Hereditary Prostate Cancer Panel

Features of Hereditary Prostate Cancer
Genetic testing with the Hereditary Prostate Cancer Panel may be appropriate if your personal and/or family history is suggestive of a hereditary predisposition to prostate cancer. This includes:

- Prostate cancer diagnosed at an early age
- Metastatic/aggressive prostate cancer
- Multiple cancers in one person (such as prostate and pancreatic cancer)
- Multiple relatives diagnosed with prostate cancer (especially aggressive cancer; Gleason score ≥ 7) and/or related cancers (including breast, ovarian, pancreatic, etc) on the same side of the family and spanning multiple generations

Genes Included on the Hereditary Prostate Cancer Panel
The genes included in the Hereditary Prostate Cancer Panel are: ATM, BRCA1, BRCA2, CHEK2, EPCAM, HOXB13, MLH1, MSH2, MSH6, NBN, PMS2, and TP53.

They can be categorized into three main groups: High-Risk, Moderate-Risk, and Newer-Risk.

Lifetime Cancer and/or Tumor Risks

<table>
<thead>
<tr>
<th>Gene</th>
<th>Lifetime Cancer and/or Tumor Risks*</th>
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</thead>
<tbody>
<tr>
<td>BRCA1</td>
<td>Female breast (57-87%), Ovarian (24-54%), Prostate, Male breast, Pancreatic, Fallopian tube, Primary peritoneal, Endometrial</td>
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<tr>
<td>BRCA2</td>
<td>Female breast (41-84%), Prostate (up to 34%), Ovarian (11-27%), Pancreatic (5-7%), Male breast (4-7%), Melanoma, Fallopian tube, Primary peritoneal, Endometrial</td>
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<tr>
<td>EPCAM**</td>
<td>Colorectal (69-75%), Endometrial (12-55%), Ovarian, Gastric, Pancreatic, Biliary tract, Urinary tract, Small bowel, Brain, Sebaceous tumors, Prostate</td>
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<tr>
<td>MLH1</td>
<td>Colorectal (22-80%), Endometrial (31-54%), Ovarian (13-20%), Gastric (6-20%), Urinary tract (1-3%), Pancreatic, Biliary tract, Small bowel, Brain, Sebaceous tumors, Prostate</td>
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<tr>
<td>MSH2</td>
<td>Colorectal (22-80%), Endometrial (31-61%), Ovarian (10-24%), Urinary tract (8-10%), Gastric (&lt;1-9%), Pancreatic, Biliary tract, Small bowel, Brain, Sebaceous tumors, Prostate</td>
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<tr>
<td>MSH6**</td>
<td>Colorectal (20-44%), Endometrial (44%), Ovarian (1-11%), Gastric, Pancreatic, Biliary tract, Urinary tract, Small bowel, Brain, Sebaceous tumors, Prostate</td>
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<tr>
<td>PMS2**</td>
<td>Colorectal (11-20%), Endometrial (12-15%), Ovarian, Gastric, Pancreatic, Biliary tract, Urinary tract, Small bowel, Brain, Sebaceous tumors, Prostate</td>
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<tr>
<td>TP53</td>
<td>Female breast, Sarcoma-bone and soft tissue, Brain, Hematologic malignancies, Adrenocortical carcinoma, among others. Overall risk for cancer: nearly 100% in females, 73% in males</td>
</tr>
</tbody>
</table>

High-Risk Genes
- Well-studied
- Greater than 4-fold risk of developing one or more cancers
- Can cause a moderate risk for other cancers
- National or expert opinion guidelines for screening and prevention are established

Moderate-Risk Genes
- Well-studied
- Approximately 2-4-fold risk of developing one or more cancers
- May increase risk for other cancers
- Limited guidelines for screening and prevention

Newer-Risk Genes
- Not as well-studied
- Precise lifetime risks and tumor spectrum not yet determined
- Guidelines for screening and prevention are limited or not available

*Most commonly associated cancers/tumors listed; lifetime risks provided when available. Risks relate to carriers of a single pathogenic variant.
**Tumor spectrum is representative of Lynch syndrome; data are limited with regard to the association of certain cancers with pathogenic variants in MSH6, PMS2 and EPCAM.
Possible Outcomes of Genetic Testing:

There are four possible outcomes of genetic testing: positive (pathogenic variant), likely pathogenic variant, variant of uncertain significance (VUS), and negative. Genetic counseling is recommended prior to genetic testing to understand the benefits and limitations of testing.

A positive result indicates a genetic variant (change) was identified in a specific gene and that variant is pathogenic (harmful). With a positive test result, the risk to develop a particular disease (in this case, cancer and/or tumors) is increased.

A likely pathogenic variant result indicates that there is a variant in a specific gene for which there is significant, but not conclusive, evidence of an increased risk to develop a particular disease (in this case, cancer and/or tumors).

A variant of uncertain significance (VUS) result means that a change in a specific gene was identified, however the effect of the variant cannot be clearly established. There may be conflicting or incomplete information in the medical literature about this variant and its association with an increased risk of cancers and/or tumors is unknown. In other words, it cannot be determined yet whether this variant is associated with an increased risk of cancer and/or tumors or it is a harmless (normal) variant.

A negative result means that no reportable variants were identified.

Medical Management Based on Genetic Test Results

Clinical guidelines may be available which provide options and recommendations for patients who have a positive (pathogenic variant) test result indicating an increased risk for cancer and/or tumors. Guidelines and recommendations for early detection and/or risk reduction are specific to the gene in which the pathogenic variant was found.

Recommendations may include:

- Clinical exams, such as prostate exams
- Blood and/or urine analysis
- Imaging exams, such as a MRI and/or CT
- Screening procedures, such as a colonoscopy
- Risk-reducing medications and/or surgery

If you have a positive or a likely pathogenic variant result, your test report will have additional information regarding the available medical management options.

If you have a negative or variant of uncertain significance (VUS) test result, medical management should be based upon your personal and/or family history of cancer and/or tumors.

Once your test results are available, a discussion with your healthcare provider is recommended to determine the most appropriate medical management options for you and your family.

Regardless of the outcome, consider sharing your test result with family members so that they may discuss them with their healthcare providers. If you have a positive or a likely pathogenic variant result, family members are at risk to have the same result, and should consider genetic testing to best understand their chance of developing cancer and/or tumors.

Patient Resources

American Cancer Society: www.cancer.org
GeneDx: www.oncogenedx.com
National Cancer Institute: www.cancer.gov/cancertopics/genetics
National Society of Genetic Counselors: www.nsgc.org