

Limb-Girdle Muscular Dystrophy (LGMD) Type 1A: *MYOT* Gene Sequencing

Test Code: STTID

Turnaround time: 4 weeks

CPT Codes: 81479 x1

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.

Visit www.ThinkGenetic.com for patient-friendly information on [limb-girdle muscular dystrophy](#).

References:

- Bonnemann, C. Limb-girdle muscular dystrophy in childhood. *Pediatric Annals*. 2005; 34(7):569-577.
- GeneTests: Limb-Girdle Muscular Dystrophy Overview: <http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=lgmd-overview>.

Genes

[MYOT](#)

Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of LGMD 1A.

Methodology

PCR amplification of 10 exons contained in the *MYOT* gene is performed on the patient's genomic DNA. Direct sequencing of amplification products is performed in both forward and reverse directions, using automated fluorescence dideoxy sequencing methods. The patient's gene sequences are then compared to a normal reference sequence. Sequence variations are classified as mutations, benign variants unrelated to disease, or variations of unknown clinical significance. Variants of unknown clinical significance may require further studies of the patient and/or family members. This assay does not interrogate the promoter region, deep intronic regions, or other regulatory elements, and does not detect large deletions.

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