

Variant: *NM_000023.4(SGCA):c.101G>A (p.Arg34His)*

Version: 1.0

CA199071 [↗](#)

92301 (ClinVar) [↗](#)

Gene: SGCA ([HGNC:6442](#))

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 5fe1934d-e35e-4f18-9095-389cc95f3639

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HGVS expressions

NM_000023.4(SGCA):c.101G>A (p.Arg34His)

NM_000023.4:c.101G>A

NC_000017.11:g.50167431G>A

CM000679.2:g.50167431G>A

NC_000017.10:g.48244792G>A

CM000679.1:g.48244792G>A

NC_000017.9:g.45599791G>A

NG_008889.1:g.6427G>A

ENST00000504073.2:c.101G>A

ENST00000511303.6:n.38-516G>A

ENST00000512526.2:c.101G>A

ENST00000682109.1:c.38-151G>A

ENST00000683294.1:c.101G>A

ENST00000262018.8:c.101G>A

ENST00000262018.7:c.101G>A

ENST00000344627.10:c.101G>A

ENST00000502555.5:c.101G>A

ENST00000511303.5:c.34-516G>A

ENST00000513821.5:c.101G>A

ENST00000513942.5:n.104-516G>A

ENST00000514934.1:c.160G>A

NM_000023.2:c.101G>A

NM_001135697.1:c.101G>A

NM_000023.3:c.101G>A

NM_001135697.2:c.101G>A

NR_135553.1:n.157G>A

NM_001135697.3:c.101G>A

NR_135553.2:n.137G>A

Likely Pathogenic

Met criteria codes 4

PM2_Supporting

PP3

PM3

PP4_Strong

Not Met criteria codes 1

PM5

Expert Panel

Limb Girdle Muscular Dystrophy VCEP [↗](#)

Criteria Specification Information

Evidence submitted by expert panel

Limb Girdle Muscular Dystrophy VCEP

The NM_000023.4: c.101G>A variant in SGCA is a missense variant predicted to cause substitution of arginine by histidine at amino acid 34 (p.Arg34His). This variant has been detected in at least two individuals with autosomal recessive limb girdle muscular dystrophy. Of those individuals, one was compound heterozygous for the variant and a pathogenic or likely pathogenic variant (p.Arg77Cys, 1.0 pt, PMID: 18285821) (PM3). At least one patient with this variant and a second presumed diagnostic SGCA variant displayed progressive limb girdle muscle weakness as well as significantly reduced or absent expression of alpha-sarcoglycan protein, which is highly specific for SGCA-related LGMD (PP4_Strong; PMID: 1828582). The filtering allele frequency of this variant is 0.000023 (the upper threshold of the 95% CI of 6/113724 exome chromosomes) in the European (non-Finnish) population in gnomAD v2.1.1, which is lower than the ClinGen LGMD VCEP threshold (0.00009) for PM2_Supporting and therefore meets this criterion (PM2_Supporting). The computational predictor REVEL gives a score of 0.708, which is above the threshold of 0.7, evidence that correlates with impact to SGCA function (PP3). 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 1.0.0; 01/09/2025): PP4_Strong, PM2_Supporting, PM3, PP3.

Met criteria codes

PM2_Supporting			The filtering allele frequency of this variant is 0.000023 (the upper threshold of the 95% CI of 6/113724 exome chromosomes) in the European (non-Finnish) population in gnomAD v2.1.1, which is lower than the ClinGen LGMD VCEP threshold (0.00009) for PM2_Supporting and therefore meets this criterion (PM2_Supporting).
PP3			The computational predictor REVEL gives a score of 0.708, which is above the threshold of 0.7, evidence that correlates with impact to SGCA function (PP3).
PM3			This variant has been detected in at least two individuals with autosomal recessive limb girdle muscular dystrophy. Of those individuals, one was compound heterozygous for the variant and a pathogenic or likely pathogenic variant (p.Arg77Cys, 1.0 pt, PMID: 18285821) (PM3).
PP4_Strong			At least one patient with this variant and a second SGCA variant displayed progressive limb girdle muscle weakness as well as significantly reduced or absent expression of alpha-sarcoglycan protein, which is highly specific for SGCA-related LGMD (PP4_Strong; PMID: 1828582).

Not Met criteria codes

PM5			Cannot use PM5 as this variant was used to apply PM5 to p.Arg34Cys.
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