**ACTA1 MUTATION ANALYSIS**

**JOHN WELSH CARDIOVASCULAR DIAGNOSTIC LABORATORY**

**ACTA1** gene encodes skeletal muscle alpha-actin, which is the principal actin isoform in adult skeletal muscle. The human gene **ACTA1** encodes a product containing 377 amino acids and encompasses six exons. It is located at 1q42.13. Muscle contraction results from the force generated between the thin filament protein actin and the thick filament protein myosin, which causes the thick and thin muscle filaments to slide past each other. There are skeletal muscle, cardiac muscle, smooth muscle, and nonmuscle isoforms of both actin and myosin. Inherited diseases in humans have been associated with defects in cardiac actin in dilated cardiomyopathy and hypertrophic cardiomyopathy. Mutations in **ACTA1** have been associated with nemaline myopathy (NEM), actin myopathy (AM) and myopathy with intranuclear rods (IRM). Recently, **ACTA1** mutations were also found in three unrelated cases of congenital fiber type disproportion (CFTD) and in a dominant congenital myopathy with cores. Dilated cardiomyopathy has been sometimes reported in association with nemaline myopathy. Hypertrophic cardiomyopathy (HCM) has been also described in four infantile cases with nemaline myopathy, one of which was genetically confirmed to have a heterozygous **ACTA1** mutation. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for **ACTA1** mutations. Individuals are tested by automatic fluorescent DNA sequencing of the coding exons of the **ACTA1** 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 muscular dystrophies with cardiomyopathy.

### METHODOLOGY

Genomic DNA is analyzed for **GAA** mutations by automatic fluorescent DNA sequencing of the coding exons of the **ACTA1** 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

<table>
<thead>
<tr>
<th>Index Case (Male or Female)</th>
<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$600 per sample</td>
<td>81405</td>
</tr>
<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 of **ACTA1**.

### SPECIMEN REQUIREMENTS

**Blood (preferred):** EDTA (purple-top) tubes: *Adult: 5 cc  Child: 5 cc  Infant: 2-3 cc*

**Tissue:** Frozen (preferred), RNA*later*, Formalin-fixed, Paraffin-embedded

**Other Body Fluids:** Call to inquire

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