**KCNE1 MUTATION ANALYSIS**

**JOHN WELSH CARDIOVASCULAR DIAGNOSTIC LABORATORY**

**KCNE1** (potassium voltage-gated channel, Isk-related family, member 1) gene encodes the KCNE1 protein, which regulates a channel made up of proteins produced by the *KCNQ1* gene. Four alpha subunits, each made from the *KCNQ1* gene, form the structure of each channel. One beta subunit (MinK), produced from the *KCNE1* gene, binds to the channel and regulates its activity. These channels are active in the inner ear and in cardiac muscle, where they transport potassium ions out of cells, playing a role in maintaining the proper ion balance needed for normal hearing and in recharging the muscle after each contraction to maintain a regular heartbeat, respectively. *KCNE1* gene contains one exon spanning 65.5 kb of genomic distance that was mapped to chromosome 21q22.12. Mutations in *KCNE1* are responsible for long QT syndrome type 5 (LQT5). In its rare homozygous forms, it can lead to Jervell and Lange-Nielsen syndrome (JLNS, an autosomal recessive form of LQTS). *KCNE1* 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 *KCNE1* mutations. Individuals are tested by DNA sequencing of the coding exons of the *KCNE1* 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 long QT syndrome type 5 (LQT5), Jervell and Lange-Nielsen syndrome (JLNS).

**METHODOLOGY**

Genomic DNA is analyzed for *KCNE1* mutations by DNA sequencing of the coding exons of the *KCNE1* 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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<thead>
<tr>
<th>Index Case (Male or Female)</th>
<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
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<tbody>
<tr>
<td>$600 per sample</td>
<td>81403</td>
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<tr>
<th>Additional Family Members</th>
<th>Direct and Institutional Billing</th>
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<td>$300 per sample; known familial mutation only</td>
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**SENSITIVITY**

DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exon of *KCNE1*.

**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

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John Welsh Cardiovascular Diagnostic Laboratory • Section of Cardiology • Department of Pediatrics
Baylor College of Medicine • 1102 Bates Avenue, Suite 480.02 • Houston, TX 77030
PHONE: (832) 824-4155 • FAX: (832) 825-5159 • E-MAIL: yuxinf@bcm.edu
Web Site: www.bcm.edu/pediatrics/welsh