PDLIM3 MUTATION ANALYSIS

JOHN WELSH CARDIOVASCULAR DIAGNOSTIC LABORATORY

PDLIM3 (PDZ and LIM domain 3) contains a PDZ domain and a LIM domain, indicating that it may be involved in cytoskeletal assembly. PDLIM3 has been shown to bind the spectrin-like repeats of alpha-actinin-2 and to colocalize with alpha-actinin-2 at the Z lines of skeletal muscle and may play a role in the organization of actin filament arrays within muscle cells. Alternatively spliced transcript variants encoding multiple isoforms have been observed. Aberrant alternative splicing of this gene may play a role in myotonic dystrophy. PDLIM3 gene contains 8 coding exons and spans a genomic distance of about 34.95 kb that has been mapped to chromosome 4q35. Diseases associated with PDLIM3 mutation include hypertrophic cardiomyopathy, dilated cardiomyopathy, myotonic dystrophy and myopathy dementia. PDLIM3 mutations demonstrate autosomal dominant inheritance with a broad range of clinical severity both within and between families. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for PDLIM3 mutations. Individuals are tested by DNA sequencing of the coding exons of the PDLIM3 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 hypertrophic cardiomyopathy, dilated cardiomyopathy, myotonic dystrophy and myopathy dementia.

METHODOLOGY

Genomic DNA is analyzed for PDLIM3 mutations by DNA sequencing of the coding exons of the PDLIM3 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

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<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
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<tr>
<td>Index Case (Male or Female)</td>
<td>$800 per sample</td>
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<tr>
<td>Additional Family Members</td>
<td>$300 per sample; known familial mutation only</td>
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SENSITIVITY

DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 1-8 of PDLIM3.

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