

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

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HGVS expressions

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

NM_000232.5:c.341C>T

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

PP4_Moderate

PM3_Strong

PS3_Moderate

PP3

PP1_Moderate

Not Met criteria codes 2

BS1

PM2

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 (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

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).
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).
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).
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).

Not Met criteria codes

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.
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.

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