The ACADVL gene stands for “Acyl-CoA Dehydrogenase, Very Long Chain”. This gene is located on chromosome 17p13.1, is 8,142 base pairs long, and makes a mitochondria protein with 655 amino acids (final product has a 40-amino acid leader peptide, yielding a mature 615-residue protein). ACADVL breaks down very long-chain fatty acids, and is an essential player in the oxidation of fatty acid. There are over 100 different ACADVL mutations that are known to cause clinically significant symptoms. Missense and nonsense mutations are common in this gene. Mutated proteins can be highly deficient in metabolizing long-chain fatty acids. Without enough functional ACADVL protein, patients can exhibit hypoglycemia, and subsequently, lethargy. Poorly-metabolized long-chain fatty acids begin building up in the liver, heart, and muscles. Any detrimental change to the ACADVL gene will cause a disease known as VLCAD deficiency. Some clinical symptoms include episodes of cardiorespiratory arrest associated with fasting. Others include hepatomegaly, cardiomegaly, hypotonia, and low plasma carnitine concentration. These mutations are passed on in an autosomal recessive fashion. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for ACADVL mutations. Individuals are tested by DNA sequencing of the coding exons of the ACADVL 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 VLCAD deficiency and cardiomyopathy.

**METHODOLOGY**

Genomic DNA is analyzed for ACADVL mutations by DNA sequencing of the coding exons of the ACADVL 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>$1,350 per sample</td>
<td>81406</td>
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<table>
<thead>
<tr>
<th>Additional Family Members</th>
<th>$300 per sample; Known familial mutation only</th>
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</thead>
</table>

<table>
<thead>
<tr>
<th>Blood (preferred): EDTA (purple-top) tubes</th>
<th>Adult: 5 cc</th>
<th>Child: 5 cc</th>
<th>Infant: 2-3 cc</th>
</tr>
</thead>
</table>

| Tissue: Frozen (preferred) or RNAlater      |

**SENSITIVITY**

DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 1-21 of ACADVL.

**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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