ALBERTA PRECISION LABORATORIES
Leaders in Laboratory Medicine

Paraganglioma/Pheochromocytoma (PGL/PCC) Predisposition Panel: Information for Ordering Providers

Paragangliomas and pheochromocytomas may occur in patients with several different inherited cancer susceptibility syndromes, including PGL/PCC syndrome, multiple endocrine neoplasia type 2, von Hippel–Lindau disease (*VHL*), and neurofibromatosis type 1 (*NF1*).[1] Hereditary cancers syndromes involving PGL/PCC are typically inherited in an autosomal dominant manner. The clinical findings associated with PGL/PCC can vary greatly within a family, despite the fact that affected individuals within a given family carry the same pathogenic variant.

Individuals who carry a pathogenic variant in a tumour predisposition gene have an increased risk of developing certain cancers compared to the general population. Cancer risks depend on the gene(s) in which the variant(s) is identified. These individuals are eligible for increased cancer screening and/or risk reducing surgeries and therapeutic interventions. In addition, results may influence treatment plans for individuals with cancer.

Indications for testing

Any patient with a pheochromocytoma or paraganglioma is eligible for testing. Patients with a personal and/or family history consistent with a pheochromocytoma/paraganglioma syndrome should be referred to a clinical geneticist for assessment.

Ordering privileges

Please refer to the APL Test Directory (http://ahsweb.ca/lab/apl-td-lab-test-directory) for specific ordering restrictions.

Paraganglioma/Pheochromocytoma NGS panel

Gene(s)	Associated cancers and/or clinical features[1,2]	Associated Hereditary Syndrome[1]
SDHA, SDHB, SDHC, SDHD SDHAF2	Head and neck paragangliomas, extra-adrenal paragangliomas and/or pheochromocytomas, GISTs and renal clear cell carcinoma (rare)	Hereditary paraganglioma/ pheochromocytoma syndromes
MAX, TMEM127	Susceptibility to paraganglioma/pheochromocytoma	
RET	Medullary thyroid carcinoma, pheochromocytoma, parathyroid adenoma or hyperplasia, mucosal neuromas of the lips and tongue, ganglioneuromatosis of the gastrointestinal tract	Multiple endocrine neoplasia, type 2 (includes MEN2A and MEN2B)
	Medullary thyroid carcinoma	Familial medullary thyroid cancer
VHL	Renal tumors, adrenal pheochromocytoma, neuroendocrine tumors and hemangioblastomas of the brain, spinal cord, and retina. The lifetime risk of renal cell carcinoma is approximately 25%-70%.	Von Hippel Lindau syndrome
FH	Renal cancer (20% lifetime risk), cutaneous and uterine leiomyomas/fibroids (~98% lifetime risk).	Hereditary leiomyomatosis and renal cell carcinoma
NF1	Multiple café au lait spots, axillary and inguinal freckling, multiple cutaneous neurofibromas, and Lisch nodules. Learning disabilities may be present. Pheochromocytomas are rare in NF1 overall; however, they occur in 20%-50% of individuals with NF1 and hypertension.	Neurofibromatosis, type 1

Associated Disorders[1,2]

Some of the genes on this panel are associated with other rare disorders including:

Fumarate Hydratase Deficiency is an autosomal recessive disorder caused by pathogenic variants in *FH*. Individuals with fumarate hydratase deficiency (two pathogenic *FH* variants) have brain anomalies, epilepsy, dysmorphic features, and global developmental delay. Most affected individuals die in early childhood.

Mitochondrial complex deficiencies are rare autosomal recessive conditions with highly variable phenotypes. Pathogenic variants have been reported in *SDHA, SDHB,* and *SDHD.*

When can I expect results?

Results may take up to 4 months.

How are results reported?

Results are sent to the ordering provider and available in Netcare and Connect Care.

Contact Information

Genetic Counsellors, Genetics & Genomics
Calgary: 403-955-3097

Requisition forms, contact information and other resources can be found at:

http://ahsweb.ca/lab/if-lab-genetics-and-genomics

References

1. Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2018 [cited 2017 Dec]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1116/

2. MedlinePlus [Internet]. Bethesda (MD): National Library of Medicine (US); [cited 2022 Sept]. Available from: https://medlineplus.gov/;