

## 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:**

- Clinically high- or very-high localized, regional, or metastatic prostate cancer
- Gleason score  $\geq 7$ , particularly with family history of prostate or other relevant cancer(s)
- Intraductal histology
- Ashkenazi Jewish ancestry
- A personal history of a second related cancer (such as prostate and pancreatic cancer)
- A father or brother with prostate cancer diagnosed  $< 60$  years of age or who died from prostate cancer
- Tumor testing which indicates an increased risk for a hereditary cancer syndrome (i.e. variant identified on tumor sequencing and/or abnormal MSI/IHC)
- Multiple relatives diagnosed with prostate cancer (especially aggressive; Gleason score  $\geq 7$ ) and/or related cancers (including breast, ovarian, pancreatic, colon, endometrial etc.) on the same side of the family

Your healthcare provider will determine if genetic testing is medically necessary for you.

## Genes Included on the Prostate Cancer Panel are Listed in the Table Below

**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- to 4-fold risk of developing one or more cancers • May increase risk for other cancers • Limited guidelines for screening and prevention

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

	Gene	Lifetime Cancer and/or Tumor Risks*
High-Risk Genes	<i>BRCA1</i>	Female breast (55-87%), Ovarian (39-59%), Prostate, Male breast, Pancreatic, Fallopian tube, Primary peritoneal, Endometrial-serous
	<i>BRCA2</i>	Female breast (33-84%), Prostate (up to 34%), Ovarian (11-27%), Pancreatic (up to 7%), Male breast (up to 7%), Melanoma, Fallopian tube, Primary peritoneal, Endometrial-serous
	<i>EPCAM**</i>	Colorectal (69-75%), Endometrial (12-55%), Ovarian, Gastric, Pancreatic, Biliary tract, Urinary tract-transitional cell, Small bowel, Brain, Sebaceous neoplasms, Prostate
	<i>MLH1</i>	Colorectal (34-46%), Endometrial (18-54%), Ovarian (10-20%), Gastric (6-20%), Urinary tract-transitional cell (1-4%), Pancreatic (1-4%), Biliary tract (2-3%), Small bowel (4-12%), Brain, Sebaceous neoplasms, Prostate
	<i>MSH2</i>	Colorectal (37-48%), Endometrial (21-57%), Ovarian (10-24%), Urinary tract-transitional cell (8-20%), Gastric ( $< 1-9\%$ ), Pancreatic (1-4%), Biliary tract, Small bowel (1%), Brain, Sebaceous neoplasms, Prostate
	<i>MSH6**</i>	Colorectal (20-44%), Endometrial (16-71%), Ovarian (1-13%), Gastric, Pancreatic, Biliary tract, Urinary tract-transitional cell, Small bowel, Brain, Sebaceous neoplasms, Prostate
	<i>PALB2</i>	Female breast (up to 58%), Male breast, Pancreatic, Ovarian, Prostate
	<i>PMS2**</i>	Colorectal (11-20%), Endometrial (12-26%), Ovarian, Gastric, Pancreatic, Biliary tract, Urinary tract-transitional cell, Small bowel, Brain, Sebaceous neoplasms, Prostate
	<i>TP53</i>	Female breast (85%), Soft tissue sarcoma, Osteosarcoma, Brain, Hematologic malignancies-Acute leukemias among others, Adrenocortical carcinoma, among others. Overall risk for cancer: up to 95% in females, 88% in males
Moderate-Risk Genes	<i>ATM</i>	Female breast (27-33%), Colorectal, Ovarian, Pancreatic, Prostate
	<i>BRIP1</i>	Ovarian, Prostate, Female Breast
	<i>CHEK2</i>	Female breast, Male breast, Colorectal, Gastric, Prostate, Renal, Thyroid
	<i>RAD51C</i>	Ovarian, Female breast, Prostate
	<i>RAD51D</i>	Ovarian, Female breast, Prostate
Newer Genes	<i>HOXB13</i>	Prostate
	<i>NBN</i>	Female breast, Non-Hodgkin lymphoma, Prostate

\*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



### Positive

- Pathogenic or likely pathogenic variant identified
- Medical management recommendations may be available
- Family member testing may be recommended



### Negative

- No significant genetic changes identified
- Medical management based on personal and/or family history



### Variant of Uncertain Significance (VUS)

- A genetic change identified, but its association with disease is unclear
- Medical management based on personal and/or family history

## Medical Management Based on Genetic Test Results

Clinical guidelines may be available which provide options and recommendations for patients who have a **positive** (pathogenic or likely 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

In some cases, guidelines for screening and prevention are limited or not available for a positive result. 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.

### Resources

#### General

American Cancer Society  
[www.cancer.org](http://www.cancer.org)

GeneDx  
[www.genedx.com/oncology](http://www.genedx.com/oncology)

National Cancer Institute  
[www.cancer.gov](http://www.cancer.gov)

#### Prostate Cancer

Prostate Cancer Foundation  
[www.pcf.org](http://www.pcf.org)

Malecare  
[www.malecare.org](http://www.malecare.org)

#### Find a Genetic Counselor

Canadian Association of Genetic Counsellors  
[www.cagc-accg.ca](http://www.cagc-accg.ca)

National Society of Genetic Counselors  
[www.nsgc.org](http://www.nsgc.org)