Cardiovascular Diseases Genetic Testing Program

CASQ2 – Catecholamine-Induced Polymorphic Ventricular Tachycardia

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.

Molecular Genetics Laboratory

Shipping Instructions

Please enclose a test requisition form with sample. All information must be complete before sample can be processed. Samples may be shipped at room temperature by overnight Federal Express to arrive Monday through Friday.

Ship to:

Molecular Genetics Lab
Cincinnati Children's Hospital
3333 Burnet Ave. NRB 1042
Cincinnati, OH 45229

Phone: 513-636-4474
Fax: 513-636-4373

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:

1. Lahat H, Pras E, Olender T, Avidan N, Ben-Asher E, Man O, Levy-Nissenbaum E, Khoury A, Lorber A, Goldman B, Lancet D, Eldar M. A missense mutation in a highly conserved region of *CASQ2* is associated with autosomal recessive catecholamine-induced polymorphic ventricular tachycardia in bedouin families from israel. *American Journal of Human Genetics*. 2001;69:1378-1384.

2. Liu N, Ruan Y, Priori SG. Catecholaminergic polymorphic ventricular tachycardia. *Progress in Cardiovascular Disease*. 2008;51:23-30.

Specimen:

Peripheral blood in EDTA tube
Adult: 3-5mL
Child: 3-5mL
Infant: 1-3mL
For other specimen types, please contact us at 513-636-4474

Turnaround Time:

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

CPT Codes:

Full Gene Sequencing	81405
Additional Family Members	81403

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