CAV3 MUTATION ANALYSIS
JOHN WELSH CARDIOVASCULAR DIAGNOSTIC LABORATORY

Caveolin-3 (CAV3) gene is composed of 2 exons and is located at 3p25. It encodes a caveolin family member, which functions as a component of the caveolae plasma membranes found in most cell types. Caveolin proteins are proposed to be scaffolding proteins for organizing and concentrating certain caveolin-interacting molecules. However, multiple other functions for these proteins have been described or postulated. Mutations identified in this gene lead to interference with protein oligomerization or intra-cellular routing, disrupting caveolae formation and resulting in caveolinopathies, a group of muscle diseases including Limb-Girdle muscular dystrophy type-1C (LGMD1C), hyperCKemia (HCK), rippling muscle disease (RMD), distal myopathy (DM) and hypertrophic cardiomyopathy (HCM) without skeletal muscle manifestations. CAV3 mutations have also been identified in patients with long QT syndrome and sudden infant death syndrome. Mutations in CAV3 have been noted to demonstrate both autosomal dominant and recessive inheritance with a variable clinical expression. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for CAV3 mutations. Individuals are tested by DNA sequencing of all 2 exons of the CAV3 gene. Genetic counseling is recommended for all individuals in order to identify additional at-risk family members and to discuss reproductive issues.

**REASONS FOR REFERRAL**
- Molecular confirmation of the diagnosis of caveolinopathies including Limb-Girdle muscular dystrophy type-1C (LGMD1C), hyperCKemia (HCK), rippling muscle disease (RMD), distal myopathy (DM) and hypertrophic cardiomyopathy (HCM) without skeletal muscle manifestations.
- Molecular confirmation of the diagnosis of CAV3-related long QT syndrome and sudden infant death syndrome.

**METHODOLOGY**

Genomic DNA is analyzed for CAV3 mutations by DNA sequencing of all 2 exons of the CAV3 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(s) by automatic fluorescent DNA sequencing.

**SERVICE FEES**

<table>
<thead>
<tr>
<th>Service Description</th>
<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
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<tbody>
<tr>
<td>Index Case (Full Gene)</td>
<td>$450 per sample</td>
<td>81404</td>
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<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% detection of mutations in exons 1-2 of CAV3

**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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