

Variant: NM_000023.4(SGCA):c.957-11C>G

Version: 1.0

CA626689269 [↗](#)

978048 (ClinVar) [↗](#)

Gene: SGCA (HGNC:6442)

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 03500fe4-c6cb-4d45-8fb2-d65d5a1d8a10

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HGVS expressions

NM_000023.4:c.957-11C>G

NM_000023.4(SGCA):c.957-11C>G

NC_000017.11:g.50170629C>G

CM000679.2:g.50170629C>G

NC_000017.10:g.48247990C>G

CM000679.1:g.48247990C>G

NC_000017.9:g.45602989C>G

NG_008889.1:g.9625C>G

ENST00000504073.2:c.807-11C>G

ENST00000511303.6:n.310-11C>G

ENST00000512526.2:c.576-11C>G

ENST00000682109.1:c.837-11C>G

ENST00000683226.1:n.1555-11C>G

ENST00000683294.1:c.*60-11C>G

ENST00000683544.1:n.600C>G

ENST00000262018.8:c.957-11C>G

ENST00000262018.7:c.957-11C>G

ENST00000344627.10:c.585-11C>G

ENST00000504073.1:c.274-11C>G

ENST00000511303.5:c.306-11C>G

ENST00000512526.1:c.420-11C>G

ENST00000513821.5:c.748-11C>G

ENST00000513942.5:n.376-11C>G

NM_000023.2:c.957-11C>G

NM_001135697.1:c.585-11C>G

NM_000023.3:c.957-11C>G

NM_001135697.2:c.585-11C>G

NR_135553.1:n.804-11C>G

NM_001135697.3:c.585-11C>G

NR_135553.2:n.784-11C>G

Likely Pathogenic

Met criteria codes 4

PM2_Supporting PP4_Strong PP3
PM3

Not Met criteria codes 22

BA1 BS1 BS4 BS3 BS2 BP5
BP7 BP4 BP3 BP1 BP2 PS1
PS2 PS3 PS4 PVS1 PP1
PP2 PM1 PM5 PM4 PM6

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.957-11C>G variant in SGCA is an intronic variant located in intron 7 of 9. This variant has been detected in at least two individuals with autosomal recessive limb girdle muscular dystrophy, where it was identified in unknown phase or confirmed in trans with a pathogenic or likely pathogenic variant (c.229C>T p.(Arg77Cys), 0.5 pts, PMID: 32153140; c.850C>T p.(Arg284Cys), 1.0 pt, UCSD internal clinic data communication) (PM3). At least one patient with this variant displayed progressive limb girdle muscle weakness as well as significantly reduced or absent expression of encoded alpha-sarcoglycan protein, which is highly specific for SGCA-related LGMD (PP4_Strong, UCSD internal clinic data communication). The highest minor allele frequency of this variant is 0.00002940 (2/68034 genome chromosomes) in the European (non-Finnish) population of gnomAD v3.1.2, which is less than the ClinGen LGMD VCEP threshold for PM2_Supporting (0.00009), meeting this criterion (PM2_Supporting). SpliceAI predicts the loss of the native acceptor site with a score of 0.49 and gain of a cryptic site with a score of 0.63, meeting criteria for 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; 01/08/2025): PP4_Strong, PM3, PP3, PM2_Supporting.

Met criteria codes

PM2_Supporting			The highest minor allele frequency of this variant is 0.00002940 (2/68034 genome chromosomes) in the European (non-Finnish) population of gnomAD v3.1.2, which is less than the ClinGen LGMD VCEP threshold for PM2_Supporting (0.00009), meeting this criterion (PM2_Supporting).
PP4_Strong			At least one patient with this 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; internal clinic data).
PP3			SpliceAI predicts the loss of the native acceptor site with a score of 0.49 and gain of a cryptic site with a score of 0.63, meeting criteria for PP3.
PM3			This variant has been detected in at least two individuals with autosomal recessive limb girdle muscular dystrophy, where it was identified in unknown phase or confirmed in trans with a pathogenic or likely pathogenic variant (1.5 pts, PMID: 32153140, internal clinic data) (PM3).

Not Met criteria codes



BA1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
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
BS2			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			The c.957-11C>G variant is an intronic variant. BP7 was not applied because although the nucleotide has a PhyloP score of -1.67 (indicating that it not highly conserved), SpliceAI does predict an impact on splicing (acceptor loss score: 0.49, BP7 threshold of 0.00).
BP4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
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
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
PS3			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

PVS1			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
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
PM6			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History [↗](#)



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See Report	Preferred Variant Title	Classification 	Condition	Published Date	Version 	Criteria Specification	Gene
View	NM_000023.4(SGCA):c.957-11C>G	Likely Pathogenic	Autosomal Recessive Limb-Girdle Muscular Dystrophy ↗	2025-01-08	1.0	ClinGen Limb Girdle Muscular Dystrophy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for SGCA Version 1.0.0 ↗	SGCA ↗

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