MIB1 (mindbomb E3 ubiquitin protein ligase 1) gene encodes a protein containing multiple ankyrin repeats and RING finger domains that functions as an E3 ubiquitin ligase. The encoded MIB1 protein positively regulates Notch signaling by ubiquitinating the Notch receptors, thereby facilitating their endocytosis. This protein may also promote the ubiquitination and degradation of death-associated protein kinase 1 (DAPK1) to promote TNF-induced apoptosis. MIB1 gene contains 21 coding exons and spans 166 kb genomic distance which was mapped to chromosome 18q11.2. Diseases associated with MIB1 mutation include left ventricular noncompaction 7 (LVNC7) and left ventricular noncompaction 1, with or without congenital heart defects. MIB1 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 MIB1 mutations. Individuals are tested by DNA sequencing of the coding exons of the MIB1 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 left ventricular noncompaction 7 (LVNC7) and left ventricular noncompaction 1 (LVNC1), with or without congenital heart defects.

**METHODOLOGY**
Genomic DNA is analyzed for MIB1 mutations by DNA sequencing of the coding exons of the MIB1 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>
</tr>
</thead>
<tbody>
<tr>
<td>Index Case (Male or Female)</td>
<td>$1,300 per sample</td>
<td>81406</td>
</tr>
<tr>
<td>Additional Family Members</td>
<td>$300 per sample; known familial mutation only</td>
<td>81403</td>
</tr>
</tbody>
</table>

**SENSITIVITY**
DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 1-21 of MIB1.

**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