. The rest are found through germline genetic testing. **Therefore, getting both types of tests will provide the most complete understanding of your treatment options.**

Other benefits

Somatic and germline genetic testing also can help you understand your prognosis, and whether you are eligible for clinical trials of new therapies. In addition, germline genetic testing can help you and your family find out if you are at increased risk for certain cancers. This can help everyone make informed choices to support the best possible health outcomes.



Getting both types of tests will give you and your doctor the most complete understanding of your treatment options.

At what point during treatment should I be tested?

Situation	Is Somatic Testing Recommended?
Advanced prostate cancer (has spread to distant places in body like bones, lungs, or liver)	**Yes**
Node-positive prostate cancer (has spread to lymph nodes)	**Consider—talk with your doctor**
Advanced prostate cancer that has progressed on treatment	**Consider repeat testing***
A new treatment or test is available	**Consider repeat testing**
Localized prostate cancer (is confined to the prostate gland)	**Not usually (you may wish to ask your doctor)**

**Tumor genes can change (mutate) in response to treatment, which can affect the next treatment choice. This is why repeat somatic testing is considered if your cancer has progressed on a treatment.*

Situation	Is Germline Genetic Testing Recommended?
Advanced prostate cancer	**Yes**
Node-positive prostate cancer	**Yes**
Very high-risk or high-risk localized prostate cancer	**Yes**
At least one first or second-degree relative with: advanced, node-positive, or high-risk/very high-risk prostate cancer, female breast cancer (at or before age 50), male breast cancer (any age), pancreatic cancer, or ovarian cancer	**Yes**
At least two close blood relatives with prostate cancer or breast cancer on the same side of the family	**Yes**
Prostate cancer and Ashkenazi Jewish ancestry	**Yes**
Diagnosed at age 55 or younger	**Consider (talk to your doctor)**
Intermediate risk and intraductal/cribriform histology	**Consider (talk to your doctor)**

Experts recommend getting both types of tests as soon as advanced prostate cancer is diagnosed.

Should I wait for my results to start a new treatment?

It can take a few weeks to get your test results. Waiting to start a new treatment can feel stressful, but it helps make sure you get the most effective and personalized care, which may improve your long-term outcomes. Talk with your doctor to see if a short delay makes sense for your specific situation and to address any concerns about waiting.

How do I read my somatic test results?

Your report will show:

MEDICAL CLINIC

Sample Somatic (Tumor) Test Report

1 Your name, date of birth, diagnosis, and the doctor who ordered the test

Patient Name	John Smith
Date of Birth	October 24, 1695
Medical Record #	157984783
Physician	Dr. Patrick Wright, MD
Medical Office	Medical Clinic Los Angeles, CA 91456

2 Type of sample and tumor

Specimen	Prostate tissue biopsy
Tumor Type	Prostate acinar adenocarcinoma

3 Which gene alterations or other changes were found (if any)

Example Biomarker Findings	Therapy and Clinical Trials
HRD signature – HRDsig Negative	
Microsatellite status – MS-Stable	
Tumor mutational burden – 1 Muts/ Mb	

Here you may see a list of any treatments or clinical trials you are eligible for, based on your test results.

Together, these tests check to see if your prostate cancer has trouble fixing mistakes in its genetic code. This will help show if certain treatment(s) may work well for you.

Your test report will also show:

A list of all the tumor genes that were tested, any gene alterations found, and how the results affect your prognosis, treatment options, and clinical trials you may be eligible to join.

How do I read my germline test results?

Your report will show:

MEDICAL CLINIC

Sample Germline Genetic Test Report

1 Your name, date of birth, diagnosis, and the doctor who ordered the test

Patient Name	John Smith
Date of Birth	October 24, 1695
Medical Record #	157984783
Physician	Dr. Patrick Wright, MD
Medical Office	Medical Clinic Los Angeles, CA 91456

2 Your sample will be blood or saliva

Sample Type Blood

3 Snapshot of key findings

Result: Positive

Gene: BRCA2

Variant (gene alteration): c.8474_841 6delinsC (p.Leu2805Serfs *6)

Variant classification: Pathogenic

This patient has an alteration in the BRCA2 gene, one of many genes linked to prostate cancer.

There are many different BRCA2 alterations. The long name you see here is an example of one specific BRCA2 alteration.

Pathogenic means it increases risk of a disease.

If instead of 'pathogenic,' you see 'unknown significance' or 'VUS,' it means you have a gene alteration with unknown health effects.

Your test report will also show:

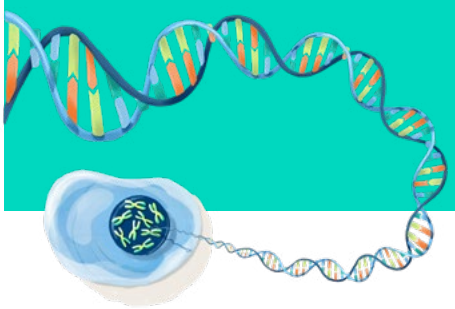
A list of all the genes the test analyzed.
What disease(s) any gene alterations you have are linked to.

What to do with your test results.

What if a gene alteration or another change is found?

The doctor who ordered the test will usually contact you to discuss the results. If not, contact them and ask for an appointment to discuss your test results. During this visit, ask your doctor to explain what the results mean as far as your treatment options, prognosis, inherited cancer risk, and clinical trial eligibility (see "Questions you can ask").

Having an inherited cancer risk gene alteration does not mean that someone will get cancer, but it can increase their risk.



My germline genetic test found a gene alteration. What should I tell my family?

If you have an inherited cancer risk gene alteration, your first and second-degree relatives (parents, children, siblings, aunts, uncles, etc.) may have it, too. This can increase their risk for certain cancers, including prostate cancer, male or female breast cancer, ovarian cancer, or pancreatic cancer. Having a gene alteration does not mean that someone will get cancer, but it can increase their risk.

Often, your doctor will refer you to a genetic counselor to discuss your test results. Talking to a genetic counselor can make your germline genetic test results much easier to understand and help you decide what information to share with family members. This will help them make decisions about germline genetic testing (to find out if they also have the gene alteration), earlier or more intensive cancer screening, and other preventive steps to help improve health outcomes. If your family members want germline genetic testing, they should first talk with their doctor or a genetic counselor, to understand what the results would mean for them.

It's a good idea to ask about tumor and genetic testing during your appointments.

Most doctors strive to provide excellent care, but they may not always know the latest testing recommendations, especially since these can change as research advances. Taking a proactive approach will help you receive the most up-to-date and personalized care.

Talking With Your Doctor

Here are some questions you can ask:

- ☑ Have my healthy cells and my tumor cells been tested for gene alterations that affect cancer treatment response, prognosis, risk, and so on? Which tests were done?
- ☑ What samples were taken (tumor tissue, blood, saliva)?
- ☑ Were any gene alterations or other changes found? If yes, which ones?
- ☑ How do the results affect my treatment options?
- ☑ How can I get a copy of my test report?
- ☑ Am I eligible for any clinical trials based on my test results?
- ☑ Should I be re-tested if the results were unclear or if my disease has progressed?
- ☑ If I have not been tested, can I be tested now?
- ☑ Should I schedule an appointment with a genetic counselor?
- ☑ Should my family members consider germline genetic testing? If yes, who can advise them about this and help them get tested if they choose to?

How much do these tests cost? Does insurance cover them?

Medicare and most private insurance plans cover somatic testing and germline genetic testing for patients with advanced prostate cancer. Out-of-pocket costs can be up to $250 for germline genetic tests, while somatic testing costs more (price varies). If you need help paying for testing, financial assistance or payment plans may be available. Ask your care team for guidance. Many testing companies also offer free phone and telemedicine services to help you learn more about tests and costs.

More Resources

Here are some more resources on somatic and germline genetic testing for patients with advanced prostate cancer.

- National Society of Genetic Counselors (lists genetic counselors in the United States and Canada)
- Prostate Cancer and Inherited Cancer Risk Genes (Prostate Cancer Foundation)
- Genetic Testing for Prostate Cancer (Urology Care Foundation)
- Metastatic Prostate Cancer Handbook
- PCF Webinar on Genetic Testing
- PCF Webinar on Germline Genetic and Somatic (Biomarker) Testing

Glossary of Terms

Many of these terms appear in this guide.
Click on a term to go to that page of the guide.

Advanced prostate cancer	Prostate cancer that has spread outside the prostate gland and pelvic lymph nodes to other places in the body like the bones, liver, or lungs. See 'metastasis.'
Ashkenazi Jewish	Someone with Jewish ancestry from Eastern Europe. In some cases, Ashkenazi Jewish ancestry is linked to with an increased risk for certain cancers and may be a reason for germline genetic testing in some situations.
Biomarker testing	Another term for tumor testing or somatic testing (these all mean the same thing).
Biopsy	A sample of tissue used to diagnose or understand features of certain diseases, including cancer.
BRCA1 and BRCA2	See homologous recombination repair (HRR) genes.
DNA	The genetic code that tells your body how to grow, look, and work. Every cell in your body (except your red blood cells) has a copy of your DNA.
Circulating tumor DNA (ctDNA)	DNA released by tumor cells into the bloodstream. ctDNA testing uses a blood sample and does not require a biopsy
Gene	A bundle of DNA. Your genes determine how you look and how your body functions.
Gene alteration	A change in the DNA sequence (code) of a gene. Some (not all) gene alterations cause or affect disease. Gene alterations are also known as gene variants and used to be called mutations.
Genetic counselor	A healthcare professional specially trained to help people understand genetic test results and decide whether to get tested.
Germline genetic testing	A blood or saliva test that checks your healthy cells for specific inherited gene alterations that affect disease risk, progression, or treatment outcomes. Also known as hereditary testing or inherited cancer risk gene testing.
Genomic testing	Another term for somatic testing. 'Genomic' comes from 'genome,' or the complete set of DNA in your body. Every person has a unique genome, and so does every tumor.
Hereditary	Passed down from a parent to a child. In cancer medicine, "hereditary" refers to inherited gene alterations that affect cancer risk, aggressiveness, and treatment response.

Homologous recombination repair (HRR) genes	Genes that help repair specific types of DNA damage. HRR genes include BRCA1, BRCA2, ATM, CHEK2, PALB2, and others. Certain alterations in these genes increase cancer risk and aggressiveness but also predict a better response to PARP inhibitor treatments. HRR alterations can be inherited (found in healthy cells) or may occur only in tumor DNA.
Immunotherapy	A treatment that helps your body's immune system locate and fight cancer cells.
Inherited cancer risk gene alterations	Gene alterations that can increase the risk of certain cancers. These alterations are inherited from a parent and can be passed down to a child. Found by testing blood or saliva.
Localized prostate cancer	Has not spread outside the prostate gland.
Metastasis	The spread of cancer cells from where they first formed to another part of the body through the bloodstream or lymphatic system. After spreading, they form a new tumor. This means that if prostate cancer metastasizes to the bones, the cancer cells in the bones are prostate cancer cells, not bone cells.
Metastatic prostate cancer	See advanced prostate cancer.
High tumor mutational burden (TMB-H)	A tumor that has many alterations in its DNA. These tumors often respond well to certain immunotherapy treatments.
Microsatellite instability-high (MSI-H)	A tumor that has trouble repairing mistakes in its DNA. These tumors also often respond well to certain immunotherapy treatments.
Mismatch repair deficiency (dMMR)	Alterations in certain genes responsible for repairing mistakes that can occur when DNA is copied. Often causes MSI-H.
Mutation	See gene alteration.
Node-positive prostate cancer	Prostate cancer that has spread from the prostate gland to nearby lymph nodes, but not to other parts of the body.
PARP inhibitor	Stands for poly (ADP-ribose) polymerase inhibitor, a type of targeted cancer drug. PARP inhibitors work by blocking a protein that tumor cells use to repair their DNA. Blocking this protein making it harder for the cancer to survive and grow.
PTEN	Stands for phosphatase and tensin homolog, a gene that controls cell growth and division. If PTEN is lost or damaged, cancer may grow faster.
Somatic testing	Looks for changes in your tumor DNA and proteins that help guide treatment selection. These changes occur in the tumor during your lifetime and are not inherited. Also known as biomarker or genomic testing.
Variant	See gene alteration.
Very high-risk or high-risk localized prostate cancer	Prostate cancer that has not spread outside the prostate gland but has characteristics that make spread much more likely.

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