

Colorectal Cancer Panel



Features of Hereditary Colorectal Cancer

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

- Colorectal or endometrial cancer diagnosed under 50 years of age
- Multiple colon polyps (especially ≥ 20 adenomas) at any age
- Tumor testing which indicates an increased risk for a hereditary cancer syndrome known as Lynch syndrome (e.g. microsatellite instability and/or lack of immunohistochemistry staining for a mismatch repair protein)
- Multiple cancers in one person either of the same origin (such as two separate colorectal cancers) or of different origin (such as colon and endometrial cancer in the same individual)
- Multiple relatives diagnosed with the same or related cancers (such as colon, endometrial, ovarian, urinary tract, gastric) on the same side of the family and spanning multiple generations

Genes Included on the Colorectal 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-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

Lifetime Cancer and/or Tumor Risks

	Gene	Lifetime Cancer and/or Tumor Risks*
High-Risk Genes	<i>APC</i>	Colorectal (up to 93%), Small bowel (4-12%), Gastric, Thyroid, Pancreatic, Brain, Liver, Desmoid tumors, Gastrointestinal polyps
	<i>BMPR1A</i>	Colorectal (40-50%), Gastric (up to 21% if gastric polyps), Small bowel, Pancreatic, Gastrointestinal polyps
	<i>CDH1</i>	Gastric (44-80%), Female breast (23-68%), Colorectal
	<i>EPCAM**</i>	Colorectal (69-75%), Endometrial (12-55%), Ovarian, Gastric, Pancreatic, Biliary tract, Urinary tract, Small bowel, Brain, Sebaceous tumors, Prostate
	<i>MLH1</i>	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
	<i>MSH2</i>	Colorectal (22-80%), Endometrial (31-61%), Ovarian (10-24%), Urinary tract (8-20%), Gastric (<1-9%), Pancreatic, Biliary tract, Small bowel, Brain, Sebaceous tumors, Prostate
	<i>MSH6**</i>	Colorectal (20-44%), Endometrial (16-71%), Ovarian (1-11%), Gastric, Pancreatic, Biliary tract, Urinary tract, Small bowel, Brain, Sebaceous tumors, Prostate
	<i>MUTYH*</i>	Colorectal (up to 80%), Small bowel (up to 4%), Endometrial, Gastrointestinal polyps
	<i>PMS2**</i>	Colorectal (11-20%), Endometrial (12-15%), Ovarian, Gastric, Pancreatic, Biliary tract, Urinary tract, Small bowel, Brain, Sebaceous tumors, Prostate
	<i>PTEN</i>	Female breast (25-85%), Thyroid (3-38%), Endometrial (5-28%), Colorectal, Renal, Melanoma, Gastrointestinal polyps
	<i>SMAD4</i>	Colorectal (40-50%), Gastric (up to 21% if gastric polyps), Small bowel, Pancreatic, Gastrointestinal polyps
	<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%), Sarcoma-bone and soft tissue, Brain, Hematologic malignancies, 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, Pancreatic, Prostate
	<i>CHEK2</i>	Female breast, Male breast, Colorectal, Gastric, Prostate, Thyroid
Newer-Risk Genes	<i>AXIN2</i>	Colorectal, Colon polyps
	<i>NTHL1*</i>	Colorectal, Colon polyps
	<i>POLD1</i>	Colorectal, Endometrial, Colon polyps
	<i>POLE</i>	Colorectal, Gastrointestinal polyps
	<i>SCG5/GREM1</i>	Colorectal, Colon polyps

*Most commonly associated cancer/tumors listed; lifetime risks provided when available. Risks relate to carriers of a single pathogenic variant with the exception of the *MUTYH* and *NTHL1* genes.

**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:

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

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

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

Resources

General

American Cancer Society
www.cancer.org

GeneDx
www.genedx.com/oncology

National Cancer Institute
www.cancer.gov

Colorectal Cancer

Colon Cancer Alliance
www.ccalliance.org

Fight Colorectal Cancer
www.fightcolorectalcancer.org

Hereditary Colon Cancer Takes Guts
www.hcctakesguts.org

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

Find a Genetic Counselor

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

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 zebras@genedx.com • www.genedx.com

