

# PGL/PCC Panel



## Features of Hereditary Paragangliomas (PGL) and Pheochromocytomas (PCC)

Paragangliomas and pheochromocytomas are tumors found in neuroendocrine tissue. These tumors may secrete excess adrenaline (in the form of epinephrine and norepinephrine) and most are not malignant (cancerous).

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

- A personal and/or family history of one or more paragangliomas or pheochromocytomas
- A pattern of cancer in which individuals with similar or related cancers (see table below) are on one side of the family and spanning multiple generations

## Genes Included on the PGL/PCC 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>FH</i>	Renal (10-19%), Paraganglioma/Pheochromocytoma, Leiomyomas-skin and uterine
	<i>MEN1</i>	Parathyroid tumors (95%), Pancreatic neuroendocrine tumors, Pituitary tumors, Pheochromocytomas and other neuroendocrine tumors
	<i>NF1</i>	Neurofibromas, Brain tumors (2-15%), Pheochromocytomas (1-13%), Sarcomas (6-13%), Female breast, Gastrointestinal stromal tumor (GIST)
	<i>RET</i>	Thyroid (greater than 90%), Pheochromocytoma (up to 50%), Hyperparathyroidism (up to 30%)
	<i>SDHB</i>	Paraganglioma/Pheochromocytoma (77%), Renal, Gastrointestinal stromal tumor (GIST)
	<i>SDHD</i>	Paraganglioma/Pheochromocytoma (up to 86%), Renal, Gastrointestinal stromal tumor (GIST)
	<i>VHL</i>	Renal (up to 69%), Pancreatic neuroendocrine tumors (up to 17%), Hemangioblastomas, Pheochromocytomas
Newer-Risk Genes	<i>MAX</i>	Paraganglioma/Pheochromocytoma
	<i>SDHA</i>	Paraganglioma/Pheochromocytoma, Gastrointestinal stromal tumor (GIST)
	<i>SDHAF2</i>	Paraganglioma/Pheochromocytoma
	<i>SDHC</i>	Paraganglioma/Pheochromocytoma, Renal, Gastrointestinal stromal tumor (GIST)
	<i>TMEM127</i>	Paraganglioma/Pheochromocytoma

\*Most commonly associated cancer/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 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:

- Blood or urine analysis
- Imaging exams, such as a MRI, CT and/or ultrasound

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)

### PGL/PCC Resources

Pheo Para Troopers  
[www.pheoparatroopers.org](http://www.pheoparatroopers.org)

### 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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