### Condition Description

Myoglobinuria is the presence of myoglobin in the urine, which can be caused by recurrent attacks of rhabdomyolysis. The onset of the episodes occurs in early childhood and occur after a febrile illness. Features during the episodes include generalized weakness, myalgia, dark urine, and the inability to walk. Early development and development between episodes is normal.

Acute recurrent myoglobinuria is inherited in an autosomal recessive manner. Zeharia et al. (2008) identified an apparently homozygous nonsense mutation in the LPIN1 gene (2p25.1) of three affected family members. This mutation was not seen in 166 control individuals. Five additional mutations in the LPIN1 gene were identified in four of 22 patients with recurrent rhabdomyolysis.

References:
- OMIM #605518: LPIN1 gene
- OMIM #268200: Myoglobinuria, acute recurrent, autosomal recessive

### Indications

This test is indicated for:
- Confirmation of a clinical diagnosis of acute recurrent, autosomal recessive, myoglobinuria.
- Carrier testing in adults with a family history of acute recurrent, autosomal recessive, myoglobinuria.

### 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**

Clinical Sensitivity: Zeharia et al. (2008) identified five mutations in the LPIN1 gene in four of 22 patients with recurrent rhabdomyolysis. 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: Ship sample 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.