The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

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
Approved on: 2025/1/9
Published on: 2025/1/9

HGVS expressions

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

PP4 PM3 PM2_Supporting 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*

Variant Interpretation Guidelines for CAPN3 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_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

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).
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).
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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