SCN4B MUTATION ANALYSIS
JOHN WELSH CARDIOVASCULAR DIAGNOSTIC LABORATORY

SCN4B (sodium channel, voltage-gated, type IV, beta subunit) gene encodes one of several sodium channel beta subunits. These subunits interact with voltage-gated alpha subunits to change sodium channel kinetics. The encoded transmembrane protein SCN4B forms interchain disulfide bonds with SCN2A. Human SCN4B gene contains 5 exons spanning 19 kb of genomic distance that was mapped to chromosome 11q23.3. Multiple mutations in SCN4B are the cause of congenital long-QT syndrome type 10 (LQT10) and have been found in patient with sudden infant death syndrome (SIDS). SCN4B 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 SCN4B mutations. Individuals are tested by DNA sequencing of the coding exons of the SCN4B 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 10 (LQT10) and sudden infant death syndrome (SIDS).

METHODOLOGY
Genomic DNA is analyzed for SCN4B mutations by DNA sequencing of the coding exons of the SCN4B 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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<tr>
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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>$750 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 SCN4B.

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