Hereditary Prostate Cancer Panel

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OPKO Health Companies

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 ≥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 ≥ 7) and/or related cancers (including breast, ovarian, pancreatic, colon, endometrial) 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	*BRCA1*	Female breast (46-87%), Ovarian, including primary peritoneal and fallopian tube (39-63%), Prostate, Male breast (1.2%), Pancreatic (1-3%)
	BRCA2	Female breast (38-84%), Ovarian, including primary peritoneal and fallopian tube (16.5-27%), Prostate (up to 20%), Pancreatic (2-7%), Male breast (up to 8.9%), Melanoma
	*EPCAM***	Colorectal (37-75%), Endometrial (12-57%), Ovarian, Gastric, Pancreatic, Biliary tract, Urinary tract-transitional cell, Small bowel, Brain, Sebaceous neoplasms, Prostate
	MLH1	Colorectal (34-46%), Endometrial (18-54%), Ovarian (10-20%), Gastric (6-20%), Urinary tract-transitional cell (1-4%), Pancreatic (1-6%), Biliary tract (2-3%), Small bowel (4-12%), Brain, Sebaceous neoplasms, Prostate
	MSH2	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
	*MSH6***	Colorectal (20-44%), Endometrial (16-71%), Ovarian (1-13%), Gastric, Pancreatic, Biliary tract, Urinary tract-transitional cell, Small bowel, Brain, Sebaceous neoplasms, Prostate
	PALB2	Female breast (33-53%), Male breast, Pancreatic (2-4%), Ovarian, Prostate
	*PMS2***	Colorectal (11-20%), Endometrial (12-26%), Ovarian, Gastric, Pancreatic, Biliary tract, Urinary tract-transitional cell, Small bowel, Brain, Sebaceous neoplasms, Prostate
	TP53	Female breast (85%), Soft tissue sarcoma, Osteosarcoma, Brain, Hematologic malignancies-Acute leukemias among others, Adrenocortical carcinoma, among others. Overall risk for cancer: approaches 100% in females, 73% in males
Moderate-Risk Genes	*ATM*	Female breast (27-33%), Colorectal, Ovarian, Pancreatic, Prostate
	BRIP1	Ovarian, Female Breast, Prostate
	CHEK2	Female breast, Colorectal, Prostate
	RAD51C	Ovarian, Female breast, Prostate
	RAD51D	Ovarian, Female breast, Prostate
Newer Genes	*HOXB13*	Prostate
	NBN	Female breast, 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, your healthcare provider will determine the most appropriate medical management options for you and your family.

Resources

General
American Cancer Society
www.cancer.org

GeneDx
www.genedx.com/oncology

National Cancer Institute
www.cancer.gov

Prostate Cancer
Prostate Cancer Foundation
www.pcf.org

Malecare
www.malecare.org

Find a Genetic Counselor
Canadian Association of Genetic Counsellors
www.cagc-accg.ca

National Society of Genetic Counselors
www.nsgc.org