

Variant: *NM_000070.3(CAPN3):c.258dup (p.Leu87fs)*

Version: 1.0

CA7510881 [↗](#)

284122 (ClinVar) [↗](#)

Gene: CAPN3 ([HGNC:825](#))

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 792ead27-5e82-4a70-8702-a85323b5b211

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HGVS expressions

NM_000070.3(CAPN3):c.258dup (p.Leu87fs)

NM_000070.3:c.258dup

NC_000015.10:g.42360063dup

CM000677.2:g.42360063dup

NC_000015.9:g.42652261dup

CM000677.1:g.42652261dup

NC_000015.8:g.40439553dup

NG_008660.1:g.16961dup

ENST00000349748.8:c.258dup

ENST00000357568.8:c.258dup

ENST00000397163.8:c.258dup

ENST00000466369.5:n.540+5610dup

ENST00000483208.5:n.540+5610dup

ENST00000495723.1:n.540+5610dup

ENST00000549793.5:n.540+5610dup

ENST00000318023.11:c.258dup

ENST00000349748.7:c.258dup

ENST00000357568.7:c.258dup

ENST00000397163.7:c.258dup

NM_000070.2:c.258dup

NM_024344.1:c.258dup

NM_173087.1:c.258dup

NM_024344.2:c.258dup

NM_173087.2:c.258dup

Pathogenic

Met criteria codes 3

PP4 PM3 PVS1

Not Met criteria codes 1

PM2

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 CAPN3 Version 2.0.0*

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

Limb Girdle Muscular Dystrophy VCEP

The NM_000070.3: c.258dup p.(Leu87SerfsTer4) variant in CAPN3 is a frameshift variant expected to cause a premature stop codon in biologically relevant exon 1/24, leading to nonsense-mediated decay in a gene in which loss of function is an established disease mechanism (PVS1). This variant has been identified in a homozygous state in at least three individuals with a clinical diagnosis or suspicion of LGMD without reported familial consanguinity (1.0 pt; PMID: 16650086, 30564623; LOVD CAPN3_000380) (PM3, PP4). The highest frequency of this variant in gnomAD v4.1.0 is 0.0002135 in the African/African American population (16/74948 alleles), which is greater than the LGMD VCEP threshold of 0.0001 (PM2_Supporting 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 Limb Girdle Muscular Dystrophy Expert Panel (specifications version 2.0.0; 02/18/2026): PVS1, PM3, PP4.

Met criteria codes

PP4			This variant has been identified in a homozygous state in at least three individuals with a clinical diagnosis or suspicion of LGMD without reported familial consanguinity (1.0 pt; PMID: 16650086, 30564623; LOVD CAPN3_000380) (PM3, PP4).
PM3			This variant has been identified in a homozygous state in at least three individuals with a clinical diagnosis or suspicion of LGMD without reported familial consanguinity (1.0 pt; PMID: 16650086, 30564623; LOVD CAPN3_000380) (PM3, PP4).
PVS1			The NM_000070.3: c.258dup p.(Leu87SerfsTer4) variant in CAPN3 is a frameshift variant expected to cause a premature stop codon in biologically relevant exon 1/24, leading to nonsense-mediated decay in a gene in which loss of function is an established disease mechanism (PVS1).

Not Met criteria codes

PM2			The highest frequency of this variant in gnomAD v4.1.0 is 0.0002135 in the African/African American population (16/74948 alleles), which is greater than the LGMD VCEP threshold of 0.0001 (PM2_Supporting not met).
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