The human *LIPI* gene encodes 481-amino-acid lipase I and encompasses 10 exons. It is located at 21q11.2. The lipase I contains a hydrophobic leader sequence with a putative cleavage site, a central lipase consensus sequence (GxSxG), a central 12-amino acid lipase lid sequence, and several conserved cysteines. The GxSxG sequence includes the active site Ser159, which forms a putative catalytic triad with Asp183 and His258. Mutations in this gene cause familial hypertriglyceridemia (FHTR), a common inherited disorder in which the concentration of very low density lipoprotein (VLDL) is elevated in the plasma. This disease leads to increased risk of heart disease, obesity, and pancreatitis. *LIPI* mutations demonstrate autosomal dominant 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 *LIPI* mutations. Individuals are tested by DNA sequencing of the coding exons of the *LIPI* 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 familial hypertriglyceridemia (FHTR).

### METHODOLOGY

Genomic DNA is analyzed for *LIPI* mutations by DNA sequencing of the coding exons of the *LIPI* 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>
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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 1-10 of *LIPI*.

### 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