

Variant: NM_000023.4(SGCA):c.739G>A (p.Val247Met)

Version: 1.0

CA203189 [↗](#)

167677 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 444cc7d1-1fa2-4d69-a8b5-9d7fd2a48eac

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HGVS expressions

NM_000023.4:c.739G>A

NM_000023.4(SGCA):c.739G>A (p.Val247Met)

NC_000017.11:g.50169246G>A

CM000679.2:g.50169246G>A

NC_000017.10:g.48246607G>A

CM000679.1:g.48246607G>A

NC_000017.9:g.45601606G>A

NG_008889.1:g.8242G>A

ENST00000504073.2:c.597+142G>A

ENST00000511303.6:n.309+674G>A

ENST00000512526.2:c.575+674G>A

ENST00000682109.1:c.619G>A

ENST00000683226.1:n.449G>A

ENST00000683294.1:c.739G>A

ENST00000262018.8:c.739G>A

ENST00000262018.7:c.739G>A

ENST00000344627.10:c.584+674G>A

ENST00000502555.5:c.*398G>A

ENST00000504073.1:c.64+142G>A

ENST00000511303.5:c.305+674G>A

ENST00000512526.1:c.419+674G>A

ENST00000513821.5:c.739G>A

ENST00000513942.5:n.375+674G>A

NM_000023.2:c.739G>A

NM_001135697.1:c.584+674G>A

NM_000023.3:c.739G>A

NM_001135697.2:c.584+674G>A

NR_135553.1:n.795G>A

NM_001135697.3:c.584+674G>A

NR_135553.2:n.775G>A

Pathogenic

Met criteria codes 4

PS3_SupportingPM3_Very StrongPP1_StrongPP4

Not Met criteria codes 3

BS1PP3PM2

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 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.739G>A variant in SGCA is a missense variant predicted to cause substitution of valine by methionine at amino acid 247, p.(Val247Met). This variant has been detected in at least 11 individuals with symptoms of limb girdle muscular dystrophy. Of those individuals, four were confirmed compound heterozygous for the variant and a pathogenic or likely pathogenic variant (c.229C>T, c.101G>A, c.850C>T, 4 pts, PMID: 30919934, 15298081, 33458577), five had a pathogenic variant in unconfirmed phase (c.229C>T, 2.5 pts, PMID: 10942431, 12566530, 31407473, 25135358) and at least three were homozygous for the variant (1 pt, PMID: 26404900, 26453141) (PM3_Very strong). The variant has been reported to segregate with autosomal recessive limb girdle muscular dystrophy in five affected family members from two families (PP1_Strong; PMID: 26404900, 15298081). At least one patient with this variant displayed progressive limb girdle muscle weakness and reduced α-sarcoglycan protein expression, which is highly specific for SGCA-related LGMD (PMID: 32528171,12566530; PP4) (capped with PP1_Strong). In an in vitro assay, this variant led to a complete loss of α-sarcoglycan at the plasma membrane, indicating that this variant impacts protein function (PMID: 22095924) (PS3_Supporting). The upper bound of the 95% confidence interval of the Grpmax variant allele frequency in gnomAD v4.1.1 is 0.0002863 for alleles in gnomAD v4.1.0 (307/1178700 European (non-Finnish) chromosomes), which is higher than the LGMD VCEP threshold (<0.00009) for PM2_Supporting, and therefore does not meet this criterion. The filtering allele frequency is also above the threshold for BS1. The computational predictor REVEL gives a score of 0.67, which is lower than the threshold of 0.7 (PP3 not met). In summary, this variant meets the criteria to be classified as 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_Very Strong, PP1_Strong, PS3_Supporting, PP4.		
Met criteria codes		
PS3_Supporting		In an in vitro assay, this variant led to a complete loss of α -sarcoglycan at the plasma membrane, indicating that this variant impacts protein function (PMID: 22095924) (PS3_Supporting).
PM3_Very Strong		This variant has been detected in at least 11 individuals with symptoms of limb girdle muscular dystrophy. Of those individuals, four were confirmed compound heterozygous for the variant and a pathogenic or likely pathogenic variant (c.229C>T, c.101G>A, c.850C>T, 4 pts, PMID: 30919934, 15298081, 33458577), five had a pathogenic variant in unconfirmed phase (c.229C>T, 2.5 pts, PMID: 10942431, 12566530, 31407473, 25135358) and at least three were homozygous for the variant (1 pt, PMID: 26404900, 26453141) (PM3_Very strong).
PP1_Strong		The variant has been reported to segregate with autosomal recessive limb girdle muscular dystrophy in five affected family members from two families (PP1_Strong; PMID: 26404900, 15298081).
PP4		At least one patient with this variant displayed progressive limb girdle muscle weakness and reduced alpha-sarcoglycan protein expression, which is highly specific for SGCA-related LGMD (PMID: 32528171,12566530; PP4) (capped with PP1_Strong).

Not Met criteria codes

BS1			The filtering allele frequency of the variant is 0.0002365 for European (non-Finnish) alleles in gnomAD v4.1.0 (the lower threshold of the 95% CI of 307/1178700), which is lower than the LGMD VCEP threshold (>0.0009) for BS1, and therefore it doesn't meet this criterion.
PP3			The computational predictor REVEL gives a score of 0.67, which is lower than the threshold of 0.7 and, therefore, this criterion is not met (PP3).
PM2			The upper bound of the 95% confidence interval of the Grpmax variant allele frequency in gnomAD v4.1.1 is 0.0002863 for alleles in gnomAD v4.1.0 (307/1178700 European (non-Finnish) chromosomes), which is higher than the LGMD VCEP threshold (<0.00009) for PM2_Supporting, and therefore does not meet this criterion.

Curation History

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