Limb-Girdle Muscular Dystrophy (LGMD) Type 1A: MYOT Gene Deletion/Duplication

**Condition Description**

Limb-girdle muscular dystrophy (LGMD) is a descriptive term applied to a clinically and genetically heterogeneous group of childhood- or adult-onset muscular dystrophies. LGMD is characterized by weakness and wasting restricted to the limb musculature, proximal greater than distal. Most individuals with LGMD show relative sparing of the heart and bulbar muscles, although exceptions occur, depending on the genetic subtype. Onset, progression, and distribution of the weakness and wasting vary considerably among individuals and genetic subtypes. Serum creatine kinase (CK) levels in individuals with LGMD are usually elevated, and muscle biopsy reveals dystrophic changes. Immunohistochemistry (IHC) testing of a muscle biopsy sample can be used to determine the presence or absence of specific proteins, and confirmatory genetic testing is available in some cases. LGMDs are distinct from the much more common X-linked dystrophinopathies, which include Duchenne and Becker muscular dystrophy (DMD/BMD).

LGMD 1A, also referred to as myotilinopathy, has an average age of onset of 27 years. Symptoms include mild proximal muscle weakness beginning in the hip girdle region and later progressing to the shoulder girdle region. Distal muscle weakness may occur later. Other symptoms can include tight Achilles tendons, nasal speech, and reduced knee and elbow tendon reflexes. LGMD 1A is slowly progressive, and lacks cardiac involvement. Serum CK levels are normal to mildly elevated, and myotilin IHC is normal. LGMD 1A is inherited in an autosomal dominant manner.

Mutations in the MYOT gene cause LGMD 1A. Mutations in the MYOT gene have also been reported in myofibrillar myopathy, which is characterized by slowly progressive weakness that can involve both proximal and distal muscles, and in spheroid body myopathy.

For patients with suspected LGMD 1A, 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**

**MYOT**

**Indications**

This test is indicated for:

- Confirmation of a clinical diagnosis of LGMD 1A in individuals who have tested negative for sequence analysis.

**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) tube:
- Infants (2 years): 3-5 ml
- Older Children & Adults: 5-10 ml

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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 *MYOT* gene is available and is required before deletion/duplication analysis.
- Sequence and deletion/duplication analysis panels are available for LGMD.
- 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.