SDHB-related Hereditary Paraganglioma-Pheochromocytoma Syndrome: SDHB Gene Sequencing

<table>
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<th>Test Code: SDHB</th>
<th>Turnaround time: 4 weeks</th>
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<td>CPT Codes: S1479 x1</td>
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**Condition Description**

Hereditary paraganglioma-pheochromocytoma (PGL/PCC) syndrome is an autosomal dominant condition characterized by paragangliomas and pheochromocytomas. Paragangliomas are tumors (usually benign) that arise from neuroendocrine tissues along the paravertebral axis. They are classified as sympathetic or parasympathetic depending on their origin. Sympathetic PGLs are usually located in the chest, abdomen, or pelvis. Parasympathetic PGLs are usually in the head or neck. Pheochromocytomas are paragangliomas that are confined to the adrenal medulla and are catecholamine-secreting. Hereditary PGL/PCC syndrome should be considered in individuals with tumors that are multiple, multifocal, recurrent, and have an onset before 40 years of age.

There are four genes known to cause hereditary PGL/PCC syndrome; SDHD, SDHC, SDHB, and SDHAF2. The SDHD, SDHC, and SDHB genes encode three of the four subunits of the mitochondrial enzyme succinate dehydrogenase (SDH) also known as mitochondrial complex II. The SDHAF2 gene is involved with the assembly of the SDH complex.

Mutations in the SDHB gene (1p36.13) are associated with extra-adrenal sympathetic paragangliomas that have a greater likelihood of being malignant. About 20-25% of hereditary PGL/PCC syndrome cases are due to mutations in the SDHB gene. Sequencing analysis will detect approximately 70-90% of disease-causing mutations. About 10% of mutations in the SDHB gene are deletions. The penetrance of hereditary PGL/PCC in individuals with SDHB mutations is approximately 77% by 50 years of age.

Please note that mutations in the SDHB gene can cause paraganglioma and gastric stromal sarcoma, also known as Carney-Stratakis syndrome.

This test is for sequencing of the SDHB gene only.

**References:**

- GeneReviews
- OMIM #185470: SDHB gene
- OMIM #115310: Hereditary PGL/PCC syndrome
- OMIM #P056564: Paraganglioma and gastric stromal sarcoma

**Genes**

SDHB

**Indications**

This test is indicated for:

- Confirmation of a clinical diagnosis of hereditary PGL/PCC syndrome.

**Methodology**

PCR amplification of 8 exons contained in the SDHB gene is performed on the patient's genomic DNA. Direct sequencing of amplification products is performed in both forward and reverse directions, using automated fluorescence dideoxy sequencing methods. The patient's gene sequences are then compared to a normal reference sequence. Sequence variations are classified as mutations, benign variants unrelated to disease, or variations of unknown clinical significance. Variants of unknown clinical significance may require further studies of the patient and/or family members. This assay does not interrogate the promoter region, deep intronic regions, or other regulatory elements, and does not detect large deletions.

**Detection**

Clinical Sensitivity: Sequence analysis will detect 70-90% of mutations in the SDHB gene. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical and/or biochemical phenotype.

Analytical Sensitivity: ~99%

**Specimen Requirements**

Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:
In EDTA (purple top) tube:
Infants (2 years): 3-5 ml
Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Type: Saliva**

Specimen Requirements:

Oragene\textsuperscript{TM} Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Related Tests**

- Custom diagnostic mutation analysis (KM) is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- Prenatal testing is available only for known familial mutations to individuals who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.