Comprehensive Germline Panel For Prostate Cancer Care

Right Decisions Start From Your Patient’s DNA

Comprehensive germline panel powered by NorthShore University HealthSystem
The Genetics of Prostate Cancer

Prostate cancer is not typically considered a hereditary disease, but studies show that inherited factors account for 57% of the risk for developing prostate cancer (including sporadic cases). In fact, the heritability of prostate cancer is stronger compared to other cancers such as breast cancer, ovarian cancer and colorectal cancer. This highlights the importance of assessing the inherited risk for prostate cancer. Inherited risk can be assessed using three available methods:

FAMILY HISTORY (FH)
FH is a common but indirect measurement of inherited risk. Men with a positive FH have a 1.5-to-2.5-fold increased risk for developing prostate cancer. However, accurate assessment of FH is often difficult because it relies on the patient's knowledge of their relatives' health conditions.

RARE PATHOGENIC MUTATIONS (RPMS)
RPMs are pathogenic DNA mutations in the coding regions of genes such as BRCA2, ATM and CHEK2. They are quite rare and are associated with a moderate-to-high risk for developing prostate cancer; some are also associated with prostate cancer aggressiveness.

GENETIC RISK SCORE (GRS)
GRS is calculated based on more than 100 single nucleotide polymorphisms (SNPs) associated with prostate cancer risk. GRS can be used to assess a man's risk of developing prostate cancer compared to other men in the general population. For example, a score of 1.5 indicates that the individual has a 50% higher chance of developing prostate cancer. GRS can identify many more high-risk men than both FH and RPMS combined.

HIGH-RISK MEN FOR PROSTATE CANCER

Because FH, RPMS and GRS each measures risk independently, a comprehensive inherited risk assessment should include ALL three tools.

QUICK FACTS ABOUT GENETIC TESTING

GERMLINE TESTING:
Used to measure RPMS and GRS in germline DNA derived from saliva and blood.

GERMLINE TESTING VS. SOMATIC TESTING:
Germline testing detects inherited alterations in the DNA passed down from parents. This is the DNA that an individual is born with. Any mutations or variations in germline DNA exist in every cell and can be passed down to offspring. In contrast, somatic testing detects genetic changes in cells specific to an organ (such as the prostate). These changes can occur and accumulate during one's lifetime and can contribute to tumor formation. Unlike germline mutations, somatic mutations are not passed down to offspring.
Who Should Be Tested?

Most prostate cancer patients and their families can benefit from germline testing. The new NCCN guidelines recommend germline testing for the following groups:13-16

**FOR PROSTATE CANCER PATIENTS**
- Patients with high to very high risk and/or regional or metastatic disease;
- Patients with high-risk family history, intraductal histologies or other conditions, regardless of risk.

**High-risk family history includes:**
- A 1st-degree relative or multiple relatives <60y who were diagnosed or died of prostate cancer;
- Ashkenazi Jewish ancestry;
- ≥3 cases of any cancer on the same side of the family.

**Other conditions include:**
- Family history of hereditary cancer syndromes and/or high-risk germline mutations (e.g. BRCA1/2, Lynch gene mutation);
- Family history of other potential high-risk germline mutations (e.g. ATM, CHEK2, PALB2, HOXB13).

**FOR UNAFFECTED MEN**
- Men with a family history of hereditary cancer syndromes (HBOC, Lynch or others);
- Men with a family history of pathogenic mutations with cancer syndromes.

### THREE REASONS FOR GERMLINE TESTING

#### PREDICTING PROGNOSIS FOR LOCALIZED PROSTATE CANCER PATIENTS:
Information on RPMs can supplement traditional clinical variables such as Gleason Score and PSA levels to predict disease progression and inform personalized decisions on prostate cancer treatment such as pursuing active surveillance vs. definitive treatment with either surgery or radiation.17-18

#### PREDICTING THERAPEUTIC RESPONSES FOR ADVANCED PROSTATE CANCER PATIENTS:
RPMs in DNA repair genes and other genes can complement clinical variables and somatic DNA testing when making a personalized decision on drug treatments.19-23

#### PREDICTING RISK FOR UNAFFECTED MEN:
Men with RPMs and a higher GRS may evaluate their chances of passing on this risk to their offspring and consider early and more frequent prostate cancer screening.10
Why ProstateNow™?

ProstateNow™ is a new, clinical grade, comprehensive germline panel offered by GoPath. The test content, result interpretation and corresponding clinical actions are developed and supported by the urology team of NorthShore University HealthSystem. The urology team is a national leader in the field of the genetics of prostate cancer, evidenced by many published peer-reviewed articles in the top medical journals such as the New England Journal of Medicine, European Urology, Nature Series, and JAMA Series and patents.

The only test...

TO SATISFY ALL THREE REASONS FOR GERMLINE TESTING

This test can be used to predict prognosis among patients with localized prostate cancer, predict therapeutic responses among advanced prostate cancer patients as well as predict prostate cancer risk among unaffected men.

TO INCLUDE BOTH RPMS AND GRS FROM STUDIES INVOLVING MULTIPLE RACES

This test includes all known prostate cancer susceptibility genes as well as >100 prostate cancer risk-associated SNPs for calculating GRS in multiple races.

BASED ON COMPREHENSIVE EVALUATION OF CURRENT EVIDENCE

This test is developed based on recommendations from up-to-date clinical guidelines, current evidence review, and proprietary data from the NorthShore team.

PROSTATENOW™ IS UNIQUE AND CUTTING-EDGE

THE LARGEST MUTATION DATABASE:
In addition to following the mutation-calling guidelines of American College of Medical Genetics (ACMG), we have the largest germline mutation database with data gathered from more than 300,000 men with or without prostate cancer. This information helps categorize relevant mutations in prostate cancer to provide accurate results.

EDUCATION BY EXPERIENCED UROLOGISTS:
Practicing urologists experienced in genetics at NorthShore University HealthSystem provide guidance and education about ProstateNow™.

RELIABILITY OF GRS IN MULTIPLE RACES:
Reported GRS values are calibrated for the general population and have been validated in many races.10

RESEARCH OPTION:
In addition to providing a clinical report of genes based on the most current evidence, patients have the choice to opt-in for research that examines hundreds of other candidate genes, helping to expand our knowledge of cancer research and impact the health of present and future generations.
# Which Genes Are Tested?

The genes tested in ProstateNow™ are based on a combination of clinical guidelines and up-to-date evidence-based review as illustrated below:

<table>
<thead>
<tr>
<th>Genes</th>
<th>Unaffected Men (PCa Screening)</th>
<th>Localized PCa (Prognosis)</th>
<th>Advanced PCa (Therapeutic response)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NCCN guideline&lt;sup&gt;16&lt;/sup&gt;</td>
<td>Evidence Review&lt;sup&gt;3,5&lt;/sup&gt;</td>
<td>NCCN guideline&lt;sup&gt;15&lt;/sup&gt; Evidence Review&lt;sup&gt;3,7,17-18&lt;/sup&gt;</td>
</tr>
<tr>
<td>ATM</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>ATR</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BRCA1</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>BRCA2</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>BRIP1</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHEK2</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>FAM175A</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FANCA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GEN1</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRE11A</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NBN</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PALB2</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>RAD51C</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RAD51D</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TP53</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>EPCAM</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MLH1</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>MSH2</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>MSH6</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>PMS2</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>HOXB13</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>HSD3B1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SNP-BASED GRS</td>
<td>X</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The core of germline testing is to know which genes/mutations have clinical validity and utility.
ProstateNow™ offered by GoPath is a comprehensive germline panel developed and supported by the urology team of NorthShore University HealthSystem. The clinical validity and utility of RPMs and GRS in cancer risk assessment are supported by hundreds of peer-reviewed papers published by the NorthShore team, including the following key publications in leading journals:

1. **Cumulative association of five genetic variants with prostate cancer**

2. **Association of GRS with age of prostate cancer diagnosis in a clinical trial**

3. **Discovered HOXB13 as a prostate cancer susceptibility gene**

4. **Relationship between BRCA2/ATM and lethal prostate cancer**

---

**Powered By NorthShore**

Comprehensive germline panel powered by NorthShore University HealthSystem
ProstateNOW™ uses the GeneticsNOW™ testing process, which is streamlined to prioritize quality and simplicity. Refer a patient and leave the rest in the hands of our skilled professional team.

THE GENETICSNOW™ TESTING PROCESS: HOW IT WORKS

- **PATHOLOGISTS:**
  Ensure the accuracy of the test and variant calls (the process of identifying variants from the sequence).

- **GENETIC COUNSELORS:**
  Nationally-accredited genetic counselors work with you side-by-side to ensure that patients understand the qualifications and benefits of germline testing.

- **SCIENTISTS:**
  Leading genomic translational researchers from NorthShore University HealthSystem perform continuous R&D to strengthen the science behind tests and bring the latest discoveries to practical clinical use.

- **TECHNOLOGISTS:**
  Perform state-of-the-art assays and ensure quality work at each step.

- **COORDINATORS:**
  Ensure smooth workflow by facilitating pre-authorization, sample collection, billing, etc.

- **UROLOGISTS:**
  Renowned urologists offer general education on prostate health programs and how the ProstateNOW™ process works.

*Under the Additional Information section of requisition, physicians may simply write, “Genetic testing will be chosen by Generic Counselor after consultation with patient”.

Comprehensive germline panel powered by NorthShore University HealthSystem
REFERENCES


