

## Limb-Girdle Muscular Dystrophy (LGMD) Type 2C: SGCG Gene Sequencing

**Test Code:** SSGCG

**Turnaround time:** 4 weeks

**CPT Codes:** 81405 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).

Mutations in any of the four genes for sarcoglycan that make up the sarcoglycan complex in skeletal muscle can cause LGMD. LGMD 2C is caused by mutation in the *SGCG* gene (13q12), LGMD 2D is caused by mutations in the *SGCA* gene (17q12-q21.3), LGMD 2E is caused by mutations in the *SGCB* gene (4q12), and LGMD 2F is caused by mutations in the *SGCD* gene (5q33). LGMD 2C-F are sometimes referred to as the sarcoglycanopathies.

Age of onset in the sarcoglycanopathies is variable and ranges from early childhood to adulthood, with the majority of affected individuals presenting in the first decade of life and loss of ambulation by the third decade. Phenotype is somewhat similar to that of Duchenne and Becker muscular dystrophy. Proximal weakness in the pelvic girdle occurs before the shoulder girdle becomes affected, which can lead to difficulty running, climbing stairs, and a positive Gowers' maneuver. There may be calf hypertrophy and about 30% of affected individuals develop dilated cardiomyopathy. Language or cognitive delays have not been reported. Significant discordance in phenotypes between siblings has been observed.

Serum CK levels are significantly elevated and IHC shows absence of the sarcoglycan complex. Mutation in any one of the sarcoglycan genes will lead to secondary deficiency of all four sarcoglycans on IHC; gene analysis is necessary to determine which gene has a mutation. LGMD 2C-F are inherited in an autosomal recessive manner, although there have been reports of individuals heterozygous for a mutation in *SGCA* with mild clinical symptoms including scapular winging and calf hypertrophy.

For patients with suspected LGMD 2C, 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](http://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>.
- Guglieri, M. et al. Limb-girdle muscular dystrophies. *Curr Opin Neurol*. 2008; 21:576-584.

### Genes

[SGCG](#)

### Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of LGMD 2C
- Carrier testing in adults with a family history of LGMD 2C

### Methodology

PCR amplification of 8 exons contained in the *SGCG* 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: 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.

### 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.

## 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 *SGCG* gene by CGH array is available for those individuals in whom sequence analysis is negative.
- A sarcoglycanopathies sequencing panel that includes the *SGCG*, *SGCA*, and *SGCB*, and *SGCD* genes is also available.
- An LGMD sequencing panel that includes 11 LGMD genes is also available.
- [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 couples who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.