

CACNA1C-related Disorders: CACNA1C Gene Deletion/Duplication

Test Code: DCACN

Turnaround time: 2 weeks

CPT Codes: 81282 x1

Condition Description

Timothy Syndrome

Timothy syndrome is characterized by cardiac abnormalities such as long QT interval and congenital heart defects, hand/foot syndactyly, and neuropsychiatric involvement such as developmental delays and autism spectrum disorder. Characteristic facial features include flat nasal bridge, low-set ears, thin upper lip, and a round face. Timothy syndrome is an autosomal dominant disorder with death occurring on average by two and a half years of age. Mutation of the *CACNA1C* gene (12p13.3) is reported to cause Timothy syndrome. There are two types; type 1 a classic form and type 2 a rare form. Most cases of Timothy syndrome result from a de novo mutation and only three different mutations have been identified at this time. The common mutation p.Gly406Arg in the *CACNA1C* gene confirms the diagnosis of Timothy syndrome type 1 while the p.Gly406Arg or p.Gly402Ser mutations in the alternatively spliced transcript of the *CACNA1C* gene result in Timothy syndrome type 2.

Brugada Syndrome

Mutation of the *CACNA1C* gene also causes Brugada syndrome, which is characterized by cardiac conduction abnormalities. These cardiac abnormalities can result in sudden death. Often, features, such as syncope and/or arrhythmias present in adulthood; however, the age of diagnosis ranges from two days to 85 years. In addition to the *CACNA1C* gene, mutation of seven other genes cause Brugada syndrome. Only 25% of individuals with Brugada syndrome have an identifiable mutation in one of the eight genes known to cause it. Most individuals with Brugada syndrome have an affected parent but approximately 1% of cases are the result of a de novo mutation.

Please note that this test is for the *CACNA1C* gene only.

For patients with suspected *CACNA1C*-related disorders, sequence analysis is recommended as the first step in mutation identification. For patients in whom mutations are not identified by full gene sequencing, deletion/duplication analysis is appropriate.

References:

- GeneReviews
- [OMIM #114205](#): *CACNA1C* gene
- [OMIM #601005](#): Timothy syndrome
- [OMIM #611875](#): Brugada syndrome

Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of *CACNA1C*-related disorders in an individual in whom sequence analysis was negative.
- Carrier testing in adults with a family history of *CACNA1C*-related disorders in whom sequence analysis was negative.

Methodology

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region.

Detection

Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations. Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

Specimen Requirements

Submit only 1 of the following specimen types

Type: Whole Blood (EDTA)

Specimen Requirements:

EDTA (Purple Top)

Infants and Young Children (2 years of age to 10 years old): 3-5 ml

Older Children & Adults: 5-10 ml

Autopsy: 2-3 ml unclotted cord or cardiac blood

Specimen Collection and Shipping:

Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

Type: DNA, Isolated

Specimen Requirements:

Microtainer

3µg

Isolation using the Perkin Elmer™ Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping:

Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

Special Instructions

Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of EGL Genetics, please submit a copy of the sequencing report with the test requisition.

Related Tests

- Sequence analysis of the *CACNA1C* gene is available and is required before deletion/duplication analysis.
- Custom diagnostic mutation analysis (KM) is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- Prenatal testing is available only for known familial mutations to individuals who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.