ANK2, also known as ankyrin B, encodes ankyrin-2 protein, which belongs to a large family of ankyrins. ANK2 gene contains 46 exons spanning 571 kb of genomic distance that was mapped to chromosome 4q25-q27. The ankyrin-2 protein is active in many cell types, particularly in the brain and in cardiac muscle. This protein targets mainly ion channels, which are complexes of proteins that transport charged atoms (ions) across cell membranes. In the heart, the flow of ions (such as sodium, potassium and calcium) through ion channels is critical for signaling the heart to beat and for maintaining a normal heart rhythm. Ankyrin-2 inserts these channels into their proper locations in the cell membrane so they can regulate the flow of ions into and out of cardiac muscle cells. Mutations in this gene cause long QT syndrome type 4 (LQT4) and cardiac arrhythmia syndrome. ANK2 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 ANK2 mutations. Individuals are tested by DNA sequencing of the coding exons of the ANK2 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 4 (LQT4) and cardiac arrhythmia syndrome.

**METHODOLOGY**

Genomic DNA is analyzed for ANK2 mutations by DNA sequencing of the coding exons of the ANK2 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>
<th>CPT Codes</th>
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<tr>
<td>Index Case (Male or Female)</td>
<td>$1,650 per sample</td>
<td>81407</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 percent detection of mutations in the coding exons 1-46 of ANK2.

**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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