

# Comprehensive Common Cancer Panel

## Features of Hereditary Cancer Syndromes

Your healthcare provider will determine if genetic testing is medically necessary for you. Genetic testing with the Comprehensive Common Cancer Panel may be appropriate if your personal and/or family history is suggestive of a hereditary predisposition to cancer. This includes:

- Cancer at a young age, such as breast, colon, or renal cancer
- Multiple cancers in one person, either of the same origin (such as two separate colon cancers) or of different origins (such as breast cancer and ovarian cancer)
- Diagnosis of ovarian, pancreatic, male breast or metastatic prostate cancer
- Multiple relatives diagnosed with the same or related cancers on the same side of the family and spanning multiple generations

## Genes Included on the Comprehensive Common 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 (up to 3%), Pancreatic, Brain, Liver, Desmoid tumors, Gastrointestinal polyps
	<i>BMPR1A</i>	Colorectal (up to 68%), Gastric (up to 21% if gastric polyps), Small bowel, Pancreatic, Gastrointestinal polyps
	<i>BRCA1</i>	Female breast (55-87%), Ovarian (39-59%), Prostate, Male breast, Pancreatic, Fallopian tube, Primary peritoneal, Endometrial
	<i>BRCA2</i>	Female breast (33-84%), Prostate (up to 34%), Ovarian (11-27%), Pancreatic (up to 7%), Male breast (up to 7%), Melanoma, Fallopian tube, Primary peritoneal, Endometrial
	<i>CDH1</i>	Gastric cancer, Female breast (39-55%), Colorectal
	<i>CDKN2A</i>	Melanoma (28-76%), Pancreatic (17%), Brain
	<i>EPCAM</i> ,** <i>MLH1</i> , <i>MSH2</i> , <i>MSH6</i> ,** <i>PMS2</i> **	Colorectal (11-75%), Endometrial (12-71%), Ovarian (1-24%), Gastric (<1-20%), Urinary tract (1-20%), Pancreatic (1-4%), Biliary tract (2-3%), Small bowel (1-12%), Brain, Sebaceous tumors, Prostate
	<i>FH</i>	Renal (10-19%), Paraganglioma/Pheochromocytoma, Leiomyomas-skin and uterine
	<i>FLCN</i>	Renal cancer and tumors (6-41%)
	<i>MUTYH</i> *	Colorectal (up to 80%), Small bowel (up to 4%), Endometrial, Gastrointestinal polyps
	<i>NF1</i>	Neurofibromas, Brain tumors (2-15%), Pheochromocytomas (1-13%), Malignant peripheral nerve sheath tumors (6-16%), Female breast, Gastrointestinal stromal tumor (GIST)
	<i>PALB2</i>	Female breast (up to 58%), Male breast, Pancreatic, Ovarian, Prostate
	<i>PTEN</i>	Female breast (25-85%), Thyroid (3-38%), Endometrial (5-28%), Colorectal, Renal, Melanoma, Gastrointestinal polyps, Lhermitte-Duclos disease
	<i>SDHB</i>	Paraganglioma/Pheochromocytoma, Renal, Gastrointestinal stromal tumor (GIST)
	<i>SDHD</i>	Paraganglioma/Pheochromocytoma, Renal, Gastrointestinal stromal tumor (GIST)
	<i>SMAD4</i>	Colorectal (up to 68%), 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
	<i>TSC1, TSC2</i>	Renal cancer (5%) and tumors, Benign central nervous system tumors, Hamartomatous tumors - cardiac rhabdomyomas and angiomyolipomas
	<i>VHL</i>	Renal (up to 69%), Hemangioblastomas (50-80%), Pheochromocytomas (11-19%), Pancreatic neuroendocrine tumors (8-17%), Endolymphatic sac tumors (up to 10%)
Moderate-Risk Genes	<i>ATM</i>	Female breast (27-33%), Colorectal, Ovarian, Pancreatic, Prostate
	<i>BRIP1</i>	Ovarian, Prostate
	<i>CHEK2</i>	Female breast, Male breast, Colorectal, Gastric, Prostate, Renal, Thyroid
	<i>RAD51C, RAD51D</i>	Ovarian, Female breast, Prostate
Newer-Risk Genes	<i>AXIN2</i>	Colorectal, Colon polyps
	<i>BAP1</i>	Renal, Melanoma, Mesothelioma, Basal cell carcinoma
	<i>BARD1</i>	Female breast, Ovarian

Please see reverse side for remainder of Newer-Risk genes

	Gene	Lifetime Cancer and/or Tumor Risks*
Newer-Risk Genes	<i>CDK4</i>	Melanoma
	<i>FANCC</i>	Female breast
	<i>FANCM</i>	Female breast
	<i>HOXB13</i>	Prostate
	<i>MET</i>	Renal
	<i>MITF</i>	Renal, Melanoma
	<i>NBN</i>	Female breast, Non-Hodgkin lymphoma, Prostate
	<i>NTHL1*</i>	Colorectal, Colon polyps
	<i>POLD1</i>	Colorectal, Endometrial, Colon polyps
	<i>POLE</i>	Colorectal, Colon polyps
	<i>POT1</i>	Melanoma, Brain
	<i>RECQL</i>	Female breast
	<i>SCG5/ GREM1</i>	Colorectal, Colon polyps
	<i>SDHC</i>	Paranglioma/Pheochromocytoma, Renal, Gastrointestinal stromal tumor (GIST)

\* 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:

- Clinical exams, such as skin or eye exams
- 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](http://www.cancer.org)

GeneDx  
[www.genedx.com/oncology](http://www.genedx.com/oncology)

National Cancer Institute  
[www.cancer.gov](http://www.cancer.gov)

### Find a Genetic Counselor

Canadian Association of Genetic  
 Counsellors  
[www.cagc-accg.ca](http://www.cagc-accg.ca)

National Society of Genetic Counselors  
[www.nsgc.org](http://www.nsgc.org)

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