

Variant: NM_000070.3(CAPN3):c.1611C>A (p.Tyr537Ter)

Version: 1.0

CA10604243 [↗](#)

282617 (ClinVar) [↗](#)

Gene: CAPN3 ([HGNC:825](#))
Condition: autosomal recessive limb-girdle muscular dystrophy ([MONDO:0015152](#))
Inheritance Mode: Autosomal recessive inheritance
UUID: c3acf1c3-9cf0-4fc8-87cc-ae989d577c39
Approved on: 2025/11/17
Published on: 2026/1/12

HGVS expressions

NM_000070.3:c.1611C>A
NM_000070.3(CAPN3):c.1611C>A (p.Tyr537Ter)
NC_000015.10:g.42402868C>A
CM000677.2:g.42402868C>A
NC_000015.9:g.42695066C>A
CM000677.1:g.42695066C>A
NC_000015.8:g.40482358C>A
NG_008660.1:g.59766C>A
ENST00000349748.8:c.1467C>A
ENST00000357568.8:c.1611C>A
ENST00000397163.8:c.1611C>A
ENST00000466369.5:n.2120C>A
ENST00000483208.5:n.2500C>A
ENST00000495723.1:n.2500C>A
ENST00000549793.5:n.1842C>A
ENST00000638141.2:n.1482C>A
ENST00000673646.1:c.75C>A
ENST00000673705.1:c.309+3216C>A
ENST00000673813.1:n.533C>A
ENST00000318023.11:c.1467C>A
ENST00000349748.7:c.1467C>A
ENST00000357568.7:c.1611C>A
ENST00000397163.7:c.1611C>A
ENST00000397200.8:c.75C>A
ENST00000567071.5:c.70C>A
ENST00000569827.5:c.75C>A
NM_000070.2:c.1611C>A
NM_024344.1:c.1611C>A
NM_173087.1:c.1467C>A
NM_173088.1:c.75C>A
NM_024344.2:c.1611C>A
NM_173087.2:c.1467C>A
NM_173088.2:c.75C>A

Pathogenic

PP1_Moderate

PP4

PM3

PM2_Supporting

PVS1

Evidence Links 0

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

Evidence submitted by expert panel

Limb Girdle Muscular Dystrophy VCEP

The NM_000070.3: c.1611C>A variant in CAPN3 is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 13/24, p.(Tyr537Ter), leading to nonsense mediated decay in a gene in which loss of function is an established disease mechanism (PVS1). This variant has been reported in at least seven unrelated individuals with features consistent with LGMD (PMID: 9150160, 16100770, 16411092, 18854869, 25046369, 33304817, 37526466), including in a homozygous state in the probands of two consanguineous families (0.25 pts x2; PMID: 9150160, 16411092) and confirmed in trans with a pathogenic variant in one patient (c.550del, p.(Thr184ArgfsTer36), 1.0 pt, PMID: 16100770) (PM3). At least one individual with this variant and a second presumed diagnostic CAPN3 variant displayed progressive limb girdle muscle weakness or had a clinical suspicion of LGMD (PMID: 9150160, 16100770, 16411092, 18854869, 25046369, 33304817, 37526466; PP4). This variant has also been reported to co-segregate with autosomal recessive LGMD in two affected family members from two families (PMID: 9150160, 16100770; PP1_Moderate). The Grpmax variant allele frequency in gnomAD v4.1.0 is 0.000002542 (3/1180032 European (non-Finnish) chromosomes), which is less than the ClinGen LGMD VCEP threshold (≤ 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 LGMD VCEP (LGMD VCEP specifications version 2.0.0; 11/17/2025): PVS1, PM3, PP4, PP1_Moderate, PM2_Supporting.

Met criteria codes

PP1_Moderate			This variant has also been reported to co-segregate with autosomal recessive LGMD in two affected family members from two families (PMID: 9150160, 16100770; PP1_Moderate)
PP4			At least one individual with this variant and a second presumed diagnostic CAPN3 variant displayed progressive limb girdle muscle weakness or had a clinical suspicion of LGMD (PMID: 9150160, 16100770, 16411092, 18854869, 25046369, 33304817, 37526466; PP4).
PM3			This variant has been reported in at least seven unrelated individuals with features consistent with LGMD (PMID: 9150160, 16100770, 16411092, 18854869, 25046369, 33304817, 37526466), including in a homozygous state in the probands of two consanguineous families (0.25 pts x2; PMID: 9150160, 16411092) and confirmed in trans with a pathogenic variant in one patient (c.550del, p.(Thr184ArgfsTer36), 1.0 pt, PMID: 16100770) (PM3). 550delA is pathogenic in VCEP = 1.0 pts (PMID: 16100770) 2 separate homozygous occurrence = 0.5 pts (PMID: 16411092) Curated variant is absent from gnomAD v2 so co-occurrence cannot be evaluated
PM2_Supporting			The Grpmax variant allele frequency in gnomAD v4.1.0 is 0.000002542 (3/1180032 European (non-Finnish) chromosomes), which is less than the ClinGen LGMD VCEP threshold (≤ 0.0001) (PM2_Supporting).
PVS1			The NM_000070.3: c.1611C>A variant in CAPN3 is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 13/24, p.(Tyr537Ter), leading to nonsense mediated decay in a gene in which loss of

function is an established disease mechanism (PVS1). Checked SpliceAI - no predicted impact

Curation History



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