

Variant: *NM\_000070.3(CAPN3):c.327\_328dup (p.Arg110fs)*

Version: 1.0

CA347357 [↗](#)

210563 (ClinVar) [↗](#)

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

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

**Inheritance Mode:** Autosomal recessive inheritance

**UUID:** 479a249a-0ed0-40c2-addc-c723d5e77120

**Approved on:** 2026/3/12

**Published on:** 2026/4/9

## HGVS expressions

**NM\_000070.3(CAPN3):c.327\_328dup (p.Arg110fs)**

**NM\_000070.3:c.327\_328dup**

NC\_000015.10:g.42384500\_42384501dup

CM000677.2:g.42384500\_42384501dup

NC\_000015.9:g.42676698\_42676699dup

CM000677.1:g.42676698\_42676699dup

NC\_000015.8:g.40463990\_40463991dup

NG\_008660.1:g.41398\_41399dup

ENST00000349748.8:c.327\_328dup

ENST00000357568.8:c.327\_328dup

ENST00000397163.8:c.327\_328dup

ENST00000466369.5:n.558\_559dup

ENST00000483208.5:n.558\_559dup

ENST00000495723.1:n.558\_559dup

ENST00000549793.5:n.558\_559dup

ENST00000638141.2:n.342\_343dup

ENST00000673705.1:c.18\_19dup

ENST00000318023.11:c.327\_328dup

ENST00000349748.7:c.327\_328dup

ENST00000357568.7:c.327\_328dup

ENST00000397163.7:c.327\_328dup

NM\_000070.2:c.327\_328dup

NM\_024344.1:c.327\_328dup

NM\_173087.1:c.327\_328dup

NM\_024344.2:c.327\_328dup

NM\_173087.2:c.327\_328dup

**Pathogenic**

Met criteria codes **4**

PVS1

PM3\_Supporting

PM2\_Supporting

PP4\_Strong

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

Evidence submitted by expert panel

*Limb Girdle Muscular Dystrophy VCEP*

The NM\_000070.3: c.327\_328dup p.(Arg110ProfsTer18) variant is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 2/24, 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 at least two patients with features consistent with LGMD (PMID: 30564623, 1805549; LOVD CAPN3\_000440), including in unconfirmed phase with a pathogenic variant (c.1993-1G>A, 0.5 pts, PMID: 30564623, LOVD Individual #00220608) (PM3\_Supporting). At least one individual with this variant and a second presumed diagnostic CAPN3 variant displayed progressive limb girdle muscle weakness as well as absent CAPN3 expression in skeletal muscle, which is highly specific for CAPN3-related LGMD (PMID: 18055493, LOVD Individual #00214565; PP4\_Strong). The upper bound of the 95% confidence interval of the Grpmax variant allele frequency in gnomAD v4.1.0 is 0.000076118 (74/1179616 European (non-Finnish) alleles), which is less than the VCEP threshold of 0.0001 (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 Limb Girdle Muscular Dystrophy Expert Panel (specification version 2.0.0; 03/12/2026): PVS1, PM3\_Supporting, PP4\_Strong, PM2\_Supporting.

Met criteria codes

|                |                                                                                     |                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|----------------|-------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| PVS1           |    |    | The NM_000070.3: c.327_328dup p.(Arg110ProfsTer18) variant is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 2/24, leading to nonsense-mediated decay in a gene in which loss of function is an established disease mechanism (PVS1). Checked SpliceAI (0.010) - no predicted impact                                                                                                 |
| PM3_Supporting |  |  | This variant has been identified in at least two patients with features consistent with LGMD (PMID: 30564623, 1805549; LOVD CAPN3_000440), including in unconfirmed phase with a pathogenic variant (c.1993-1G>A, 0.5 pts, PMID: 30564623, LOVD Individual #00220608) (PM3_Supporting). c.1993-1G>A is independently classified as P; co-occurrence could not be checked since one of the variants is absent from gnomAD v2 exomes |
| PM2_Supporting |  |  | The upper bound of the 95% confidence interval of the Grpmax variant allele frequency in gnomAD v4.1.0 is 0.000076118 (74/1179616 European (non-Finnish) alleles), which is less than the VCEP threshold of 0.0001 (PM2_Supporting).                                                                                                                                                                                               |
| PP4_Strong     |  |  | At least one individual with this variant and a second presumed diagnostic CAPN3 variant displayed progressive limb girdle muscle weakness as well as absent CAPN3 expression in skeletal muscle, which is highly specific for CAPN3-related LGMD (PMID: 18055493, LOVD Individual #00214565; PP4_Strong).                                                                                                                         |

Curation History [↗](#)

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