Myoclonus-Dystonia: SGCE Gene Sequencing

Test Code: SSGCE
Turnaround time: 6 weeks
CPT Codes: 81479 x1

Condition Description

Myoclonus-dystonia (M-D) is a movement disorder characterized by a combination of rapid, brief muscle contractions (myoclonus) and/or sustained twisting and repetitive movements that result in abnormal postures (dystonia). Onset of myoclonus is usually in the first or second decade of life. The myoclonic jerks typical of M-D are brief, lightning-like movements that most often affect the neck, trunk, and upper limbs with less common involvement of the legs. Dystonia is observed in more than half of affected individuals, but is only rarely seen without myoclonus. Affected individuals can have focal or segmental dystonia, presenting as cervical dystonia and/or writer's cramp. Most affected adults report a dramatic reduction in myoclonus in response to alcohol ingestion. The most prominent non-motor features have been psychiatric problems including depression, anxiety, obsessive-compulsive disorder (OCD), personality disorders, addiction, and panic attacks.

The diagnosis of myoclonus-dystonia is based on clinical findings, family history, absence of other neurologic deficits, and normal neuroimaging studies. In general, all laboratory tests are normal in individuals with M-D. Abnormal liver function tests may be the result of chronic alcohol use.

Myoclonus-dystonia is inherited in an autosomal dominant manner. Mutations in the SGCE gene (7q21) are identified in approximately 30-50% of individuals with familial M-D and 10-15% of simplex cases. Simplex and familial cases without identifiable SGCE mutations have been reported, suggesting locus heterogeneity. Reduced penetrance on maternal transmission of the disease allele has been observed, suggesting maternal genomic imprinting of the SGCE gene. Almost all children who inherit the mutation from their fathers develop symptoms. About 5% of children who inherit the mutation from their mothers develop symptoms.

For patients with suspected myoclonus-dystonia, 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: Myoclonus-Dystonia
- OMIM #159900 Myoclonic Dystonia

Genes
SGCE

Indications

This test is indicated for:
- Confirmation of a clinical diagnosis of myoclonus-dystonia

Methodology

PCR amplification of 11 exons contained in the SGCE gene is performed on the patient's genomic DNA. Direct sequencing of amplification products is performed in both forward and reverse directions, using automated fluorescence dideoxy sequencing methods. The patient's gene sequences are then compared to a normal reference sequence. Sequence variations are classified as mutations, benign variants unrelated to disease, or variations of unknown clinical significance. Variants of unknown clinical significance may require further studies of the patient and/or family members. This assay does not interrogate the promoter region, deep intronic regions, or other regulatory elements, and does not detect large deletions.

Detection

Clinical Sensitivity: Mutations in the SGCE gene (7q21) are identified in approximately 30-50% of individuals with familial M-D and 10-15% of simplex cases. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's biochemical phenotype.

Analytical Sensitivity: ~99%

Specimen Requirements

Submit only 1 of the following specimen types
- Preferred specimen type: Whole Blood

Type: Whole Blood

Specimen Requirements:

In EDTA (purple top) tube:
Infants (2 years): 3-5 ml
Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Type: Saliva**

Specimen Requirements:

Oragene\textsuperscript{TM} Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Special Instructions**

Submit copies of diagnostic biochemical test results with the sample, if appropriate. Contact the laboratory if further information is needed.

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**

- Deletion/duplication analysis of the \textit{SGCE} gene by CGH array is available for those individuals in whom sequence analysis is negative.
- \textit{Custom diagnostic mutation analysis (KIM)} is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- Prenatal testing is available to individuals who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.