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Variant: NM_000023.4(SGCA):c.502G>A (p.Gly168Arg)

Version: 1.0

CA8643815

498275 (ClinVar)

Gene: SGCA (HGNC:6442)
Condition: autosomal recessive limb-girdle muscular dystrophy (MONDO:0015152)
Inheritance Mode: Autosomal recessive inheritance
UUID: 6ab30f87-9161-449b-aa5c-d25719909456
Approved on: 2026/4/29
Published on: 2026/5/7

HGVS expressions

NM_000023.4(SGCA):c.502G>A (p.Gly168Arg)
NM_000023.4:c.502G>A
NC_000017.11:g.50168490G>A
CM000679.2:g.50168490G>A
NC_000017.10:g.48245851G>A
CM000679.1:g.48245851G>A
NC_000017.9:g.45600850G>A
NG_008889.1:g.7486G>A
ENST00000504073.2:c.502G>A
ENST00000511303.6:n.227G>A
ENST00000512526.2:c.493G>A
ENST00000682109.1:c.382G>A
ENST00000683226.1:n.212G>A
ENST00000683294.1:c.502G>A
ENST00000262018.8:c.502G>A
ENST00000262018.7:c.502G>A
ENST00000344627.10:c.502G>A
ENST00000502555.5:c.*161G>A
ENST00000511303.5:c.223G>A
ENST00000512526.1:c.337G>A
ENST00000513821.5:c.502G>A
ENST00000513942.5:n.293G>A
ENST00000514934.1:c.*208G>A
NM_000023.2:c.502G>A
NM_001135697.1:c.502G>A
NM_000023.3:c.502G>A
NM_001135697.2:c.502G>A
NR_135553.1:n.558G>A
NM_001135697.3:c.502G>A
NR_135553.2:n.538G>A

Likely Pathogenic

Met criteria codes 4

PM2_Supporting PP4 PM3 PS3_Moderate

Not Met criteria codes 2

PP3 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 SGCA 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_000023.4: c.502G>A variant in SGCA is a missense variant predicted to cause substitution of glycine by arginine at amino acid 168, p.(Gly168Arg). This variant has been detected in at least three individuals with limb-girdle muscular dystrophy, where it was reported in unconfirmed phase with a likely pathogenic variant in two patients (c.241C>T p.(Arg81Cys), 0.25 pts, PMID: 31268554; c.246C>A p.(Ser82Arg), 0.25 pts, GRASP-LGMD Consortium internal data communication) and in unconfirmed phase with a pathogenic variant in the third patient (c.229C>T p.(Arg77Cys), 0.5 pts, PMID: 39678382) (PM3). At least one of these patients displayed progressive limb girdle muscle weakness (PP4; PMID: 39678382). The Grpmax variant allele frequency in gnomAD v4.1.1 is 0.00004605 (2/43432 East Asian alleles), which is less than the LGMD VCEP threshold for PM2_Supporting. In vitro assay in a heterologous cell system has demonstrated that this variant disrupts membrane localization of the sarcoglycan complex (PS3_Moderate, Washington University internal data). The computational predictor REVEL gives a score of 0.548, which is below the threshold of 0.7 (PP3 not met). In summary, this variant meets 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 2.0.0; 04/29/2026): PM3, PP4, PM2_Supporting, PS3_Moderate.

Met criteria codes

PM2_Supporting	✔	The Grpmax variant allele frequency in gnomAD v4.1.1 is 0.00004605 (2/43432 East Asian alleles), which is less than the LGMD VCEP threshold for PM2_Supporting. The upper bound of the 95% confidence interval for the European (non-Finnish) population also meets the criterion.
PP4	✔	At least one patient with this variant displayed progressive limb girdle muscle weakness (PP4; PMID: 39678382).
PM3	✔	This variant has been detected in at least three individuals with Limb-girdle muscular dystrophy, where it was reported in unconfirmed phase with a likely pathogenic variant in two patients (c.241C>T p.(Arg81Cys), 0.25 pts, PMID: 31268554; c.246C>A p.(Ser82Arg), 0.25 pts, GRASP-LGMD Consortium internal data communication) and in unconfirmed phase with a pathogenic variant in the third patient (c.229C>T p.(Arg77Cys), 0.5 pts, PMID: 39678382) (PM3). c.229C>T, c.241C>T predicted on different haplotypes; c.246C>A not present in gnomAD v2 all variant classifications independent
PS3_Moderate	✔	In vitro assay in a heterologous cell system has demonstrated that this variant disrupts membrane localization of the sarcoglycan complex (PS3_Moderate, Washington University internal data). Concordant results across two sarcoglycan membrane localization assays: Functional score -0.85 in the WashU assay and -1.5 in Yale assay

Not Met criteria codes

PP3	✖	The computational predictor REVEL gives a score of 0.548, which is below the threshold of 0.7 (PP3 not met). SpliceAI: 0.00
BS1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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