The human ANGPTL3 gene encodes a product containing 460 amino acids and encompasses 7 exons. It is located at 1p31.3. The ANGPTL3 protein is expressed predominantly in the liver, and is further processed into an N-terminal coiled-coil domain-containing chain and a C-terminal fibrinogen chain. The N-terminal chain is important for lipid metabolism, while the C-terminal chain may be involved in angiogenesis. Mutations in this gene have been associated with familial hypobetalipoproteinemia type 2. ANGPTL3 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 ANGPTL3 mutations. Individuals are tested by DNA sequencing of the coding exons of the ANGPTL3 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 familial hypobetalipoproteinemia type 2.

**METHODOLOGY**

Genomic DNA is analyzed for ANGPTL3 mutations by DNA sequencing of the coding exons of the ANGPTL3 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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<tr>
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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>$600 per sample</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 1-7 of ANGPTL3.

**SPECIMEN REQUIREMENTS**

**Blood (preferred):** EDTA (purple-top) tubes: 
- Adult: 5 cc
- Child: 5 cc
- Infant: 2-3 cc

**Tissue:** Frozen (preferred), RNAalater

**Other Body Fluids and Formalin-fixed, Paraffin-embedded Tissue:** Call to inquire