Congenital Muscular Dystrophy with Integrin Alpha 7 Deficiency: \textit{ITGA7} Gene Sequencing

\textbf{Test Code:} SITG7  
\textbf{Turnaround time:} 4 weeks  
\textbf{CPT Codes:} 81479 x1

\section*{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 \textit{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.

\section*{Genes}

\textbf{ITGA7}

\section*{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

\section*{Methodology}

\textbf{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.

\section*{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: \(\sim 99\%\)

\section*{Specimen Requirements}

Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

\section*{Type: Whole Blood}

Specimen Requirements:

In EDTA (purple top) or ACD (yellow 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™ 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 Emory Genetics Laboratory, 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.