The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000023.4(SGCA):c.37+6T>C

Version: 1.0

CA8643646

281148 (ClinVar)

Gene: SGCA (HGNC:6442)
Condition: autosomal recessive limb-girdle muscular dystrophy (MONDO:0015152)
Inheritance Mode: Autosomal recessive inheritance
UUID: e79733a4-e6ed-4858-ace3-45c65283a72e
Approved on: 2026/4/29
Published on: 2026/5/7

HGVS expressions

NM_000023.4:c.37+6T>C
NM_000023.4(SGCA):c.37+6T>C
NC_000017.11:g.50166083T>C
CM000679.2:g.50166083T>C
NC_000017.10:g.48243444T>C
CM000679.1:g.48243444T>C
NC_000017.9:g.45598443T>C
NG_008889.1:g.5079T>C
ENST00000504073.2:c.37+6T>C
ENST00000511303.6:n.37+6T>C
ENST00000512526.2:c.37+6T>C
ENST00000682109.1:c.37+6T>C
ENST00000683294.1:c.37+6T>C
ENST00000262018.8:c.37+6T>C
ENST00000262018.7:c.37+6T>C
ENST00000344627.10:c.37+6T>C
ENST00000502555.5:c.37+6T>C
ENST00000511303.5:c.33+6T>C
ENST00000513821.5:c.37+6T>C
ENST00000513942.5:n.103+1767T>C
ENST00000514934.1:c.43T>C
NM_000023.2:c.37+6T>C
NM_001135697.1:c.37+6T>C
NM_000023.3:c.37+6T>C
NM_001135697.2:c.37+6T>C
NR_135553.1:n.93+6T>C
NM_001135697.3:c.37+6T>C
NR_135553.2:n.73+6T>C

Pathogenic

Met criteria codes 5

PP1 PM3 PP4_Strong PM2_Supporting PVS1_Moderate

Not Met criteria codes 1

PS1

Expert Panel

Limb Girdle Muscular Dystrophy VCEP

Criteria Specification Information

Evidence Links 0

Criteria Specification: *ClinGen Limb Girdle Muscular Dystrophy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for SGCA Version 2.0.0*

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Limb Girdle Muscular Dystrophy VCEP

The NM_000023.4: c.37+6T>C variant in SGCA occurs outside the canonical splice donor site (+/- 1,2) of intron 1. SpliceAI gives a delta score of 0.51 for loss of the canonical donor and of 0.25 for gain of a cryptic donor 59 bp into the intron. RNA-seq on a LGMD patient carrying the variant and a second missense variant (c.725T>C, p.Val242Arg) showed a reduced number of reads with normal splicing at the junction compared to a control sample. The patient sample also showed a 59-bp partial intron 1 retention that was not observed in the control sample and introduces a frameshift with nonsense mediated decay expected (PMID: 39755676; PVS1_RNA_Moderate). This variant has been detected in at least six individuals with limb-girdle muscular dystrophy, including in a homozygous state in 5 patients (1 pt, PMID: 35416532, 39755676; International Centre for Genomic Medicine in Neuromuscular Diseases internal data communication) (PM3). At least one patient with this variant and a second presumed diagnostic SGCA variant displayed progressive limb girdle muscle weakness and significantly reduced or absent expression of alpha-sarcoglycan in skeletal muscle, which is highly specific for SGCA-related LGMD (PP4_Strong; PMID: 39755676). The variant has also been reported to segregate with autosomal recessive limb girdle muscular dystrophy in 3 affected family members from one family (PP1, capped with PP4_Strong; International Centre for Genomic Medicine in Neuromuscular Diseases internal data communication). The upper bound of the 95% confidence interval of the Grpmax variant allele frequency in gnomAD v4.1.1 is 0.000085 (3/91042 South Asian alleles), which is lower than the LGMD VCEP threshold (<0.00009) for PM2_Supporting, and therefore meets this criterion. In summary, this variant meets the criteria to be classified as Pathogenic for autosomal recessive limb girdle muscular dystrophy based on the ACMG/AMP criteria applied, as specified by the ClinGen LGMD VCEP (LGMD VCEP specifications version 2.0.0; 04/29/2026): PVS1_RNA_Moderate, PM3, PP1, PM2_Supporting, PP4_Strong.

Met criteria codes

PP1	✔	The variant has been reported to segregate with autosomal recessive limb girdle muscular dystrophy in 3 affected family members from one family (PP1, capped with PP4_Strong; International Centre for Genomic Medicine in Neuromuscular Diseases internal data communication).
PM3	✔	This variant has been detected in at least six individuals with limb-girdle muscular dystrophy, including in a homozygous state in 5 patients (1 pt, PMID: 35416532, 39755676; International Centre for Genomic Medicine in Neuromuscular Diseases internal data communication) (PM3). Eurofins Ntd Llc (ga) Accession: SCV000331524.5 1 homozygote Labcorp Genetics (formerly Invitae), Labcorp Accession: SCV000649768.8 observed in individuals with clinical features of limb-girdle muscular dystrophy (PMID: 35116532; internal data) PreventionGenetics, part of Exact Sciences Accession: SCV004716399.2 At PreventionGenetics, we have observed this variant with a second SGCA variant in a patient tested for metabolic myopathy (internal data). Neuberg Centre For Genomic Medicine, NCGM Accession: SCV004047074.3 1 affected observation Salient Features : Difficulty in getting up from a squatting position since the age of 10 Younger brother with similar complaint Clinical suspicion : Limb Girdle Muscular Dystrophy (India)
PP4_Strong	✔	At least one patient with this variant and a second presumed diagnostic SGCA variant displayed progressive limb girdle muscle weakness and significantly reduced or absent expression of alpha-sarcoglycan in skeletal muscle, which is highly specific for SGCA-related LGMD (PP4_Strong; PMID: 39755676).
PM2_Supporting	✔	

The upper bound of the 95% confidence interval of the Grpmax variant allele frequency in gnomAD v4.1.1 is 0.000085 (3/91042 South Asian alleles), which is lower than the LGMD VCEP threshold (<0.00009) for PM2_Supporting, and therefore meets this criterion.

PVS1_Moderate ✔

The NM_000023.4: c.37+6T>C variant in SGCA, occurs outside the canonical splice donor site (+/- 1,2) of intron 1. SpliceAI gives a delta score of 0.51 for loss of the canonical donor and of 0.25 for gain of a cryptic donor 59 bp into the intron. RNA-seq on a LGMD patient carrying the variant and a second missense variant (c.725T>C, p.Val242Arg) showed a reduced number of reads with normal splicing at the junction compared to a control sample. The patient sample also showed a 59-bp partial intron 1 retention that was not observed in the control sample and introduces a frameshift with nonsense mediated decay expected (PMID: 39755676; PVS1_RNA_Moderate). The score was reduced given inability to quantify the proportion of transcripts with altered splicing.

Not Met criteria codes

PS1 ✖

c.37+1G>T donor loss 0.7 (alt 0 vs 0.19 for curated variant) strengthens same two alternative donors as curated variant, but strongest alternative donor for comparison variant is at a different position than the strongest alternative for the curated variant both alternative donors are out of frame

Curation History

Showing 1 to 1 of 1 rows

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