

Variant: NM_000023.4(SGCA):c.700G>A (p.Asp234Asn)

Version: 1.0

CA246512 [↗](#)

198031 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 3c873079-f7a8-4078-bc51-56af80495f40

Approved on: 2025/1/7

Published on: 2025/1/7

HGVS expressions

NM_000023.4(SGCA):c.700G>A (p.Asp234Asn)

NM_000023.4:c.700G>A

NC_000017.11:g.50169207G>A

CM000679.2:g.50169207G>A

NC_000017.10:g.48246568G>A

CM000679.1:g.48246568G>A

NC_000017.9:g.45601567G>A

NG_008889.1:g.8203G>A

ENST00000504073.2:c.597+103G>A

ENST00000511303.6:n.309+635G>A

ENST00000512526.2:c.575+635G>A

ENST00000682109.1:c.580G>A

ENST00000683226.1:n.410G>A

ENST00000683294.1:c.700G>A

ENST00000262018.8:c.700G>A

ENST00000262018.7:c.700G>A

ENST00000344627.10:c.584+635G>A

ENST00000502555.5:c.*359G>A

ENST00000504073.1:c.64+103G>A

ENST00000511303.5:c.305+635G>A

ENST00000512526.1:c.419+635G>A

ENST00000513821.5:c.700G>A

ENST00000513942.5:n.375+635G>A

NM_000023.2:c.700G>A

NM_001135697.1:c.584+635G>A

NM_000023.3:c.700G>A

NM_001135697.2:c.584+635G>A

NR_135553.1:n.756G>A

NM_001135697.3:c.584+635G>A

NR_135553.2:n.736G>A

Likely Pathogenic

Met criteria codes 2

PP4_StrongPM3

Not Met criteria codes 23

PS1PS2PS4PP1PP2PP3BA1BS2PM6PM2PM1PM5PM4BS1BS4BS3BP5BP7BP4BP3BP1BP2PVS1

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 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.700G>A variant in SGCA is a missense variant predicted to cause substitution of aspartic acid by asparagine at amino acid 234 (p.Asp234Asn). This variant has been detected in at least three individuals with autosomal recessive limb girdle muscular dystrophy, including in a homozygous state in two patients (1.0 pt, ClinVar SCV000769867.5 internal data communication) and in unknown phase with a variant classified as at least likely pathogenic (c.100C>T (p.Arg34Cys), 0.25 pts, Washington University internal clinic data communication) (PM3). At least one patient with this variant displayed progressive limb girdle muscle weakness as well as absent expression of alpha-sarcoglycan protein in skeletal muscle, which is highly specific for SGCA-related LGMD (PP4_Strong, Washington University internal clinic data communication). The highest minor allele frequency of this variant is 0.0005498 (19/34560 exome chromosomes) in the Admixed American population in gnomAD v2.1.1 (PM2_Supporting, BS1 not met). The computational predictor REVEL gives a score of 0.491 (BP4, 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 1.0.0; 01/07/2025)(LGMD VCEP specifications version 1.0.0; 01/07/2025): PM3, PP4_Strong.

Met criteria codes

PP4_Strong		At least one patient with this variant displayed progressive limb girdle muscle weakness as well as absent expression of alpha-sarcoglycan protein in skeletal muscle, which is highly specific for SGCA-related LGMD (PP4_Strong, Personal Contact of Dr. Wehl).
PM3		This variant has been detected in 3 individuals with autosomal recessive limb-girdle muscular dystrophy. One individual was compound heterozygous for another variant which has been curated to be likely pathogenic and confirmed in trans by family testing. 2 individuals were homozygous for the variant (2.0pt total, Personal contact of Dr. Wehl, SCV000769867.5) (PM3_Strong). ARC: phase not confirmed in GRASP-LGMD case (downgrade to PM3)

Not Met criteria codes

PS1		No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2		No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

PS4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3			0.491 vs. ≥ 0.70 (REVEL)
BA1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM6			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM2			The greatest minor allele frequency of this variant is 0.0005498 (19/34560 exome chromosomes) in the Admixed American population in gnomAD v2.1.1 (PM2, BS1 not met).
PM1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM5			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1			The highest population minor allele frequency in gnomAD v2.1.1 is 0.00055 (19/34560 alleles)
BS4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP5			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP7			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

BP4			0.491 vs. ≤ 0.10 (REVEL) AND 0.05 vs. 0.00 (SpliceAI)
BP3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PVS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History 		
Showing 1 to 1 of 1 rows		

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.