The CALR3 gene is located at 19p13.11 and encodes a member of the calreticulin family, the calcium-binding chaperones localized mainly in the endoplasmic reticulum. Mutation in this gene has been associated with familial hypertrophic cardiomyopathy and syncope. These mutations are passed on in an autosomal dominant fashion. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for CALR3 mutations. Individuals are tested by DNA sequencing of the coding exons of the CALR3 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 familial hypertrophic cardiomyopathy and syncope.

**METHODOLOGY**

Genomic DNA is analyzed for CALR3 mutations by DNA sequencing of the coding exons of the CALR3 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></th>
<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
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<tbody>
<tr>
<td>Index Case (Male or Female)</td>
<td>$800 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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</tbody>
</table>

**SENSITIVITY**

DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 1-9 of CALR3.

**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