The human LPIN1 gene encompasses 20 exons and is located at 2p25.1. The LPIN1 encoded by this gene plays important roles in controlling the metabolism of fatty acids at different levels, acts as a magnesium-dependent phosphatidate phosphatase enzyme which catalyzes the conversion of phosphatidic acid to diacylglycerol during triglyceride, phosphatidylcholine and phosphatidylethanolamine biosynthesis in the reticulum endoplasmic membrane, and also acts as a nuclear transcriptional coactivator for PPARGC1A/PPARA to modulate lipid metabolism gene expression. Mutations in this gene are associated with metabolic syndrome, type 2 diabetes and autosomal recessive acute recurrent myoglobinuria (ARARM) characterized by recurrent attacks of rhabdomyolysis (necrosis or disintegration of skeletal muscle) associated with muscle pain and weakness and followed by excretion of myoglobin in the urine. LPIN1 mutations demonstrate autosomal recessive inheritance with a broad range of clinical severity both within and between families. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for LPIN1 mutations. Individuals are tested by DNA sequencing of the coding exons of the LPIN1 gene. We strongly recommend initial testing of a clearly affected individual, if available, in order to provide the greatest test sensitivity and clearest interpretation of results for subsequent family members. Genetic counseling is recommended for all individuals.

**REASONS FOR REFERRAL**

Molecular confirmation of the diagnosis of autosomal recessive acute recurrent myoglobinuria (ARARM) and the association of metabolic syndrome and type 2 diabetes.

**METHODOLOGY**

Genomic DNA is analyzed for LPIN1 mutations by DNA sequencing of the coding exons of the LPIN1 gene, as well as the exon/intron junctions and a portion of the 5’ and 3’ untranslated region. Patient DNA is sequenced in both the forward and reverse orientations. If a mutation is identified, additional family members are analyzed only for the familial mutation by automatic fluorescent DNA sequencing.

**SERVICE FEES**

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<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
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<td>Index Case (Male or Female)</td>
<td>$1200 per sample</td>
<td>81406</td>
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<tr>
<td>Additional Family Members</td>
<td>$300 per sample; Known familial mutation only</td>
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**SENSITIVITY**

DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 1-20 of LPIN1.

**SPECIMEN REQUIREMENTS**

- **Blood (preferred):** EDTA (purple-top) tubes: 
  - **Adult:** 5 cc
  - **Child:** 5 cc
  - **Infant:** 2-3 cc
- **Tissue:** Frozen (preferred), RNAlater
- **Other Body Fluids and Formalin-fixed, Paraffin-embedded Tissue:** Call to inquire