

Variant: *NM_000232.5(SGCB):c.265G>A (p.Val89Met)*

Version: 1.0

CA2918446 [↗](#)

551805 (ClinVar) [↗](#)

Gene: SGCB ([HGNC:6443](#))

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

Inheritance Mode: Autosomal recessive inheritance

UUID: f98879f1-c7ae-43f8-9b74-3c53efca968b

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HGVS expressions

NM_000232.5(SGCB):c.265G>A (p.Val89Met)

NM_000232.5:c.265G>A

NC_000004.12:g.52029842C>T

CM000666.2:g.52029842C>T

NC_000004.11:g.52896008C>T

CM000666.1:g.52896008C>T

NC_000004.10:g.52590765C>T

NG_008891.1:g.13478G>A

ENST00000381431.10:c.265G>A

ENST00000381431.9:c.265G>A

ENST00000506357.5:c.348G>A

ENST00000514133.1:c.342G>A

NM_000232.4:c.265G>A

Likely Pathogenic

Met criteria codes **5**

PM2_Supporting

PP1

PP3

PP4

PM3_Strong

Evidence Links **0**

Expert Panel

Limb Girdle Muscular Dystrophy VCEP [↗](#)

Criteria Specification Information

[↗](#) **Criteria Specification:** ClinGen Limb Girdle Muscular Dystrophy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for SGCB Version 1.0.0

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Limb Girdle Muscular Dystrophy VCEP

The NM_000232.5: c.265G>A variant in SGCB is a missense variant predicted to cause substitution of valine by methionine at amino acid 89 (p.Val89Met). This variant has been detected in at least four individuals with symptoms of limb girdle muscular dystrophy. Of those individuals, one was compound heterozygous for the variant and a pathogenic variant (c.391C>T p.(Arg131Ter), 1 pt, ClinVar SCV000748307.5 internal data communication), and three patients were homozygous for the variant (1 pt, PMID: 28889091, 30838351, 29797799) (PM3_Strong). At least one of these patients displayed progressive limb girdle muscle weakness (PP4). This variant was also

shown to co-segregate with autosomal recessive LGMD in one affected family member (PMID: 28889091; PP1). The highest population minor allele frequency in gnomAD v2.1.1 is 0.00003 in the Admixed American population (1/34588 exome alleles), which is lower than the LGMD VCEP threshold (<0.00009) for PM2_Supporting, meeting this criterion (PM2_Supporting). The computational predictor REVEL gives a score of 0.932, which is above the threshold of 0.7, evidence that correlates with impact to SGCB 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 1.0.0; 01/08/2025): PM3_Strong, PP4, PM2_Supporting, PP3, PP1.

Met criteria codes

PM2_Supporting			The highest population minor allele frequency in gnomAD v2.1.1 is 0.00003 (1/34588 exome alleles) in the Admixed American population, which is lower than the ClinGen Limb-Girdle Muscular Dystrophy threshold (<0.00009) for PM2_Supporting, meeting this criterion (PM2_Supporting).
PP1			This variant was shown to co-segregate with autosomal recessive LGMD in one affected family member (PMID: 28889091).
PP3			The computational predictor REVEL gives a score of 0.932, which is above the threshold of 0.7, evidence that correlates with impact to SGCB function (PP3).
PP4			At least one patient with this variant and a second presumed diagnostic variant in SGCB displayed progressive limb girdle muscle weakness (PP4). ARC note: all SGC genes screened in Yis et al. patient but "deficient" provides insufficient detail about magnitude of reduction. Cannot confirm all SGC genes screened in GeneDx patient though it seems likely.
PM3_Strong			This variant has been detected in at least four individuals with autosomal recessive limb girdle muscular dystrophy. Of those individuals, one was compound heterozygous for the variant and a pathogenic variant (c.391C>T p. (Arg131Ter), 1 pt, SCV000748307.5 internal data communication), and three patients were homozygous for the variant (1 pt, PMID: 28889091, 30838351, 29797799) (PM3_Strong).

Curation History

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