MYOM1 MUTATION ANALYSIS

JOHN WELSH CARDIOVASCULAR
DIAGNOSTIC LABORATORY

MYOM1 gene encodes myomesin 1, one of the two sarcomere M-band components. Myomesin 1, like myomesin 2, titin, and other myofibrillar proteins contains structural modules with strong homology to either fibronectin type III (motif I) or immunoglobulin C2 (motif II) domains. Myomesin 1 and myomesin 2 each have a unique N-terminal region followed by 12 modules of motif I or motif II, in the arrangement II-II-I-I-I-I-II-II-II-II-II. The two proteins share 50% sequence identity in this repeat-containing region. The head structure formed by these 2 proteins on one end of the titin string extends into the center of the M band. The integrating structure of the sarcomere arises from muscle-specific members of the superfamily of immunoglobulin-like proteins. Alternatively spliced transcript variants encoding different isoforms have been identified. MYOM1 gene contains 37 coding exons and spans a genomic distance about 153.3 kb mapped to chromosome 18p11.31. Mutations in this gene have been associated with hypertrophic cardiomyopathy (HCM). MYOM1 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 MYOM1 mutations. Individuals are tested by DNA sequencing of the coding exons of the MYOM1 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 (HCM).

METHODOLOGY

Genomic DNA is analyzed for MYOM1 mutations by DNA sequencing of the coding exons of the MYOM1 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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<td>Index Case (Male or Female)</td>
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<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 1-37 of MYOM1.

SPECIMEN REQUIREMENTS

Blood (preferred): EDTA (purple-top) tubes: Adult: 5 cc  Child: 5 cc  Infant: 2-3 cc
Tissue: Frozen (preferred), RNA later
Other Body Fluids and Formalin-fixed, Paraffin-embedded Tissue: Call to inquire