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Variant: NM_000232.5(SGCB):c.341C>T (p.Ser114Phe)

Version: 1.0

CA202230

42035 (ClinVar)

Gene: SGCB (HGNC:6443)
Condition: autosomal recessive limb-girdle muscular dystrophy (MONDO:0015152)
Inheritance Mode: Autosomal recessive inheritance
UUID: 454cbdbd-ffd5-4e34-87c4-44c95d6f4b7e
Approved on: 2026/4/29
Published on: 2026/5/7

HGVS expressions

NM_000232.5:c.341C>T
NM_000232.5(SGCB):c.341C>T (p.Ser114Phe)
NC_000004.12:g.52029766G>A
CM000666.2:g.52029766G>A
NC_000004.11:g.52895932G>A
CM000666.1:g.52895932G>A
NC_000004.10:g.52590689G>A
NG_008891.1:g.13554C>T
ENST00000381431.10:c.341C>T
ENST00000381431.9:c.341C>T
ENST00000506357.5:c.424C>T
ENST00000514133.1:c.418C>T
NM_000232.4:c.341C>T

Pathogenic

Met criteria codes 5

PP3 PS3_Moderate PP1_Moderate PP4_Moderate PM3_Strong

Not Met criteria codes 2

PM2 BS1

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 2.0.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Limb Girdle Muscular Dystrophy VCEP

The NM_000232.5(SGCB): c.341C>T variant in SGCB is a missense variant predicted to cause substitution of serine by phenylalanine at amino acid 114, p.(Ser114Phe). This variant has been detected in at least 29 individuals with limb girdle muscular dystrophy. Of those individuals, five had a likely pathogenic variant in unconfirmed phase (c.31C>T p.(Gln11Ter), 0.25 pts x5, PMIDs: 32875335, 30919934). Another 24 individuals were homozygous for the variant (1 pt, PMIDs: 25862795, 29970176, 25135358, 20071171, 30919934, 18996010, 26404900, 18285821, 9032047, 10942431) (PM3_Strong). The variant has been reported to segregate with autosomal recessive limb-girdle

muscular dystrophy in two pairs of affected siblings from two families (PP1_Moderate; PMIDs: 30919934, 20071171). At least one patient homozygous for this variant displayed progressive limb girdle muscle weakness and absent beta-sarcoglycan protein expression, which is highly specific for SGCB-related LGMD (PMID: 10942431; PP4_Moderate) (capped with PP1_Moderate). An in vitro assay in a heterologous cell system has demonstrated that this variant disrupts membrane localization of the sarcoglycan complex (PMID: 37317968; PS3_Moderate). The computational predictor REVEL gives a score of 0.855, which is above the threshold of 0.7, evidence that correlates with impact to SGCB function (PP3). The upper bound of the 95% confidence interval of the Grpmax variant allele frequency in gnomAD v4.1.1 (725/1179486 European (non-Finnish) chromosomes), which is higher than the LGMD VCEP threshold (<0.00009) for PM2_Supporting, and therefore does not meet 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 (specifications version v2.0.0; 04/29/2026): PM3_Strong, PS3_Moderate, PP1_Moderate, PP4_Moderate, PP3.

Met criteria codes

PP3	✔	The computational predictor REVEL gives a score of 0.855, which is above the threshold of 0.7, evidence that correlates with impact to SGCB function (PP3).
PS3_Moderate	✔	In vitro assay in an heterologous cell system has demonstrated that this variant disrupts membrane localization of the sarcoglycan complex (PMID: 37317968; PS3_Moderate).
PP1_Moderate	✔	The variant has been reported to segregate with Limb-girdle muscular dystrophy in two pairs of affected siblings from two families (PP1_Moderate; PMIDs: 30919934, 20071171).
PP4_Moderate	✔	At least one patient with this variant displayed progressive limb girdle muscle weakness and reduced Beta-sarcoglycan protein expression, which is highly specific for SGCB-related LGMD (PMID: 10942431; PP4_Moderate) (capped with PP1_Moderate).
PM3_Strong	✔	This variant has been detected in at least 29 individuals with limb girdle muscular dystrophy. Of those individuals, five had a likely pathogenic variant in unconfirmed phase (c.31C>T p.(Gln11Ter), 0.25 pts x5, PMIDs: 32875335, 30919934). Another 24 individuals were homozygous for the variant (1 pt, PMIDs: 25862795, 29970176, 25135358, 20071171, 30919934, 18996010, 26404900, 18285821, 9032047, 10942431) (PM3_Strong).

Not Met criteria codes

PM2	✖	The upper bound of the 95% confidence interval of the Grpmax variant allele frequency in gnomAD v4.1.1 (725/1179486 European (non-Finnish) chromosomes), which is higher than the LGMD VCEP threshold (<0.00009) for PM2_Supporting, and therefore does not meet this criterion.
BS1	✖	The filtering allele frequency of the variant is 0.0005776 for Non-Finnish European alleles in gnomAD v4.1.0 (the lower threshold of the 95% CI of 725/1179486), which is higher than the LGMD VCEP threshold (>0.0009) for BS1, and therefore does not meet this criterion.

Curation History

Showing 1 to 1 of 1 rows

See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_000232.5(SGCB):c.341C>T (p.Ser1…	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 SGCB Version 2.0.0	SGCB

Showing 1 to 1 of 1 rows

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