

Variant: *NM_000070.3(CAPN3):c.717del (p.Phe239fs)*

Version: 1.0

CA7511095 [↗](#)

284807 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 27330316-f60e-491c-8a82-8a1f1bde9ac8

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HGVS expressions

NM_000070.3:c.717del

NM_000070.3(CAPN3):c.717del (p.Phe239fs)

NM_000070.3:c.717delT

NC_000015.10:g.42389012del

CM000677.2:g.42389012del

NC_000015.9:g.42681210del

CM000677.1:g.42681210del

NC_000015.8:g.40468502del

NG_008660.1:g.45910del

ENST00000349748.8:c.717del

ENST00000357568.8:c.717del

ENST00000397163.8:c.717del

ENST00000466369.5:n.1226del

ENST00000483208.5:n.948del

ENST00000495723.1:n.948del

ENST00000549793.5:n.948del

ENST00000638141.2:n.732del

ENST00000673705.1:c.70+4460del

ENST00000318023.11:c.717del

ENST00000349748.7:c.717del

ENST00000357568.7:c.717del

ENST00000397163.7:c.717del

NM_000070.2:c.717del

NM_024344.1:c.717del

NM_173087.1:c.717del

NM_024344.2:c.717del

NM_173087.2:c.717del

Pathogenic

Met criteria codes 4

PP4_Strong

PM3

PM2_Supporting

PVS1

Not Met criteria codes 1

PS4

Expert Panel

Limb Girdle Muscular Dystrophy VCEP [↗](#)

Criteria Specification Information

[↗](#) **Criteria Specification:** ClinGen Limb Girdle Muscular Dystrophy Expert Panel Specifications to the ACMG/AMP

Evidence submitted by expert panel

Limb Girdle Muscular Dystrophy VCEP

The NM_000070.3: c.717del (p.Phe239LeufsTer14) variant in CAPN3 is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 5/24, 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 six patients with signs of LGMD (1.0 pt; PMID: 10330340, 18073330, 17236769; PM3). At least one of the patients had a clinical diagnosis of LGMD and absent calpain-3 protein expression, which is highly specific for CAPN3-related LGMD (PMID: 17236769; PP4_Strong). The upper bound of the 95% confidence interval of the Grpmax variant allele frequency in gnomAD v4.1.1 is 0.00001 (6/1180006 European (non-Finnish) chromosomes), which is lower than the ClinGen LGMD VCEP threshold (<0.0001) for PM2_Supporting, and therefore meets 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 (specifications v2.0.0; 04/29/2026): PVS1, PM3, PP4_Strong, PM2_Supporting.

Met criteria codes

PP4_Strong			At least one of the patients had a clinical diagnosis of LGMD and absent calpain-3 protein expression, which is highly specific for CAPN3-related LGMD (PMID: 17236769; PP4_Strong).
PM3			This variant has been identified in a homozygous state in six patients with signs of LGMD (1.0 pt; PMID: 10330340, 18073330, 17236769; PM3).
PM2_Supporting			The upper bound of the 95% confidence interval of the Grpmax variant allele frequency in gnomAD v4.1.1 is 0.00001 (6/1180006 European (non-Finnish) chromosomes), which is lower than the ClinGen LGMD VCEP threshold (<0.0001) for PM2_Supporting, and therefore meets this criterion (PM2_Supporting).
PVS1			The NM_000070.3: c.717del (p.Phe239LeufsTer14) variant in CAPN3 is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 5/24 leading to nonsense mediated decay in a gene in which loss of function is an established disease mechanism (PVS1). SpliceAI: 0.00

Not Met criteria codes

PS4			PS4_Mod mentioned in ClinVar submission ?
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