The AARS2 gene encodes mitochondrial alanyl-tRNA synthetase, which is responsible for the charging of tRNA-ala with alanine during mitochondrial translation. The AARS2 gene contains 22 exons and spans 13.7kb that were mapped to chromosome 6. Mutations in this gene are associated with infantile mitochondrial cardiomyopathy which is caused by defective oxidative phosphorylation. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for AARS2 mutations. Individuals are tested by DNA sequencing of the coding exons of the AARS2 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 HCM and pancardiomyopathy.

METHODOLOGY

Genomic DNA is analyzed for AARS2 mutations by DNA sequencing of the coding exons of the AARS2 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>
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<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
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<tbody>
<tr>
<td>Index Case (Male or Female)</td>
<td>$1,100 per sample</td>
<td>81406</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 of AARS2.

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

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