Peroxisome proliferator-activated receptors (PPARs) belong to the steroid hormone receptor superfamily, which may regulate the expression of target genes involved in cell proliferation, cell differentiation, immune and inflammation responses. Three closely related subtypes (alpha, beta/delta, and gamma) have been identified so far. *PPARA* gene encodes the subtype PPAR-alpha, contains 6 exons, and spans 83.7 kb genomic distance. *PPARA* has been mapped to chromosome 22q12-q13. The encoded protein is a nuclear transcription factor for the ACOX1 and P450 genes. It is the key regulator of lipid metabolism. Diseases associated with this protein include diabetes mellitus, atherosclerosis, fatty liver disease, hyperglycemia, hypertension, heart disease and hyperapobetalipoproteinemia. *PPARA* 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 *PPARA* mutations. Individuals are tested by DNA sequencing of the coding exons of the *PPARA* 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 of diabetes mellitus, atherosclerosis, fatty liver disease, hyperglycemia, hypertension, heart disease and hyperapobetalipoproteinemia.

### METHODOLOGY

Genomic DNA is analyzed for *PPARA* mutations by DNA sequencing of the coding exons of the *PPARA* 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>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$600 per sample</td>
<td>81405</td>
</tr>
<tr>
<td>Additional Family Members</td>
<td>$300 per sample; Known familial mutation only</td>
<td>81403</td>
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</tbody>
</table>

### SENSITIVITY

DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 1-6 of *PPARA*.

### 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