**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.

Merosin-deficient congenital muscular dystrophy type 1A (MDC1A) usually presents in the neonatal period with marked muscle weakness and severe hypotonia, and ventilatory assistance may be required. Most infants stabilize and do not require further mechanical ventilation, although noninvasive night-time ventilation may be necessary. Feeding difficulties due to decreased suck and swallow can result in recurrent aspiration and poor nutrition. Joint contractures in the elbows, hips, knees, and ankles and scoliosis are common, and typically affected individuals are not able to ambulate or stand unsupported.

Affected individuals generally show normal cognitive development. By six months of age all affected individuals show characteristic white matter changes on MRI, including hypomyelination and hypodensity of white matter; these changes are not, however, unique to CMD. Occasionally structural brain abnormalities may be seen including occipital agryia and pontocerebellar hypoplasia. Individuals with more extensive brain abnormalities may have lower IQ. Approximately 30% of affected individuals have epilepsy.

Individuals affected with MDC1A usually show markedly elevated serum creatine kinase from birth. Muscle biopsies in the neonatal period may show significant inflammation which usually resolves into a typically more dystrophic pattern. Immunohistochemistry staining of a muscle or skin biopsy usually shows complete merosin (also called laminin alpha 2) protein deficiency and can be performed for diagnostic purposes. In some instances, merosin deficiency is not complete; these individuals may have a milder phenotype and later onset than individuals with complete deficiency, resembling limb-girdle muscular dystrophy.

MDC1A is an autosomal recessive disorder caused by mutations in the laminin alpha 2 gene \textit{LAMA2} (6q22-q23). Common mutations have not been observed.

For patients with suspected MDC1A, 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**


**Genes**

\textit{LAMA2}

**Indications**

This test is indicated for:

- Confirmation of a clinical diagnosis of MDC1A in an individual in whom sequence analysis was negative
- Carrier testing in adults with a family history of MDC1A 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.

Please note that a "backbone" of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient's phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

**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

* Preferred specimen type: Whole Blood

**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 EGL Genetics, please submit a copy of the sequencing report with the test requisition.

**Related Tests**

- Sequence analysis of the *LAMA2* is required before deletion/duplication 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.