SCN5A MUTATION ANALYSIS
JOHN WELSH CARDIOVASCULAR DIAGNOSTIC LABORATORY

SCN5A, mapped to chromosome 3p21, is composed of 28 exons spanning approximately 80 kb genomic distance. SCN5A, a cardiac sodium channel gene, encodes a 2,016-amino acid protein that has a structure similar to that of previously characterized sodium channels and contains 4 homologous domains, each of which has six putative membrane-spanning regions. Multiple mutations in SCN5A have been identified in patients with Brugada syndrome, long QT syndrome-3 and idiopathic ventricular fibrillation. SCN5A mutations demonstrate autosomal dominant inheritance with a broad range of clinical severity both within and between families. Definitive genotype/phenotype correlations have not been established.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for SCN5A mutations. Individuals are tested by DNA sequencing of the coding exons of the SCN5A 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 Brugada Syndrome, Long QT Syndrome, and Idiopathic Ventricular Fibrillation

METHODOLOGY

Genomic DNA is analyzed for SCN5A mutations by DNA sequencing of all coding exons of the SCN5A gene, as well as the 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

<table>
<thead>
<tr>
<th>Index Case (Male or Female)</th>
<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>$1100 per sample</td>
<td>81407</td>
</tr>
<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% detection of mutations in the coding exons of SCN5A.

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