CACNA1C MUTATION ANALYSIS
JOHN WELSH CARDIOVASCULAR DIAGNOSTIC LABORATORY

CACNA1C gene encodes the alpha-1C subunit of the voltage-dependent long-lasting (L-type) calcium channels that present in the membrane of most excitable cells and mediate calcium influx in response to depolarisation, and are also involved in a variety of calcium-dependent processes, including muscle contraction, hormone or neurotransmitter release, gene expression, cell motility, cell division and cell death. Calcium channels containing the alpha-1C subunit play an important role in excitation-contraction coupling in the heart. The protein encoded by this gene binds to and is inhibited by dihydropyridine. Alternative splicing results in many transcript variants encoding different proteins. CACNA1C gene contains 47 exons spanning 727 kb of human genome that was mapped to chromosome 12p13.33. Multiple mutations in CACNA1C gene have been found in patients associated with Brugada syndrome 3, Timothy syndrome, long-QT syndrome type 8 (LQT8) and short-QT syndrome (SQT). CACNA1C 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 CACNA1C mutations. Individuals are tested by DNA sequencing of the coding exons of the CACNA1C 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 3, Timothy syndrome, long-QT syndrome type 8 (LQT8) and short-QT syndrome (SQT).

METHODOLOGY
Genomic DNA is analyzed for CACNA1C mutations by DNA sequencing of the coding exons of the CACNA1C gene, as well as the exon/intron junctions and a portion of the 3’ and 5’ untranslated regions. 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>$1,500 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>
<td>81403</td>
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SENSITIVITY
DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 1-47 of CACNA1C.

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