APOA1 MUTATION ANALYSIS
JOHN WELSH CARDIOVASCULAR DIAGNOSTIC LABORATORY

APOA1 gene encodes apolipoprotein A-I, which is the major protein component of high density lipoprotein (HDL) in plasma. The human gene encodes a product containing 267 amino acids and encompasses 3 exons. It is located at 11q23-q24. The APOA1 protein promotes cholesterol efflux from tissues to the liver for excretion, and is a cofactor for lecithin cholesterolacyltransferase (LCAT), which is responsible for the formation of most plasma cholesteryl esters. APOA1 is closely linked with two other apolipoprotein genes on chromosome 11. Defects in this gene are associated with HDL deficiencies, including Tangier’s disease, and with systemic non-neuropathic amyloidosis. APOA1 mutations demonstrate autosomal dominant inheritance in HDL deficiencies and autosomal recessive inheritance in Tangier’s disease 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 APOA1 mutations. Individuals are tested by DNA sequencing of the coding exons of the APOA1 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 hypoalphalipoproteinemia, Tangier’s disease and familial visceral amyloidosis (Ostertag type).

METHODOLOGY
Genomic DNA is analyzed for APOA1 mutations by DNA sequencing of the coding exons of the APOA1 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>Index Case (Male or Female)</th>
<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>$500 per sample</td>
<td>81404</td>
</tr>
<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 1-3 of APOA1.

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

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