

Variant: *NM_000023.4(SGCA):c.197T>A (p.Leu66His)*

Version: 1.0

CA501057 [↗](#)

286025 (ClinVar) [↗](#)

Gene: SGCA ([HGNC:6442](#))

Condition: autosomal recessive limb-girdle muscular dystrophy
([MONDO:0015152](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: 56729249-dce6-49b4-914a-03a511954b23

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HGVS expressions

NM_000023.4:c.197T>A

NM_000023.4(SGCA):c.197T>A (p.Leu66His)

NC_000017.11:g.50167621T>A

CM000679.2:g.50167621T>A

NC_000017.10:g.48244982T>A

CM000679.1:g.48244982T>A

NC_000017.9:g.45599981T>A

NG_008889.1:g.6617T>A

ENST00000504073.2:c.197T>A

ENST00000511303.6:n.38-326T>A

ENST00000512526.2:c.197T>A

ENST00000682109.1:c.77T>A

ENST00000683294.1:c.197T>A

ENST00000262018.8:c.197T>A

ENST00000262018.7:c.197T>A

ENST00000344627.10:c.197T>A

ENST00000502555.5:c.157+134T>A

ENST00000511303.5:c.34-326T>A

ENST00000512526.1:c.41T>A

ENST00000513821.5:c.197T>A

ENST00000513942.5:n.104-326T>A

ENST00000514934.1:c.*18+134T>A

NM_000023.2:c.197T>A

NM_001135697.1:c.197T>A

NM_000023.3:c.197T>A

NM_001135697.2:c.197T>A

NR_135553.1:n.253T>A

NM_001135697.3:c.197T>A

NR_135553.2:n.233T>A

Likely Pathogenic

Met criteria codes **4**

PP4_Strong

PS3_Moderate

PP3

PM3

Not Met criteria codes **2**

Expert Panel

Limb Girdle Muscular Dystrophy VCEP [↗](#)

Criteria Specification Information

Evidence submitted by expert panel

Limb Girdle Muscular Dystrophy VCEP

The NM_000023.4: c.197T>A variant in SGCA is a missense variant predicted to cause substitution of leucine by histidine at amino acid 66, p.(Leu66His). This variant has been detected in at least 10 individuals with limb-girdle muscular dystrophy, all of them were homozygous for the variant (1 pt; PMIDs: 33552634, 30564623, 31069529, 35416532) (PM3). At least one patient homozygous for this variant displayed progressive limb girdle muscle weakness and absent alpha-sarcoglycan protein expression, which is highly specific for SGCA-related LGMD (PP4_Strong; PMID: 35416532). The upper bound of the 95% confidence interval of the Grpmax variant allele frequency in gnomAD v4.1.1 is 0.0001724 (9/91072 South Asian alleles), which is higher than the LGMD VCEP threshold (<0.00009) for PM2_Supporting, and therefore does not meet this criterion. An in vitro assay in a heterologous cell system has demonstrated that this variant disrupts membrane localization of the sarcoglycan complex, indicating disruption of protein function (PS3_Moderate, Washington University internal data). The computational predictor REVEL also gives a score of 0.887, which is above the threshold of 0.7, evidence that correlates with impact to SGCA function (PP3). In summary, this variant meets the criteria to be classified as Likely 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): PM3, PP4_Strong, PS3_Moderate, PP3.

Met criteria codes

PP4_Strong	i	✓	At least one patient homozygous for this variant displayed progressive limb girdle muscle weakness and absent alpha-sarcoglycan protein expression, which is highly specific for SGCA-related LGMD (PP4_Strong; PMID: 35416532).
PS3_Moderate	i	✓	An in vitro assay in a heterologous cell system has demonstrated that this variant disrupts membrane localization of the sarcoglycan complex, indicating disruption of protein function (PS3_Moderate, Washington University internal data). score -0.97 (WashU assay), -2.21 (Lek Yale assay)
PP3	i	✓	The computational predictor REVEL gives a score of 0.887, which is above the threshold of 0.7, evidence that correlates with impact to SGCA function (PP3).
PM3	i	✓	This variant has been detected in at least 10 individuals with limb-girdle muscular dystrophy, all of whom were homozygous for the variant (1 pt; PMIDs: 33552634, 30564623, 31069529, 35416532) (PM3).

Not Met criteria codes

BS1	i	✗	The filtering allele frequency of the variant is 0.000051556 for South Asian alleles in gnomAD v4.1.0 (the lower threshold of the 95% CI of 9/91072), which is lower than the LGMD VCEP threshold (>0.0009) for BS1, and therefore does not meet this criterion.
PM2		✗	The upper bound of the 95% confidence interval of the Grpmax variant allele frequency in gnomAD v4.1.1 is 0.0001724 (9/91072 South Asian alleles), which is higher than the LGMD VCEP threshold (<0.00009) for

PM2_Supporting, and therefore does not meet this criterion. This variant seems to be a South Asian founder variant.

Curation History [↗](#)

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See Report	Preferred Variant Title	Classification ⓘ	Condition	Published Date	Version ⓘ	Criteria Specification	Gene
View	NM_000023.4(SGCA):c.197T>A (p.Leu6...	Likely Pathogenic	Autosomal Recessive Limb-Girdle Muscular Dystrophy ↗	2026-05-07	1.0	ClinGen Limb Girdle Muscular Dystrophy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for SGCA Version 2.0.0 ↗	SGCA ↗

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