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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
Approved on: 2025/1/8
Published on: 2025/1/8

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

PM3 PP4_Strong PVS1 PM2_Supporting

Not Met criteria codes 22

PP1 PP2 PP3 PM6 PM1 PM5 PM4 BA1 BS1 BS4 BS3 BS2 PS1 PS2 PS3 PS4 BP5 BP7 BP4 BP3 BP1 BP2

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

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).
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).

Not Met criteria codes

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
PM6	✖	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	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS4	ℹ	✖	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
PS1	ℹ	✖	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	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS4	ℹ	✖	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	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4	ℹ	✖	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

Curation History

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