Comprehensive Common Cancer Panel

Features of Hereditary Cancer Syndromes

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 certain rare cancers, such as ovarian or male breast 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	*APC*	Colorectal (up to 93%), Small bowel (4-12%), Gastric, Thyroid, Pancreatic, Brain, Liver, Desmoid tumors, Gastrointestinal polyps
	BMPR1A	Colorectal (40-50%), Gastric (up to 21% if gastric polyps), Small bowel, Pancreatic, Gastrointestinal polyps
	BRCA1	Female breast (55-87%), Ovarian (39-59%), Prostate, Male breast, Pancreatic, Fallopian tube, Primary peritoneal, Endometrial
	BRCA2	Female breast (32.6-84%), Prostate (up to 34%), Ovarian (11-27%), Pancreatic (5-7%), Male breast (4-7.1%), Melanoma, Fallopian tube, Primary peritoneal, Endometrial
	CDH1	Gastric cancer (44-80%), Female breast (23-68%), Colorectal
	CDKN2A	Melanoma (28-76%), Pancreatic (14%)
	EPCAM, MLH1, MSH2, MSH6, PMS2	Colorectal (11-80%), Endometrial (12-71%), Ovarian (1-24%), Gastric (<1-20%), Urinary tract (1-20%), Pancreatic, Biliary tract, Small bowel, Brain, Sebaceous tumors, Prostate 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*
	FH	Renal (10-19%), Paraganglioma/Pheochromocytoma, Leiomyomas-skin and uterine
	FLCN	Renal cancer and tumors (6-41%)
	*MUTYH**	Colorectal (up to 80%), Small bowel (up to 4%), Endometrial, Gastrointestinal polyps
	NF1	Neurofibromas, Brain tumors (2-15%), Pheochromocytomas (1-13%), Sarcomas (6-13%), Female breast, Gastrointestinal stromal tumor (GIST)
	PALB2	Female breast (up to 58%), Male breast, Pancreatic, Ovarian, Prostate
	PTEN	Female breast (25-85%), Thyroid (3-38%), Endometrial (5-28%), Colorectal, Renal, Melanoma, Gastrointestinal polyps
	SDHB	Paraganglioma/Pheochromocytoma (77%), Renal, Gastrointestinal stromal tumor (GIST)
	SDHD	Paraganglioma/Pheochromocytoma (up to 86%), Renal, Gastrointestinal stromal tumor (GIST)
	SMAD4	Colorectal (40-50%), Gastric (up to 21% if gastric polyps), Small bowel, Pancreatic, Gastrointestinal polyps
	STK11	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
	TP53	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
	TSC1, TSC2	Renal cancer (5%) and tumors, Benign central nervous system tumors, Hamartomatous tumors
	VHL	Renal (up to 69%), Pancreatic neuroendocrine tumors (up to 17%), Hemangioblastomas, Pheochromocytomas
Moderate-Risk Genes	*ATM*	Female breast (27-33%), Colorectal, Pancreatic, Prostate
	BRIP1	Ovarian, Prostate
	CHEK2	Female breast, Male breast, Colorectal, Gastric, Prostate, Thyroid
	RAD51C, RAD51D	Ovarian, Female breast, Prostate
Newer-Risk Genes	*AXIN2*	Colorectal, Colon polyps
	BAP1	Renal, Melanoma, Mesothelioma, Basal cell carcinoma
	BARD1	Female breast, Ovarian
	CDK4	Melanoma, Non-melanoma skin cancer, Pancreatic
	FANCC	Female breast
	HOXB13	Prostate

Please see reverse side for remainder of Newer-Risk genes

	Gene	Lifetime Cancer and/or Tumor Risks*
Newer-Risk Genes	*MET*	Renal
	MITF	Renal, Melanoma
	NBN	Female breast, Non-Hodgkin lymphoma, Prostate
	*NTHL1**	Colorectal, Colon polyps
	POLD1	Colorectal, Endometrial, Colon polyps
	POLE	Colorectal, Gastrointestinal polyps
	POT1	Melanoma
	RECQL	Female breast
	SCG5/GREM1	Colorectal, Colon polyps
	SDHC	Paraganglioma/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.

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

GeneDx
www.genedx.com/oncology

National Cancer Institute
www.cancer.gov

Find a Genetic Counselor

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

National Society of Genetic Counselors
www.nsgc.org

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