

Variant: *NM_000070.3(CAPN3):c.1027G>T (p.Glu343Ter)*

Version: 1.0

CA7511222 [↗](#)

497182 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: ab17cccd-85f9-45dc-b929-4b146a0be469

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HGVS expressions

NM_000070.3:c.1027G>T

NM_000070.3(CAPN3):c.1027G>T (p.Glu343Ter)

NC_000015.10:g.42392720G>T

CM000677.2:g.42392720G>T

NC_000015.9:g.42684918G>T

CM000677.1:g.42684918G>T

NC_000015.8:g.40472210G>T

NG_008660.1:g.49618G>T

ENST00000349748.8:c.883G>T

ENST00000357568.8:c.1027G>T

ENST00000397163.8:c.1027G>T

ENST00000466369.5:n.1536G>T

ENST00000483208.5:n.1258G>T

ENST00000495723.1:n.1258G>T

ENST00000549793.5:n.1258G>T

ENST00000638141.2:n.898G>T

ENST00000673658.1:n.11G>T

ENST00000673705.1:c.71-4080G>T

ENST00000318023.11:c.883G>T

ENST00000349748.7:c.883G>T

ENST00000357568.7:c.1027G>T

ENST00000397163.7:c.1027G>T

NM_000070.2:c.1027G>T

NM_024344.1:c.1027G>T

NM_173087.1:c.883G>T

NM_024344.2:c.1027G>T

NM_173087.2:c.883G>T

Pathogenic

Met criteria codes **4**

PM2_Supporting

PP4

PM3

PVS1

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

Evidence submitted by expert panel

Limb Girdle Muscular Dystrophy VCEP

The NM_000070.3: c.1027G>T (p.Glu343Ter) variant in CAPN3, which is also known as p.(Glu343del), is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 7/24, 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 five individuals with features of limb girdle muscular dystrophy (PMID: 34628793, 30564623; LOVD CAPN3_000602; ClinVar SCV000953543.3 internal data communication), including in unknown phase with a pathogenic variant in two cases (c.1468C>T p.(Arg490Trp), 1.0 pt, PMID: 30564623; LOVD Individual #00222348; ClinVar SCV000953543.3 internal data communication) (PM3). At least one patient with this variant was clinically suspected to have limb girdle muscular dystrophy (PP4). The highest population minor allele frequency of the variant is 0.00005787 (2/34560 exome chromosomes) in the Admixed American population of gnomAD v2.1.1, which is less than the LGMD VCEP threshold (<0.0001) for PM2_Supporting, 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; 01/09/2025): PVS1, PM3, PP4, PM2_Supporting.

Met criteria codes

PM2_Supporting			The highest population minor allele frequency of the variant is 0.00005787 (2/34560 exome chromosomes) in the Admixed American population of gnomAD v2.1.1, which is less than the LGMD VCEP threshold (<0.0001) for PM2_Supporting, meeting this criterion (PM2_Supporting).
PP4			At least one patient with this variant was clinically suspected to have limb girdle muscular dystrophy (PP4).
PM3			This variant has been detected in at least fives individuals with features of limb girdle muscular dystrophy (PMID: 34628793, 30564623; LOVD CAPN3_000602; SCV000953543.3), including in unknown phase with a pathogenic variant in two cases (c.1468C>T p.(Arg490Trp), 1.0 pt, PMID: 30564623; LOVD CAPN3_000602; SCV000953543.3) (PM3).
PVS1			The NM_000070.3: c.1027G>T (p.Glu343Ter) variant in CAPN3 is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 7/24 leading to nonsense mediated decay in a gene in which loss of function is an established disease mechanism.

Curation History

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See Report	Preferred Variant Title	Classification ⓘ	Condition	Published Date	Version ⓘ	Criteria Specification	Gene
View	NM_000070.3(CAPN3):c.1027G>T (p.Gl...	Pathogenic	Autosomal Recessive Limb-Girdle Muscular Dystrophy ↗	2025-01-09	1.0	ClinGen Limb Girdle Muscular Dystrophy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for CAPN3 Version 1.0.0 ↗	CAPN3 ↗

Showing 1 to 1 of 1 rows

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