Limb-Girdle Muscular Dystrophy (LGMD) Type 1C: CAV3 Gene Deletion/Duplication

**Test Code:** DCAV3  
**Turnaround time:** 2 weeks  
**CPT Codes:** 81228 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 1C, also referred to as caveolinopathy, has an average age of onset of five years, although it can range from early childhood to late adulthood. Individuals with childhood onset typically show a Gower sign, calf hypertrophy, mild to moderate proximal weakness, and muscle cramps after exercise. LGMD 1C may also present with muscle cramping and pain, hyperCKemia, or both instead of weakness. Serum CK levels are 4-25 times normal levels and caveolin-3 is reduced on IHC and Western blot. LGMD 1C is inherited in an autosomal dominant manner.

Mutations in the \( \text{CAV3} \) gene (3p25) cause LGMD 1C. Mutations in the \( \text{CAV3} \) gene also cause ripping muscle disease, familial hypertrophic cardiomyopathy, and distal myopathy, in addition to LGMD 1C and hyperCKemia. These phenotypes all demonstrate intrafamilial variability.

For patients with suspected LGMD 1C, 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

### CAV3

## Indications

This test is indicated for:
- Confirmation of a clinical diagnosis of LGMD 1C 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
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 CAV3 gene is available and is required before deletion/duplication analysis.
- Sequence and deletion/duplication analysis panels are available for 11 LGMD genes.
- 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.