**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.

A single individual has been recognized with congenital muscular dystrophy type 1D (MDC1D). This individual was 17 years of age at the time of diagnosis and did not have any problems at birth, but was recognized to be developmentally delayed at 5 months of age. She was able to sit unsupported at two and a half years of age, and walked independently at four and a half years of age. Maximal motor function was obtained by nine years of age, after which she gradually worsened. She had contractures at the ankles and elbows, muscle hypertrophy of the quadriceps, calves, and arm muscles, and mild facial weakness.

The affected individual was profoundly mentally retarded with abnormal brain MRI that showed extensive and symmetrical cerebral white matter changes and neuronal migration defects, although brain MRI at age 4 years only showed minimal changes. Serum creatine kinase (CK) levels were elevated 2-20 times normal levels. Muscle biopsy showed uneven reduced staining of alpha dystroglycan, and normal laminin alpha 2 and beta-dystroglycan staining. Two mutations were identified in the LARGE1 gene (22q12.3-q13.1).

For patients with suspected MDC1D, 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**

**LARGE1**

**Indications**

This test is indicated for:

- Confirmation of a clinical diagnosis of MDC1D in an individual in whom sequence analysis was negative
- Carrier testing in adults with a family history of MDC1D 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.

**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**

**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
3µg
Isolation using the Perkin Elmer™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

- Sequence analysis of the LARGE1 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.