The TNNI3 gene encodes troponin I (TnI), which is one of 3 subunits that form the troponin complex of the thin filaments of striated muscle. Troponin I binds actin and inhibits actomyosin ATPase activity in the absence of calcium. Cardiac muscle troponin I is expressed only in the heart. The TNNI3 gene contains 8 exons mapped to chromosome 19q13.4. Mutations in this gene are related with hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM) and restrictive cardiomyopathy-1 (RCM1). HCM is an autosomal dominant inherited disease characterized by a portion of the myocardium been hypertrophied (thickened). DCM is a type of cardiomyopathy in which the heart becomes weakened and enlarged and cannot pump blood efficiently. RCM1 is characterized with diastolic dysfunction and atrial enlargement without ventricular dilatation. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for TNNI3 mutations. Individuals are tested by DNA sequencing of the coding exons of the TNNI3 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 dilated, hypertrophic and restrictive cardiomyopathy-1 (DCM, HCM and RCM1).

**METHODOLOGY**

Genomic DNA is analyzed for TNNI3 mutations by DNA sequencing of the coding exons of the TNNI3 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**

<table>
<thead>
<tr>
<th>Index Case (Male or Female)</th>
<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>$750 per sample</td>
<td>81405</td>
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<tr>
<td>Additional Family Members</td>
<td>$300 per sample;</td>
<td>81403</td>
</tr>
<tr>
<td></td>
<td>Known familial mutation only</td>
<td></td>
</tr>
</tbody>
</table>

**SENSITIVITY**

DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 1-8 of TNNI3.

**SPECIMEN REQUIREMENTS**

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

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