JPH2 gene encodes Junctophilin type 2, a cardiac specific member of the junctophilins family of junctional membrane complex proteins which physically approximates the plasmalemmal L type calcium channel and the sarcoplasmic reticulum (SR). The human gene JPH2 encompasses 5 exons. It is located at 20q13.12. JPH2 knockout mice showed that disrupted calcium transients, altered junctional membrane complex formation, cardiomyopathy, and embryonic lethality. Furthermore, JPH2 gene expression is down-regulated in murine cardiomyopathy models. To this end, JPH2 was explored as a novel candidate gene for the pathogenesis of hypertrophic cardiomyopathy (HCM) in humans. The molecular and functional evidence implicates defective junctophilin-2 and disrupted calcium signaling as a novel pathogenic mechanism for HCM and establishes HCM as the first human disease associated with genetic defects in JPH2. Susceptibility for other cardiomyopathies, such as dilated cardiomyopathy, can be conferred by mutations in JPH2 warrants investigation. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for JPH2 mutations. Individuals are tested by DNA sequencing of the coding exons of the JPH2 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 HCM and DCM.

**METHODOLOGY**
Genomic DNA is analyzed for JPH2 mutations by DNA sequencing of the coding exons of the JPH2 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**

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<th>Direct and Institutional Billing</th>
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<td>Index Case (Male or Female)</td>
<td>$600 per sample</td>
<td>81404</td>
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<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 1-5 of JPH2.

**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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