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Variant: NM_000232.5(SGCB):c.85A>T (p.Arg29Ter)

Version: 1.0

CA2918507

370775 (ClinVar)

Gene: SGCB (HGNC:6443)
Condition: autosomal recessive limb-girdle muscular dystrophy (MONDO:0015152)
Inheritance Mode: Autosomal recessive inheritance
UUID: 3ecc72a9-be2b-4c08-9471-c6d726ba0543
Approved on: 2025/1/9
Published on: 2025/1/9

HGVS expressions

NM_000232.5(SGCB):c.85A>T (p.Arg29Ter)
NM_000232.5:c.85A>T
NC_000004.12:g.52033589T>A
CM000666.2:g.52033589T>A
NC_000004.11:g.52899755T>A
CM000666.1:g.52899755T>A
NC_000004.10:g.52594512T>A
NG_008891.1:g.9731A>T
ENST00000381431.10:c.85A>T
ENST00000381431.9:c.85A>T
ENST00000506357.5:c.71A>T
ENST00000514133.1:c.52A>T
NM_000232.4:c.85A>T

Pathogenic

Met criteria codes 4

PVS1_Moderate PP4_Strong PM3_Strong PM2_Supporting

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.85A>T p.(Arg29Ter) variant in SGCB is a nonsense variant that may cause loss of function of the protein. However, the premature stop encoded by this variant occurs within the first 100 base pairs, and the resulting transcript may escape nonsense mediated decay. The next in-frame methionine is at amino acid 100, and non-truncating variants upstream of this alternative start site are classified as likely pathogenic or pathogenic (c.265G>A p.(Val89Met), c.271C>T p.(Arg91Cys)) (PVS1_Moderate). This variant has been detected in at least five individuals with signs of limb girdle muscular dystrophy (PMID: 11369190, 17994539, 25862795), including confirmed in trans

with a likely pathogenic or pathogenic variant (c.377_384dup p.(Gly128GlnfsTer2), 1.0 pt; c.271C>T p.(Arg91Cys), 1.0 pt; PMID: 17994539, 25862795, 11369190) (PM3_Strong). At least one patient with this variant showed progressive limb girdle muscle weakness and absent or severely reduced expression of β-sarcoglycan protein in skeletal muscle, which is highly specific for SGCB-related LGMD (PP4_Strong; PMID: 25862795). The highest minor allele frequency of this variant is 0.00001758 in the European (non-Finnish) population in gnomAD v2.1.1 (2/113756 exome chromosomes), which is lower than the LGMD VCEP threshold (<0.00009) for PM2_Supporting, meeting this criterion (PM2_Supporting). 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 1.0.0; 01/09/2025): PVS1_Moderate, PM3_Strong, PP4_Strong, PM2_Supporting.

Met criteria codes

PVS1_Moderate ✔	The NM_000232.5: c.85A>T p.(Arg29Ter) variant in SGCB is a nonsense variant that may cause loss of function of the protein. However, the premature stop encoded by this variant occurs within the first 100 base pairs, and the resulting transcript may escape nonsense mediated decay. The next in-frame methionine is at amino acid 100, and non-truncating variants upstream of this alternative start site are classified as likely pathogenic or pathogenic (c.265G>A p.(Val89Met), c.271C>T p.(Arg91Cys)) (PVS1_Moderate).
PP4_Strong ✔	At least one patient with this variant showed progressive limb girdle muscle weakness and absent or severely reduced expression of β-sarcoglycan in skeletal muscle, which is highly specific for SGCB-related LGMD (PP4_Strong; PMID: 25862795).
PM3_Strong ✔	This variant has been detected in at least five individuals with signs of limb girdle muscular dystrophy (PMID: 11369190, 17994539, 25862795), including confirmed in trans with a likely pathogenic or pathogenic variant (c.377_384dup p.(Gly128GlnfsTer2), 1.0 pt; c.271C>T p.(Arg91Cys), 1.0 pt; PMID: 17994539, 25862795, 11369190) (PM3_Strong).
PM2_Supporting ✔	The minor allele frequency of this variant is 0.00001758 in the European (non-Finnish) population in gnomAD v2.1.1 (2/113756 exome chromosomes), which is lower than the LGMD VCEP threshold (<0.00009) for PM2_Supporting, meeting this criterion (PM2_Supporting).

Curation History

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