MYLK gene encodes the Myosin Light Chain Kinases (MLCKs), which are a group of protein serine/threonine kinases that is currently divided into two subtypes, MLCK1 and MLCK2. MLCK1 is found in smooth muscle and phosphorylates myosin II regulatory light chains at Ser19, allowing myosin crossbridges to bind to actin filaments and initiate contraction. In addition to smooth muscle contraction, MLCK1 is involved in a diverse range of biological processes including control of endothelial and vascular permeability, growth initiation of astrocytes processes, neurotransmitter release in the sympathetic nervous system and apoptosis of fibroblasts. MLCK2 is found in striated muscle and co-localizes with phosphorylated MLC filaments to mediate skeletal and cardiac muscle contraction. Full length MYLK gene contains 31 exons spanning 272 kb of genomic that had been mapped to chromosome 3q21.1. Multiple mutations in MYLK have been identified in patients with familial aortic dissection and familial thoracic aortic aneurysm type 7 (AAT7). MYLK 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 MYLK mutations. Individuals are tested by DNA sequencing of the coding exons of the MYLK 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 familial thoracic aortic aneurysm/dissections.

METHODOLOGY

Genomic DNA is analyzed for MYLK mutations by DNA sequencing of the coding exons of the MYLK gene, as well as the exon/intron junctions and a portion of the 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>
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<td>Index Case (Male or Female)</td>
<td>$1200 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% detection of mutations in the coding exons of MYLK.

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