Kir2.1 is an inward rectifying potassium channel that 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 KCNJ2 gene. KCNJ2 is composed of two exons, one of which is coding, and is located at 17q23.1-q24.2.

Multiple autosomal dominant mutations in KCNJ2 have been identified in patients with Andersen-Tawil syndrome, which is composed of a clinical triad of 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, 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 KCNJ2 mutations demonstrate non-penetrance.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for KCNJ2 mutations. Individuals are tested by DNA sequencing of the 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 is analyzed for KCNJ2 mutations by DNA sequencing of exon 2 of the KCNJ2 gene, as well as its exon/intron junctions and a portion of the 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>
<th>CPT Codes</th>
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<td>Index Case (Male or Female)</td>
<td>$450 per sample</td>
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<tr>
<td>Additional Family Members</td>
<td>$300 per sample; known familial mutation only</td>
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**SENSITIVITY**

DNA Sequencing Analysis: Approximately 99% detection of mutations in coding exon of KCNJ2.

**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