

Congenital Muscular Dystrophy with Integrin Alpha 7 Deficiency: *ITGA7* Gene Sequencing

Test Code: SITG7

Turnaround time: 4 weeks

CPT Codes: 81479 x1

Condition Description

The congenital muscular dystrophies are a group of genetically and clinically heterogeneous hereditary myopathies characterized by congenital hypotonia and muscle weakness, contractures, and delayed motor development. Muscle biopsy usually reveals a nonspecific dystrophic pattern. The clinical course is broadly variable and can involve the brain and eyes. Initial testing often includes clinical evaluation, muscle imaging, electromyography, and muscle biopsy, followed by targeted genetic testing.

Congenital muscular dystrophy with integrin alpha 7 deficiency is an extremely rare autosomal recessive CMD that has been reported in only a few patients. Reported symptoms include proximal weakness, congenital torticollis, congenital hip dislocation, multiple joint contractures, and motor delays characteristic of a congenital myopathy. One patient was reported to have mental retardation without brain MRI changes.

Affected individuals have mildly elevated serum creatine kinase levels and immunohistochemistry can reveal absent integrin alpha 7 with normal laminin alpha 2 (merosin). Muscle biopsy is consistent with congenital myopathy. Mutations in the *ITGA7* gene (12q13), including deletions, splice-site mutations, and missense mutations, have been found in affected individuals.

For patients with suspected CMD with integrin alpha 7 deficiency, 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

- Bonnemann, Carsten. Personal communication. July 8, 2009.
- Conti Reed, U. Congenital muscular dystrophy part I: A review of phenotypical and diagnostic aspects. *Arq Neuropsiquiatr.* 2009; 67:144-168.
- GeneTests: Congenital Muscular Dystrophy Overview. <http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=genet?cmd=overview>
- Mendell, JR et al. The congenital muscular dystrophies: Recent advances and molecular insights. *Ped and Dev Pathology.* 2006; 9:427-443.

Genes

[ITGA7](#)

Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of CMD with integrin alpha 7 deficiency
- Carrier testing in adults with a family history of CMD with integrin alpha 7 deficiency

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

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 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

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: 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

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.

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 *ITGA7* gene by CGH array is available for those individuals in whom sequence analysis is negative.
- [Familial mutation testing](#) is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- Prenatal testing is available to couples who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.