CAV1 MUTATION ANALYSIS

JOHN WELSH CARDIOVASCULAR
DIAGNOSTIC LABORATORY

The integral membrane protein caveolin-1 is the main component of caveolae membranes. The CAV1 gene contains 3 exons and spans around 36 kb genomic distance that has been mapped to 7q31.2. Mutations in the CAV1 gene are associated with congenital generalized lipodystrophy type 3. Recent studies have demonstrated that receptor signaling cascades relevant to pulmonary arterial hypertension (PAH) such as the TGF beta superfamily, nitric oxide pathway, and G-protein coupled receptors rely heavily on proper caveolar function. Caveolin-1 modifies TGF-beta signaling at the plasma membrane, which provides a mechanistic link between CAV1 and BMPR2 mutations in the pathogenesis of PAH. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for CAV1 mutations. Individuals are tested by DNA sequencing of the coding exons of the CAV1 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 pulmonary arterial hypertension (PAH) and congenital generalized lipodystrophy type 3.

METHODOLOGY

Genomic DNA is analyzed for CAV1 mutations by DNA sequencing of the coding exons of the CAV1 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

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<tr>
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<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
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<tbody>
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<td>Index Case (Male or Female)</td>
<td>$600 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 percent detection of mutations in the coding exons 1-3 of CAV1.

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