

Hereditary Breast and Gynecologic Cancer

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

- Breast cancer or endometrial (uterine) diagnosed under the age of 50 or triple negative breast cancer diagnosed under the age of 60
- Multiple cancers in one person, either of same origin (such as two separate breast cancers) or of different origins (such as breast and ovarian cancer, or endometrial and colon cancer)
- Diagnosis of ovarian cancer, pancreatic cancer*, metastatic prostate cancer*, or male breast cancer at any age
- Multiple relatives diagnosed with the same or related cancers (including breast, ovarian, endometrial, pancreatic, and/or metastatic/aggressive prostate cancer) on the same side of the family and spanning multiple generations
- Ashkenazi Jewish ancestry
- Tumor testing which indicates an increased risk for a hereditary cancer syndrome (i.e. variant identified on tumor sequencing and or abnormal MSI/IHC)

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

*If this is the primary indication for testing, a more comprehensive panel specifically geared at this diagnosis is available

Genes Included on the Breast/Gyn 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 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

Lifetime Cancer and/or Tumor Risks

Gene	Lifetime Cancer and/or Tumor Risks*
<i>BRCA1</i>	Female breast (43-87%), Ovarian, including primary peritoneal and fallopian tube (39-63%), Prostate, Male breast (1.2%), Pancreatic (1-3%)
<i>BRCA2</i>	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
<i>CDH1</i>	Gastric-diffuse, Female breast-lobular (42-55%), Colorectal
<i>EPCAM**</i>	Colorectal (37-75%), Endometrial (12-57%), 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>MUTYH</i>	Colorectal (up to 80%), Small bowel (up to 4%), Gastrointestinal polyps
<i>NF1</i>	Neurofibromas, Optic nerve gliomas (15%), Pheochromocytomas (1-13%), Malignant peripheral nerve sheath tumors (6-16%), Brain tumors (2-3%), Female breast (up to 26%), Gastrointestinal stromal tumor (GIST)
<i>PALB2</i>	Female breast (33-53%), Male breast, Pancreatic (2-4%), Ovarian, Prostate
<i>PMS2**</i>	Colorectal (11-20%), Endometrial (12-26%), Ovarian, Gastric, Pancreatic, Biliary tract, Urinary tract-transitional cell, Small bowel, Brain, Sebaceous tumors, Prostate
<i>PTEN</i>	Female breast (25-85%), Thyroid (3-38%), Endometrial (5-28%), Colorectal, Renal, Melanoma, Gastrointestinal polyps, Lhermitte-Duclos disease
<i>STK11</i>	Female breast (up to 54%), Colorectal (39%), Pancreatic (11-36%), Gastric (29%), Ovarian tumors (21%), Lung (7-17%), Small bowel (13%), Cervical (10%), Testicular tumors (9%), Endometrial (9%), Gastrointestinal polyps
<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: approaches 100% in females, 73% in males

High-Risk Genes

	Gene	Lifetime Cancer and/or Tumor Risks*
Moderate-Risk Genes	ATM	Female breast (27-33%), Colorectal, Ovarian, Pancreatic, Prostate
	BRIP1	Ovarian, Female Breast, Prostate
	CHEK2	Female breast, Male breast, Colorectal, Gastric, Prostate, Renal, Thyroid
	RAD51C	Ovarian, Female breast, Prostate
	RAD51D	Ovarian, Female breast, Prostate
Newer Genes	BARD1	Female breast
	FANCC	Female breast
	FANCM	Female breast
	NBN	Female breast, Prostate
	POLD1	Colorectal, Endometrial, Colon polyps
	RECQL	Female breast

*Most commonly associated cancer/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



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:

- Breast awareness, including breast self-examination for both men and women
- Imaging exams, such as a MRI, mammography, CT and/or ultrasound
- Screening procedures, such as a colonoscopy
- Risk-reducing medications and/or surgeries

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

GeneDx
www.genedx.com/oncology

National Cancer Institute
www.cancer.gov

Breast and Gynecologic Cancer

Bright Pink
www.brightpink.org

Colon Cancer Alliance for Research and Education for Lynch Syndrome (CCARE)
www.fightlynch.org

Facing Our Risk of Cancer Empowered (FORCE)
www.facingourrisk.org

Find a Genetic Counselor

Canadian Association of Genetic Counsellors
www.cagc-accg.ca

National Society of Genetic Counselors
www.nsgc.org