The HADH gene contains 9 exons and spans around 49 kb mapped to 4q25. HADH (hydroxyacyl-CoA dehydrogenase) is a member of the 3-hydroxyacyl-CoA dehydrogenase gene family. The encoded protein functions in the mitochondrial matrix to catalyze the oxidation of straight-chain 3-hydroxyacyl-CoAs as part of the beta-oxidation pathway. Its enzymatic activity is highest with medium-chain-length fatty acids. Mutations in this gene cause are associated with 3-hydroxyacyl-CoA dehydrogenase deficiency and familial hyperinsulinemic hypoglycemia 4. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for HADH mutations. Individuals are tested by DNA sequencing of the coding exons of the HADH 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 dyslipidemia, 3-hydroxyacyl-CoA dehydrogenase deficiency and familial hyperinsulinemic hypoglycemia 4.

METHODOLOGY

Genomic DNA is analyzed for HADH mutations by DNA sequencing of the coding exons of the HADH gene, as well as the exon/intron junctions and a portion of the 5’ and 3’ untranslated regions. 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>$900 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 1-9 of HADH.

SPECIMEN REQUIREMENTS

Blood (preferred): EDTA (purple-top) tubes: Adult: 5 cc Child: 5 cc Infant: 2-3 cc
Tissue: Frozen (preferred) or RNAlater
Other Body Fluids or Formalin-Fixed, Paraffin-Embedded Tissue: Call to inquire