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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
Approved on: 2025/1/9
Published on: 2025/1/30

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

PM3 PP4_Strong PM2_Supporting PP3

Not Met criteria codes 1

PM5

Expert Panel

Limb Girdle Muscular Dystrophy VCEP

Criteria Specification Information

Evidence Links 0

Criteria Specification: *ClinGen Limb Girdle Muscular Dystrophy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for SGCA 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_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

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).
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).

Not Met criteria codes

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

Curation History

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