Kir2.1 is an inward rectifying potassium channel which is expressed in multiple cell types, including cardiac, skeletal, and smooth muscle cells, osteoclasts, and neurons. Kir2.1, which shapes the cardiac action potential and stabilizes the resting membrane potential of excitable cells, is encoded by the \textit{KCNJ2} gene, which is composed of two exons, one of which is coding, and is located at 17q23.1-q24.2.

Multiple autosomal dominant mutations in \textit{KCNJ2} have been identified in patients with Andersen-Tawil syndrome, which is composed of a clinical triad including, periodic paralysis of the skeletal muscles, cardiac arrhythmias, and dysmorphic features. Patients frequently present with episodic muscle weakness during early childhood to late adolescence. Cardiac manifestations include, Long QT syndrome, ventricular arrhythmias, supraventricular or ventricular tachycardia, \textit{torsades de pointes}, prominent U wave, and premature ventricular contractions. Multiple dysmorphic features, including micrognathia, hypertelorism, low-set ears, scoliosis, cleft palate, 2-3 finger or toe syndactyly, fifth finger clinodactyly, and a broad nasal root have also been described. Andersen-Tawil syndrome demonstrates great variability in age of onset, severity, and clinical manifestations. 6% to 20% of individuals with \textit{KCNJ2} mutations demonstrate non-penetrance.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for \textit{KCNJ2} mutations. Individuals will be tested by automatic fluorescent DNA sequencing of the \textit{KCNJ2} gene coding region. We strongly recommend initial testing of an 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 in order to identify additional at-risk family members and to discuss reproductive issues.

**REASONS FOR REFERRAL**

- Molecular confirmation of the diagnosis of Andersen-Tawil syndrome or Long QT syndrome
- Family history of Andersen-Tawil syndrome or Long QT syndrome

**METHODOLOGY**

Genomic DNA will be analyzed for \textit{KCNJ2} mutations by automatic fluorescent DNA sequencing of exon 2 of the \textit{KCNJ2} gene, as well as its exon/intron junctions and a portion of the 3’ untranslated region. Patient DNA will be sequenced in both the forward and reverse orientations. If a mutation is identified, additional family members will be analyzed only for the familial mutation by automatic fluorescent DNA sequencing.

**SERVICE FEES**

<table>
<thead>
<tr>
<th>Index Case (Male or Female)</th>
<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$450 per sample</td>
<td>83891, 83898x3, 83904x6, 83912</td>
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</tbody>
</table>

| Additional Family Members  | $200 per sample; known familial mutation only |

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<th>CPT Codes</th>
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<tbody>
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<td>83891, 83898, 83904x2, 83912</td>
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**SENSITIVITY**

DNA Sequencing Analysis: Approximately 99% detection of mutations in exon 2 of \textit{KCNJ2}

**SPECIMEN REQUIREMENTS**

**Blood (preferred):** EDTA (purple-top) tubes: \textit{Adult:} 5 cc \textit{Child:} 5 cc \textit{Infant:} 2-3 cc

**Tissue:** Frozen (preferred), RNA\textit{later}, Formalin-fixed, Paraffin embedded

**Other Body Fluids:** Call to inquire

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