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Variant: NM_000231.3(SGCG):c.787G>A (p.Glu263Lys)

Version: 1.0

CA220515

2009 (ClinVar)

Gene: SGCG (HGNC:6445)
Condition: autosomal recessive limb-girdle muscular dystrophy (MONDO:0015152)
Inheritance Mode: Autosomal recessive inheritance
UUID: fd3c2a91-dc99-4b9c-b672-14ea492dd40d
Approved on: 2026/4/29
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HGVS expressions

NM_000231.3:c.787G>A
NM_000231.3(SGCG):c.787G>A (p.Glu263Lys)
NC_000013.11:g.23324452G>A
CM000675.2:g.23324452G>A
NC_000013.10:g.23898591G>A
CM000675.1:g.23898591G>A
NC_000013.9:g.22796591G>A
NG_008759.1:g.148532G>A
ENST00000682775.1:c.2186-12337C>T
ENST00000683210.1:c.2185+29333C>T
ENST00000684325.1:c.2186-2778C>T
ENST00000684497.1:c.2186-1808C>T
ENST00000218867.4:c.787G>A
ENST00000218867.3:c.787G>A
NM_000231.2:c.787G>A
NM_001378244.1:c.841G>A
NM_001378245.1:c.787G>A
NM_001378246.1:c.787G>A

Pathogenic

Met criteria codes 5

PP1_Strong PP3 PP4 PM3_Strong PS3_Supporting

Not Met criteria codes 2

PM2 BS1

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 SGCG 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_000231.3: c.787G>A variant in SGCG is a missense variant predicted to cause substitution of glutamic acid by lysine at amino acid 263, p.(Glu263Lys). This variant has been detected in at least eight individuals with limb-girdle muscular dystrophy. Of those individuals, three were presumed compound heterozygous for the variant and a second pathogenic variant (c.525del, 1.5 pts, PMID: 32875335, 18285821). Another five individuals were homozygous for the variant (1 pt, PMID: 27708273, 16832103, 28877744, Newcastle University internal data communication) (PM3_Strong). The variant has been reported to segregate with autosomal recessive LGMD in three affected family members from two families (PP1_Strong; PMID: 28877744, Newcastle University internal data communication). At least one patient with this variant displayed progressive limb girdle muscle weakness and reduced gamma-sarcoglycan protein expression, which is highly specific for SGCG-related LGMD (PMID: 16832103; PP4, capped with PP1_Strong). In vitro assays have demonstrated that this variant disrupts membrane localization of the sarcoglycan complex (PMID: 22095924; PS3_Supporting). The computational predictor REVEL gives a score of 0.825, which is above the threshold of 0.7, evidence that correlates with impact to SGCG function (PP3). The upper bound of the 95% confidence interval of the Grpmax variant allele frequency in gnomAD v4.1.1 is 0.000678 (30/60008 Admixed American alleles), which is higher than the LGMD VCEP threshold (<0.00009) for PM2_Supporting and therefore does not meet this criterion. 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_Strong, PP1_Strong, PS3_Supporting, PP3, PP4.

Met criteria codes

PP1_Strong	✔	The variant has been reported to segregate with autosomal recessive LGMD in three affected family members from two families (PP1_Strong; PMID: 28877744, Newcastle University internal data communication).
PP3	✔	The computational predictor REVEL gives a score of 0.825, which is above the threshold of 0.7, evidence that correlates with impact to SGCG function (PP3).
PP4	✔	At least one patient with this variant displayed progressive limb girdle muscle weakness and reduced gamma-sarcoglycan protein expression, which is highly specific for SGCG-related LGMD (PMID: 16832103; PP4, capped with PP1_Strong).
PM3_Strong	✔	This variant has been detected in at least eight individuals with limb-girdle muscular dystrophy. Of those individuals, three were presumed compound heterozygous for the variant and a second pathogenic variant (c.525del, 1.5 pts, PMID: 32875335, 18285821). Another five individuals were homozygous for the variant (1 pt, PMID: 27708273, 16832103, 28877744, Newcastle University internal data communication) (PM3_Strong).
PS3_Supporting	✔	In vitro assays have demonstrated that this variant disrupts membrane localization of the sarcoglycan complex (PMID: 22095924; PS3_Supporting).

Not Met criteria codes

PM2	✖	The upper bound of the 95% confidence interval of the Grpmax variant allele frequency in gnomAD v4.1.1 is 0.000678 (30/60008 Admixed American alleles), which is higher than the LGMD VCEP threshold (<0.00009) for PM2_Supporting and therefore does not meet this criterion.
BS1	✖	The filtering allele frequency of the variant is 0.0003599 for Admixed American alleles in gnomAD v4.1.0 (the lower threshold of the 95% CI of 30/60008), which is lower than the LGMD VCEP threshold (>0.0009) for BS1, and therefore it does not meet this criterion.

Curation History

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