Endometrial Cancer Panel

Features of Hereditary Endometrial Cancer

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

- Endometrial cancer diagnosed under 50 years of age
- Multiple cancers in one person (such as colon cancer and endometrial cancer)
- Tumor testing which indicates an increased risk for a hereditary cancer syndrome known as Lynch syndrome
- Multiple relatives diagnosed with endometrial cancer and/or related cancers (including breast, ovarian, colon etc.) on the same side of the family and spanning multiple generations

Genes Included on the Endometrial Cancer Panel

The genes included in Endometrial Cancer Panel are: *BRCA1, BRCA2, CHEK2, EPCAM, MLH1, MSH2, MSH6, MUTYH, PMS2, POLD1, PTEN,* and *TP53.*

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

Lifetime Cancer and/or Tumor Risks

		Gene	Lifetime Cancer and/or Tumor Risks*
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	*BRCA1*	Female breast (57-87%), Ovarian (24-54%), Prostate, Male breast, Pancreatic, Fallopian tube, Primary peritoneal, Endometrial
		BRCA2	Female breast (41-84%), Prostate (up to 34%), Ovarian (11-27%), Pancreatic (5-7%), Male breast (4-7%), Melanoma, Fallopian tube, Primary peritoneal, Endometrial
		*EPCAM***	Colorectal (69-75%), Endometrial (12-55%), Ovarian, Gastric, Pancreatic, Biliary tract, Urinary tract, Small bowel, Brain, Sebaceous tumors, Prostate
		MLH1	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
		MSH2	Colorectal (22-80%), Endometrial (31-61%), Ovarian (10-24%), Urinary tract (8-10%), Gastric (<1-9%), Pancreatic, Biliary tract, Small bowel, Brain, Sebaceous tumors, Prostate
		*MSH6***	Colorectal (20-44%), Endometrial (44%), Ovarian (1-11%), Gastric, Pancreatic, Biliary tract, Urinary tract, Small bowel, Brain, Sebaceous tumors, Prostate
		*MUTYH**	Colorectal (up to 80%), Small bowel (up to 4%), Endometrial, Gastrointestinal polyps
		*PMS2***	Colorectal (11-20%), Endometrial (12-15%), Ovarian, Gastric, Pancreatic, Biliary tract, Urinary tract, Small bowel, Brain, Sebaceous tumors, Prostate
		PTEN	Female breast (25-85%), Thyroid (3-38%), Endometrial (5-28%), Colorectal, Renal, Melanoma, Gastrointestinal polyps
		TP53	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
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	*CHEK2*	Female breast, Male breast, Colorectal, Gastric, Prostate, Thyroid, Endometrial, Ovarian
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	*POLD1*	Colorectal, Endometrial, Colon polyps

*Most commonly associated cancers/tumors listed; lifetime risks provided when available. Risks relate to carriers of a single pathogenic variant with the exception of *MUTYH*.
**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 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 skin and/or breast exams
- Blood and/or urine analysis
- Imaging exams, such as a mammogram, MRI, CT and/or ultrasound
- Screening procedures, such as a colonoscopy and/or endometrial biopsy
- 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

207 Perry Parkway
Gaithersburg, MD 20877
T 1 888 729 1206 (Toll Free), 1 301 519 2100 • **F** 1 201 421 2010
E wecare@genedx.com • www.genedx.com

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