

Variant: *NM_000337.6(SGCD):c.493C>T (p.Arg165Ter)*

Version: 1.0

CA340747 [↗](#)

8172 (ClinVar) [↗](#)

Gene: SGCD ([HGNC:6444](#))

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 0582aab2-d2d4-408f-99b6-f015a93bb3c5

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HGVS expressions

NM_000337.6(SGCD):c.493C>T (p.Arg165Ter)

NM_000337.6:c.493C>T

NC_000005.10:g.156595042C>T

CM000667.2:g.156595042C>T

NC_000005.9:g.156022052C>T

CM000667.1:g.156022052C>T

NC_000005.8:g.155954630C>T

NG_008693.2:g.729699C>T

ENST00000337851.9:c.493C>T

ENST00000337851.8:c.493C>T

ENST00000435422.7:c.490C>T

ENST00000517913.5:c.493C>T

NM_000337.5:c.493C>T

NM_001128209.1:c.490C>T

NM_172244.2:c.493C>T

NM_001128209.2:c.490C>T

NM_172244.3:c.493C>T

Pathogenic

Met criteria codes 4

PVS1

PM2_Supporting

PM3

PP4_Strong

Not Met criteria codes 22

BS2

BS1

BS4

BS3

BP4

BP3

BP1

BP2

BP5

BP7

BA1

PS1

PS2

PS3

PS4

PP1

PP2

PP3

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 SGCD 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_000337.6: c.493C>T p.(Arg165Ter) variant in SGCD is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 6/9, leading to nonsense mediated decay in a gene in which loss of function is an established disease mechanism (PVS1). This variant has been detected in at least three patients with limb girdle muscular dystrophy, including in homozygous state in at least two patients from two families (1.0 pt, PMID: 19770540, 10735275) (PM3). At least one patient with this variant displayed progressive limb girdle muscle weakness as well as absent delta-sarcoglycan protein expression in skeletal muscle by IHC, which is highly specific for SGCD-related LGMD (PP4_Strong; PMID: 19770540). The highest population minor allele frequency for this variant is 0.00004827 (2/41432 genome chromosomes) in the African/African American population of gnomAD v3.1.2, which is lower than the ClinGen LGMD VCEP threshold for PM2_Supporting (<0.00009), meeting this criterion (PM2_Supporting). 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 1.0.0; 01/08/2025): PVS1, PP4_Strong, PM3, PM2_Supporting.

Met criteria codes

PVS1			The NM_000337.6: c.493C>T p.(Arg165Ter) variant in SGCD is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 6/9, leading to nonsense mediated decay in a gene in which loss of function is an established disease mechanism (PVS1).
PM2_Supporting			The highest population minor allele frequency for this variant is 0.00004827 (2/41432 genome chromosomes) in the African/African American population of gnomAD v3.1.2, which is lower than the ClinGen LGMD VCEP threshold for PM2_Supporting (<0.00009), meeting this criterion (PM2_Supporting).
PM3			This variant has been detected in at least three patients with limb girdle muscular dystrophy, including in homozygous state in at least two patients from two families (1.0 pt, PMID: 19770540, 10735275) (PM3).
PP4_Strong			At least one patient with this variant displayed progressive limb girdle muscle weakness as well as absent delta-sarcoglycan protein expression in skeletal muscle by IHC, which is highly specific for SGCD-related LGMD (PP4_Strong; PMID: 19770540).

Not Met criteria codes

BS2			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
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
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
BA1		✖	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
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		✖	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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