

Variant: *NM_000023.4(SGCA):c.92T>C (p.Leu31Pro)*

Version: 1.0

CA291535993 [↗](#)

550333 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 2156a9b5-22cf-4671-bde6-58a8a5941ae2

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HGVS expressions

NM_000023.4:c.92T>C

NM_000023.4(SGCA):c.92T>C (p.Leu31Pro)

NC_000017.11:g.50167422T>C

CM000679.2:g.50167422T>C

NC_000017.10:g.48244783T>C

CM000679.1:g.48244783T>C

NC_000017.9:g.45599782T>C

NG_008889.1:g.6418T>C

ENST00000504073.2:c.92T>C

ENST00000511303.6:n.38-525T>C

ENST00000512526.2:c.92T>C

ENST00000682109.1:c.38-160T>C

ENST00000683294.1:c.92T>C

ENST00000262018.8:c.92T>C

ENST00000262018.7:c.92T>C

ENST00000344627.10:c.92T>C

ENST00000502555.5:c.92T>C

ENST00000511303.5:c.34-525T>C

ENST00000513821.5:c.92T>C

ENST00000513942.5:n.104-525T>C

ENST00000514934.1:c.151T>C

NM_000023.2:c.92T>C

NM_001135697.1:c.92T>C

NM_000023.3:c.92T>C

NM_001135697.2:c.92T>C

NR_135553.1:n.148T>C

NM_001135697.3:c.92T>C

NR_135553.2:n.128T>C

Pathogenic

Met criteria codes 4

PS3_Supporting

PM3_Very Strong

PP4

PM2_Supporting

Not Met criteria codes 2

PP1

PP3

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.92T>C variant in SGCA is a missense variant predicted to cause substitution of leucine by proline at amino acid 131, p. (Leu31Pro). This variant has been detected in at least nine individuals with limb-girdle muscular dystrophy. Of those individuals, eight were presumed compound heterozygous for the variant and a second pathogenic or likely pathogenic variant (c.229C>T, c.739G>A, c.850C>T, c.101G>A, c.957-11C>G; 3.5 pts, PMID: 39678382, 32875335, 32528171, 12566530, 9032047, 17994539, ClinVar SCV001432771.2 internal data communication). Another individual was homozygous for the variant without reported consanguinity (0.5 pts; PMID: 18285821) (PM3_Very Strong). At least one patient heterozygous for this variant and a second diagnostic SGCA variant displayed progressive limb girdle muscle weakness and partial loss of alpha-sarcoglycan protein expression, the extent of which could not be confirmed (PP4; ClinVar SCV001432771.2 internal data communication). The variant has been reported to segregate with autosomal recessive limb girdle muscular dystrophy in two affected siblings from one family, but phase was not confirmed (PMID: 32875335; PP1 not met). The upper bound of the 95% confidence interval of the Grpmax variant allele frequency in gnomAD v4.1.1 is 0.000004598 (10/1180008 European (non-Finnish) alleles), which is lower than the LGMD VCEP threshold (<0.00009) for PM2_Supporting, and therefore meets this criterion. In vitro assays have demonstrated that this variant disrupts membrane localization of the sarcoglycan complex (PMID: 22095924; PS3_Supporting). The computational predictor REVEL gives a score of 0.586, which is below the threshold of 0.7 (PP3 not met). 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; 05/01/2026): PM3_Very Strong, PP4, PM2_Supporting, PS3_Supporting.

Met criteria codes

PS3_Supporting			In vitro assays have demonstrated that this variant disrupts membrane localization of the sarcoglycan complex (PMID: 22095924; PS3_Supporting). -0.44 in WashU assay, -1.9 in Lek/Yale assay
PM3_Very Strong			This variant has been detected in at least nine individuals with limb-girdle muscular dystrophy. Of those individuals, eight were presumed compound heterozygous for the variant and a second pathogenic or likely pathogenic variant (c.229C>T, c.739G>A, c.850C>T, c.101G>A, c.957-11C>G; 3.5 pts, PMID: 39678382, 32875335, 32528171, 12566530, 9032047, 17994539, ClinVar SCV001432771.2 internal data communication). Another individual was homozygous for the variant without reported consanguinity (0.5 pts; PMID: 18285821) (PM3_Very Strong). co-occurrence checked, classifications independent
PP4			At least one patient heterozygous for this variant and a second diagnostic SGCA variant displayed progressive limb girdle muscle weakness and partial loss of alpha-sarcoglycan protein expression, the extent of which could not be confirmed (PP4; ClinVar SCV001432771.2 internal data communication).
PM2_Supporting			The upper bound of the 95% confidence interval of the Grpmax variant allele frequency in gnomAD v4.1.1 is 0.000004598 (10/1180008 European (non-Finnish) alleles), which is lower than the LGMD VCEP threshold (<0.00009) for PM2_Supporting, and therefore meets this criterion.

Not Met criteria codes

PP1



The variant has been reported to segregate with autosomal recessive limb girdle muscular dystrophy in two affected siblings from one family, but phase was not confirmed (PMID: 32875335; PP1 not met).

PP3



The computational predictor REVEL gives a score of 0.586, which is below the threshold of 0.7 (PP3 not met).

Curation History

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