Congenital Myasthenic Syndromes: Sequencing Panel

Test Code: MM110
Turnaround time: 6 weeks
CPT Codes: 81406 x1, 81479 x1

Condition Description

Congenital myasthenic syndromes (CMS) are a highly variable group of diseases characterized by fatigable weakness of skeletal muscle. Symptoms range from mild to progressive disabling weakness. The age of onset is also variable ranging from birth to early childhood. Infections, fever, or excitement may precipitate severe exacerbations of weakness or episodes of respiratory insufficiency. Additional features of the neonatal onset subtypes include feeding difficulties, choking spells, poor suck and cry, eyelid ptosis, and weakness. Additional features of the childhood onset subtypes include delayed motor milestones, fluctuating eyelid ptosis, and fluctuating extraocular muscle weakness. CMS can be inherited in an autosomal recessive or an autosomal dominant manner; however, the autosomal recessive manner is more common.

References:

- GeneReviews
- OMIM

Genes

ALG2, CHAT, CHRNA1, CHRNB1, CHRND, CHRNE, COLQ, DOK7, MUSK, RAPSN, SCN4A

Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of congenital myasthenic syndromes (CMS).
- Carrier testing in adults with a family history of congenital myasthenic syndromes (CMS).

Methodology

Next Generation Sequencing: In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

Detection

Next Generation Sequencing: Clinical Sensitivity: Unknown. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions/duplications will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical/biochemical phenotype.

Analytical Sensitivity: ~99%.

Specimen Requirements

Submit only 1 of the following specimen types

Type: Saliva

Specimen Requirements:
Oragene™ Saliva Collection Kit
Oragene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

Specimen Collection and Shipping:
Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

Type: DNA, Isolated

Specimen Requirements:
Microtainer
8µg
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.

**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 24 hours of collection. Do not refrigerate or freeze.

**Related Tests**

- Congenital Myasthenic Syndromes: Deletion/Duplication Panel