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Variant: NM_000023.4(SGCA):c.246C>A (p.Ser82Arg)

Version: 1.0

CA400177611

813953 (ClinVar)

Gene: SGCA (HGNC:6442)
Condition: autosomal recessive limb-girdle muscular dystrophy (MONDO:0015152)
Inheritance Mode: Autosomal recessive inheritance
UUID: 687cc694-7cdd-495d-80da-00e0e769be3f
Approved on: 2026/4/29
Published on: 2026/5/7

HGVS expressions

NM_000023.4(SGCA):c.246C>A (p.Ser82Arg)
NM_000023.4:c.246C>A
NC_000017.11:g.50167670C>A
CM000679.2:g.50167670C>A
NC_000017.10:g.48245031C>A
CM000679.1:g.48245031C>A
NC_000017.9:g.45600030C>A
NG_008889.1:g.6666C>A
ENST00000504073.2:c.246C>A
ENST00000511303.6:n.38-277C>A
ENST00000512526.2:c.246C>A
ENST00000682109.1:c.126C>A
ENST00000683294.1:c.246C>A
ENST00000262018.8:c.246C>A
ENST00000262018.7:c.246C>A
ENST00000344627.10:c.246C>A
ENST00000502555.5:c.157+183C>A
ENST00000511303.5:c.34-277C>A
ENST00000512526.1:c.90C>A
ENST00000513821.5:c.246C>A
ENST00000513942.5:n.104-277C>A
ENST00000514934.1:c.*18+183C>A
NM_000023.2:c.246C>A
NM_001135697.1:c.246C>A
NM_000023.3:c.246C>A
NM_001135697.2:c.246C>A
NR_135553.1:n.302C>A
NM_001135697.3:c.246C>A
NR_135553.2:n.282C>A

Likely Pathogenic

Met criteria codes 4

PM3 PS3_Moderate PM2_Supporting PP4

Not Met criteria codes 1

Expert Panel

Limb Girdle Muscular Dystrophy VCEP

Criteria Specification Information

PP3

Evidence Links 0

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.246C>A variant in SGCA is a missense variant predicted to cause substitution of serine by arginine at amino acid 82, p.(Ser82Arg). This variant has been detected in at least four homozygous individuals with limb-girdle muscular dystrophy of Iranian ancestry (1 pt, ClinVar: SCV001164458.1; PMID: 39678382, 38374194, 32528171, 41315541) (PM3). At least one patient with this variant displayed progressive limb girdle muscle weakness (PP4; PMID: 32528171, 41315541). 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). This variant is absent from gnomAD v4.1.1 (PM2_Supporting). The computational predictor REVEL gives a score of 0.504, which is below the threshold of 0.7 (PP3 not met). In summary, this variant meets the 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, PS3_Moderate, PM2_Supporting.

Met criteria codes

PM3	✔	This variant has been detected in at least four homozygous individuals with limb-girdle muscular dystrophy of Iranian ancestry (1 pt, ClinVar: SCV001164458.1; PMID: 39678382, 38374194, 32528171, 41315541) (PM3). Note: Three reported cases are of Iranian origin
PS3_Moderate	✔	In vitro assay in an heterologous cell system has demonstrated that this variant disrupts membrane localization of the sarcoglycan complex (PS3_Moderate, Washington University internal data). Variant was tested by Gabe Haller's team using their previously reported approach for SGCB variants. The assay has been clinically validated with over 11 control variants. The variant presented a score of -1, which is les than the -0.5 threshold for non-functional variants that was used for SGCB. This variant was also classified as non-functional in Monkol's membrane localization assay, which used a slightly different method.
PM2_Supporting	✔	This variant is absent from gnomAD v4.1.1 (PM2_Supporting).
PP4	✔	At least one patient with this variant displayed progressive limb girdle muscle weakness (PP4; PMID: 32528171, 41315541).

Not Met criteria codes

PP3	✖	The computational predictor REVEL gives a score of 0.504, which is below the threshold of 0.7 (PP3 not met). SpliceAI 0.03

Curation History

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