Catecholamine-Induced Polymorphic Ventricular Tachycardia (CPVT) is an arrhythmogenic disorder of the heart muscle in the absence of structural heart defects. The prevalence of CPVT is estimated to be 1/10,000 individuals. CPVT is unique in that acute emotion or exercise can trigger polymorphic ventricular arrhythmias in an affected individual. CPVT is caused by mutations in the RYR2 (autosomal dominant form) and CASQ2 (autosomal recessive form) genes. CASQ2 encodes a calsequestrin protein which is produced in the sarcoplasmic reticulum of the heart muscle. Mutations in the CASQ2 gene can cause leakage of calcium from the sarcoplasmic reticulum, triggering cardiac electrical instability during times of stress (1). The CASQ2 gene contains 11 exons and is located on chromosome 1p11-13.3.

Causative mutations can be identified in 50-70% of individuals with CPVT (2). Mutations in RYR2 account for 70% of cases, while mutations in CASQ2 account for 7% of cases (2). Since causative mutations cannot be identified in all affected individuals, it is likely that other unidentified genes also contribute to the development of CPVT. Parents of a child with CASQ2 autosomal recessive CPVT are obligate heterozygotes, or carriers of the pathogenic mutation. Heterozygote carriers of CASQ2 mutations are unlikely to have any symptoms.

It is not unusual for patients with CPVT to be misdiagnosed as having Long Q-T Syndrome (LQTS) with normal Q-T intervals (2). Individuals with LQTS generally do not develop arrhythmias during exercise stress testing, whereas CPVT patients often do.

**Indication**

CASQ2 gene testing is utilized to confirm a diagnosis of CPVT in patients with clinically evident disease. RYR2 gene testing should always be done before CASQ2 gene testing, unless there is a clear autosomal recessive pattern of inheritance. Genetic testing also allows for early identification and diagnosis of individuals at greatest risk prior to the expression of typical clinical manifestations and can be used for prenatal diagnosis.
Methodology:

All 11 exons of the *CASQ2* gene, as well as the exon/intron boundaries and portion of untranslated regions of the gene are amplified by PCR. Genomic DNA sequences from both forward and reverse directions are obtained by automatic fluorescent detection using an *ABI PRISM® 3730 DNA Analyzer*. Sequence variants different from National Center for Biotechnology Information GenBank references are further evaluated for genetic significance. If a mutation is identified, a known familial mutation analysis will be available for additional family members.

Sensitivity & Accuracy:

Greater than 98.5% of the mutations in exons 1-11 of *CASQ2* are detectable by sequence based methods. Sequencing does not detect deletions or duplications.

References:


Specimen:

Peripheral blood in EDTA tube
- Adult: 5-10mL
- Child: 3-5mL
- Infant: 1-3mL

For other specimen types, please contact Amy Shikany at 513-803-3317

Turnaround Time:

Full Mutation Analysis 2-4 weeks
Known Mutation Analysis 1-2 weeks

CPT Codes:

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