### Mabry Syndrome: Sequencing Panel

| Test Code: MM670 | Turnaround time: 6 weeks | CPT Codes: 81479 x1 |

#### Condition Description

Mabry syndrome is a rare genetic condition characterized by hyperphosphatasia (persistent elevation of alkaline phosphatase in the blood), moderate- to severe intellectual disability, and delayed development. The clinical spectrum may also consist of seizures, hypotonia, nail hypoplasia, brachytelephalangy (shortened bones at the ends of fingers), distinctive facial features, and abnormalities of the digestive system. A variation of signs and symptoms is observed among individuals with this syndrome.

Mabry syndrome is inherited an autosomal recessive manner. Genetic changes in the *PIGV*, *PIGY*, *PIGO*, *PIGW*, *PGAP2*, or *PGAP3* genes cause Mabry syndrome, also known as hyperphosphatasia with mental retardation syndrome. The prevalence of Mabry syndrome is currently unknown; however, more than 20 cases have been reported in the scientific literature.

#### References:

1. OMIM. Hyperphosphatasia with Mental Retardation syndromes.

#### Genes

*PGAP2*, *PGAP3*, *PIGO*, *PIGV*, *PIGW*, *PIGY*

#### Indications

This test is indicated for:

- Individuals with a clinical or suspected diagnosis of Mabry syndrome.

#### 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

* 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: Ship sample at room temperature with overnight delivery.

**Type: Isolated DNA**
Specimen Requirements:

In microtainer: 60 ug.

Isolation using the QiagenTM Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping: Refrigerate until time of shipment in 100 ng/ul of TE buffer. Ship sample at room temperature with overnight delivery.