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. This includes:

- Colon cancer or endometrial cancer under 50 years of age
- Multiple cancers in one person, either of the same origin (such as two separate colon cancers) or of different origins (such as colon and endometrial cancer)
- Diagnosis of multiple colon polyps at any age
- 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

The genes included in the Colorectal Cancer Panel are: APC, ATM, AXIN2, BMPR1A, CDH1, CHEK2, EPCAM, MLH1, MSH2, MSH6, MUTYH, PMS2, POLD1, POLE, PTEN, SCG5/GREM1, SMAD4, STK11, and TP53.

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

Lifetime Cancer and/or Tumor Risks

<table>
<thead>
<tr>
<th>Gene</th>
<th>Lifetime Cancer and/or Tumor Risks*</th>
</tr>
</thead>
<tbody>
<tr>
<td>APC</td>
<td>Colorectal (up to 93%), Small bowel (4-12%), Gastric, Thyroid, Pancreatic, Brain, Liver, Desmoid tumors, Gastrointestinal polyps</td>
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<tr>
<td>BMPR1A</td>
<td>Colorectal (40-50%), Gastric (up to 21% if gastric polyps), Small bowel, Pancreatic, Gastrointestinal polyps</td>
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<tr>
<td>CDH1</td>
<td>Gastric cancer (40-83%), Female breast (39-52%), Colon</td>
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<tr>
<td>EPCAM**</td>
<td>Colorectal (69-75%), Endometrial (12-55%), Ovarian, Gastric, Pancreatic, Biliary tract, Urinary tract, Small bowel, Brain, Sebaceous tumors</td>
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<tr>
<td>MLH1</td>
<td>Colorectal (22-80%), Endometrial (31-54%), Ovarian (13-20%), Gastric (6-20%), Urinary tract (1-3%), Biliary tract, Small bowel, Brain, Sebaceous tumors</td>
</tr>
<tr>
<td>MSH2</td>
<td>Colorectal (22-80%), Endometrial (31-61%), Ovarian (10-24%), Urinary tract (8-10%), Gastric (&lt;1-9%), Biliary tract, Small bowel, Brain, Sebaceous tumors</td>
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<tr>
<td>MSH6**</td>
<td>Colorectal (20-44%), Endometrial (44%), Ovarian (1-11%), Gastric, Pancreatic, Biliary tract, Urinary tract, Small bowel, Brain, Sebaceous tumors</td>
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<tr>
<td>MUTYH*</td>
<td>Colorectal (up to 80%), Small bowel (up to 4%), Endometrial, Gastrointestinal polyps</td>
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<tr>
<td>PMS2**</td>
<td>Colorectal (11-20%), Endometrial (12-15%), Ovarian, Gastric, Pancreatic, Biliary tract, Urinary tract, Small bowel, Brain, Sebaceous tumors</td>
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<tr>
<td>PTEN</td>
<td>Female breast (25-85%), Thyroid (3-38%), Endometrial (5-28%), Colon, Renal, Melanoma, Gastrointestinal polyps</td>
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<tr>
<td>SMAD4</td>
<td>Colorectal (40-50%), Gastric (up to 21% if gastric polyps), Small bowel, Pancreatic, Gastrointestinal polyps</td>
</tr>
<tr>
<td>STK11</td>
<td>Female breast (45-54%), Colorectal (39%), Pancreatic (11-36%), Gastric (29%), Ovarian tumors (21%), Lung (15-17%), Small bowel (13%), Cervical (10%), Testicular tumors (8%), Endometrial (8%), Gastrointestinal polyps</td>
</tr>
<tr>
<td>TP53</td>
<td>Female breast, Sarcoma-bone and soft tissue, Brain, Hematologic malignancies, Adrenocortical carcinoma, among others. Overall risk for cancer: nearly 100% in females, 70% in males</td>
</tr>
</tbody>
</table>

*Lifetime risks are 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 indicates a genetic variant (change) was identified in a specific gene that 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 that there is a 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 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](http://www.cancer.org)
Colon Cancer Alliance:  [www.ccalliance.org](http://www.ccalliance.org)
C3 Colorectal Cancer Coalition:  [www.fightcolorectalcancer.org](http://www.fightcolorectalcancer.org)
GeneDx:  [www.oncogenedx.com](http://www.oncogenedx.com)
Hereditary Colon Cancer Takes Guts:  [www.hcctakesguts.org](http://www.hcctakesguts.org)
National Cancer Institute:  [www.cancer.gov/cancertopics/genetics](http://www.cancer.gov/cancertopics/genetics)
National Society of Genetic Counselors:  [www.nsgc.org](http://www.nsgc.org)