

Variant: *NM_000232.5(SGCB):c.452C>G (p.Thr151Arg)*

Version: 1.0

CA119849 [↗](#)

8712 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 4e43b5fa-2280-41ca-9107-05d165133751

Approved on: 2025/1/9

Published on: 2025/1/9

HGVS expressions

NM_000232.5(SGCB):c.452C>G (p.Thr151Arg)

NM_000232.5:c.452C>G

NC_000004.12:g.52028899G>C

CM000666.2:g.52028899G>C

NC_000004.11:g.52895065G>C

CM000666.1:g.52895065G>C

NC_000004.10:g.52589822G>C

NG_008891.1:g.14421C>G

ENST00000381431.10:c.452C>G

ENST00000381431.9:c.452C>G

ENST00000506357.5:c.535C>G

ENST00000514133.1:c.529C>G

NM_000232.4:c.452C>G

Pathogenic

Met criteria codes **6**

PM3_Strong

PP1_Moderate

PS3_Moderate

PP3

PP4

PM2_Supporting

Evidence Links **1**

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.452C>G variant in SGCB is a missense variant predicted to cause substitution of threonine by arginine at amino acid 151 p.(Thr151Arg). This variant has been detected in at least five individuals with signs of limb girdle muscular dystrophy, including in a homozygous state (1.0 pt; PMID: 30564623, 21480868, 7581448) and confirmed in trans with a pathogenic variant (c.271C>T p.(Arg91Cys), 1.0 pt, PMID: 9565988) (PM3_Strong). At least one patient with this variant was clinically suspected to have limb girdle muscular dystrophy (PP4). The variant has also been shown to segregate with autosomal recessive LGMD in at least 5 affected family members in

families from the Plain community in southern Indiana and has been proposed as a founder variant for this population (PP1_Moderate; PMID: 7581448, 9565988, 28615891, 3083835). The minor allele frequency of this variant is 0.00006498 for European (non-Finnish) chromosomes in gnomAD v2.1.1 (1/15390), which is lower than the LGMD VCEP threshold (<0.00009) for PM2_Supporting, and therefore meets this criterion (PM2_Supporting). In vitro assays of membrane localization in HEK293 and HER-911 cells showed that expression of p.Thr151Arg in β -sarcoglycan disrupted localization of both the β -sarcoglycan subunit and the sarcoglycan complex to the plasma membrane, indicating an impact of the variant on protein function (PMID: 37317968, 22095924) (PS3_Moderate). The computational predictor REVEL gives a score of 0.87, which is above the LGMD VCEP threshold of 0.70, evidence that correlates with impact to SGCB function (PP3). 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): PM3_Strong, PP4, PP1_Moderate, PM2_Supporting, PS3_Moderate, PP3.

Met criteria codes

PM3_Strong			This variant has been detected in at least five individuals with signs of limb girdle muscular dystrophy, including in a homozygous state (1.0 pt; PMID: 30564623, 21480868, 7581448) and confirmed in trans with a pathogenic variant (c.271C>T p.(Arg91Cys), 1.0 pt, PMID: 9565988) (PM3_Strong).
PP1_Moderate			The variant has been reported to segregate with LGMD in at least 5 affected family members in families from the Plain community in southern Indiana and has been proposed as a founder variant for this population (PP1_Moderate; PMID: 7581448, 9565988, 28615891, 3083835).
PS3_Moderate			In vitro assays of membrane localization in HEK293 and HER-911 cells showed that expression of p.Thr151Arg in β -sarcoglycan disrupted localization of both the β -sarcoglycan subunit and the sarcoglycan complex to the plasma membrane, indicating an impact of the c.452C>G p.(Thr151Arg) variant on protein function (PMID: 37317968, 22095924) (PS3_Moderate).
			Disrupts sarcoglycan complex cell surface localization in a cell culture assay. PubMed:37317968 
PP3			The computational predictor REVEL gives a score of 0.87, which is above the LGMD VCEP threshold of 0.70, evidence that correlates with impact to SGCB function (PP3).
PP4			At least one patient with this variant was clinically suspected to have limb girdle muscular dystrophy (PP4).
PM2_Supporting			The minor allele frequency of this variant is 0.00006498 for European (non-Finnish) chromosomes in gnomAD v2.1.1 (1/15390), which is lower than the LGMD VCEP threshold (<0.00009) for PM2_Supporting, and therefore meets this criterion (PM2_Supporting).

Curation History 

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Showing 1 to 1 of 1 rows

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