ANGPTL4 MUTATION ANALYSIS

JOHN WELSH CARDIOVASCULAR DIAGNOSTIC LABORATORY

ANGPTL4 gene encodes a glycosylated, secreted protein, angiopoietin-like 4, containing a C-terminal fibrinogen domain. The human gene encodes a product containing 406 amino acids and encompasses 7 exons. It is located at 19p13.3. The ANGPTL4 protein is induced by peroxisome proliferation activators and functions as a serum hormone that regulates glucose homeostasis, lipid metabolism, and insulin sensitivity. It also acts as an apoptosis survival factor for vascular endothelial cells and prevents metastasis by inhibiting vascular growth and tumor cell invasion. The C-terminal domain may be proteolytically-cleaved from the full-length secreted protein. Common variants at 30 loci of ANGPTL4 contribute to polygenic dyslipidemia. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for ANGPTL4 mutations. Individuals are tested by DNA sequencing of the coding exons of the ANGPTL4 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 association with polygenic dyslipidemia.

METHODOLOGY

Genomic DNA is analyzed for ANGPTL4 mutations by DNA sequencing of the coding exons of the ANGPTL4 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

<table>
<thead>
<tr>
<th>Service</th>
<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
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<tbody>
<tr>
<td>Index Case (Male or Female)</td>
<td>$600 per sample</td>
<td>81405</td>
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<tr>
<td>Additional Family Members</td>
<td>$300 per sample; Known familial mutation only</td>
<td>81403</td>
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SENSITIVITY

DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 1-7 of ANGPTL4.

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