Pancreatic Cancer Panel

Features of Hereditary Pancreatic Cancer

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

- Pancreatic cancer diagnosed at an early age
- Multiple cancers in one person (such as pancreatic cancer and breast cancer)
- Multiple relatives diagnosed with pancreatic cancer and/or related cancers (including breast, colon, melanoma etc.) on the same side of the family and spanning multiple generations

Genes Included on the Pancreatic 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
	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
	CDKN2A	Melanoma (28-76%), Pancreatic (14%)
	*EPCAM***	Colorectal (69-75%), Endometrial (12-55%), Ovarian, Gastric, Pancreatic, Biliary tract, Urinary tract, Small bowel, Brain, Sebaceous tumors, Prostate
	MLH1	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
	MSH2	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
	*MSH6***	Colorectal (20-44%), Endometrial (16-71%), Ovarian (1-11%), Gastric, Pancreatic, Biliary tract, Urinary tract, Small bowel, Brain, Sebaceous tumors, Prostate
	PALB2	Female breast (up to 58%), Male breast, Pancreatic, Ovarian, Prostate
	*PMS2***	Colorectal (11-20%), Endometrial (12-15%), Ovarian, Gastric, Pancreatic, Biliary tract, Urinary tract, Small bowel, Brain, Sebaceous tumors, Prostate
	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
	VHL	Renal (up to 69%), Pancreatic neuroendocrine tumors (up to 17%), Hemangioblastomas, Pheochromocytomas
Moderate-Risk Genes	*ATM*	Female breast (27-33%), Colorectal, Pancreatic, Prostate
Newer-Risk Genes	*CDK4*	Melanoma, Non-melanoma skin cancer, Pancreatic

*Most commonly associated cancer/tumors listed; lifetime risks provided when available. Risks relate to carriers of a single pathogenic variant.

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

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

Pancreatic Cancer

Pancreatic Cancer Action Network
www.pancan.org

Pancreatic Cancer Alliance
www.pancreaticalliance.org

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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