Integrin-linked kinase (ILK) is a highly conserved serine/threonine protein kinase capable of interacting with the cytoplasmic region of the integrin β1- and β3-subunit and is widely expressed, including in endothelial cells, skeletal muscle, and cardiomyocytes. The human gene ILK encodes a protein containing 452 amino acids and encompasses 12 exons. It is located at 11p15.4. Researchers reported on a novel function for ILK, which is to maintain cardiomyocyte cell shape and morphology of the ventricle during embryonic development, which depends on the presence of the extracellular matrix molecule LAMA4. Deletion of ILK results in disaggregation of cardiomyocytes, associated with disruption of adhesion signaling through the β1-integrin/FAK (focal adhesion kinase) complex. Importantly, the loss of ILK is accompanied by a reduction in cardiac Akt phosphorylation, which normally provides a protective response against stress. Together, these results suggest that ILK plays a central role in protecting the mammalian heart against cardiomyopathy and heart failure. ILK mutation was found in patients affected with severe cardiomyopathy and not in unaffected individuals. This mutation was also associated with a defect in endothelial cells and heart failure. Definitive genotype/phenotype correlations have not been described.

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

**METHODOLOGY**
Genomic DNA is analyzed for ILK mutations by DNA sequencing of the coding exons of the ILK 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>Description</th>
<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
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</thead>
<tbody>
<tr>
<td>Index Case (Male or Female)</td>
<td>$900 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>
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</table>

**SENSITIVITY**
DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 1-12 of ILK.

**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 or Formalin-fixed, Paraffin-embedded Tissue:** Call to inquire

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