

Melanoma Panel



Features of Hereditary Melanoma

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

- Personal history of melanoma (especially multiple melanomas) and/or a personal or family history of related cancers (such as melanoma, pancreatic, mesothelioma, or renal cancer)
- Multiple relatives diagnosed with the same or related cancers (including melanoma, pancreatic, mesothelioma, or renal cancer) on the same side of the family and spanning multiple generations

Genes Included on the Melanoma 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
- 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>BRCA2</i>	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-serous
	<i>CDKN2A</i>	Melanoma (28-76%), Pancreatic (14%)
	<i>PTEN</i>	Female breast (25-85%), Thyroid (3-38%), Endometrial (5-28%), Colorectal, Renal, Melanoma, Gastrointestinal polyps, Lhermitte-Duclos disease
	<i>RB1</i>	Retinoblastoma (greater than 90%), Brain-pineoblastoma (5-10%), Soft tissue sarcoma-leiomyosarcoma and rhabdomyosarcoma, Osteosarcoma, Leukemia, Melanoma
	<i>TP53</i>	Female breast (85%), Soft tissue sarcoma, Osteosarcoma, Brain, Hematologic malignancies, Adrenocortical carcinoma, among others. Overall risk for cancer: up to 95% in females, 88% in males
Newer-Risk Genes	<i>BAP1</i>	Renal, Melanoma, Mesothelioma, Basal cell carcinoma
	<i>CDK4</i>	Melanoma, Non-melanoma skin cancer, Pancreatic
	<i>MITF</i>	Renal, Melanoma
	<i>POT1</i>	Melanoma

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

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 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
- Imaging exams, such as a MRI, CT and/or ultrasound
- Lifestyle changes, such as sun protection strategies

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

National Cancer Institute
www.cancer.gov

GeneDx
www.genedx.com/oncology

Skin Cancer

American Academy of Dermatology
www.aad.org

Skin Cancer Foundation
www.skincancer.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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