Paraganglioma-Pheochromocytoma: Sequencing Panel

**Test Code:** MM203  
**Turnaround time:** 4 weeks  
**CPT Codes:** 81404 x1, 81405 x1, 81406 x1, 81479 x1

**Condition Description**

The estimated prevalence of pheochromocytomas (PHEOs) is 1:4500 and 1:1700 for paragangliomas (PGLs), with an annual incidence of 3 to 8 cases per 1 million a year in the general population. The age of onset for PGL individuals is between 15 and 45 years of age, with early symptoms typically consisting of local swelling and cranial nerve injury. Although the tumors are benign in nature, only 4-16% shows malignant degeneration, giving rise to swelling causing cranial nerve damage, facial asymmetry, deafness, or hoarseness. PGLs are composed of pheochromocytomas (PCC, fPGLs, PH, or PHEOs) and extra-adrenal PGLs, and are characterized by the tumor production and secretion of catecholamines arising from the adrenal medulla (pheochromocytoma) or sympathetic nervous ganglia. Diagnosis for PGLs is determined by a biochemical assay, tumor location, function, inheritance, and gene mutation. If the tumor has metastasized the overall five year survival rate in patients is 40-72%. Size and location of the primary tumor has been correlated with risk for metastasis and the duration of survival.

**Reference:**

**Genes**

**FH, MAX, RET, SDHAF2, SDHB, SDHC, SDHD, TMEM127, VHL**

**Indications**

The test is indicated for:
- Individuals with a clinical or suspected diagnosis of pheochromocytomas and paragangliomas.

**Methodology**

**Next Generation Sequencing:** In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

**Detection**

**Next Generation Sequencing:** Clinical Sensitivity: Unknown. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions/duplications will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical/biochemical phenotype.

**Analytical Sensitivity:** ~99%.

**Specimen Requirements**

Submit only 1 of the following specimen types

**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: Ship sample at room temperature with overnight delivery.

**Type: Isolated DNA**

Specimen Requirements:

In microtainer: 60 ug

Isolation using the Qiagen™ Puregene kit for DNA extraction is recommended.
Specimen Collection and Shipping: Refrigerate until time of shipment in 100 ng/μl of TE buffer. Ship sample at room temperature with overnight delivery.

**Special Instructions**

This test is for germline mutation analysis. DNA isolated from FFPE tumor samples is not suitable for this test.

**Related Tests**

- Hereditary Cancer Syndrome: Sequencing Panel.
- Paraganglioma-Pheochromocytoma: Deletion/Duplication Panel.