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Variant: NM_000070.3(CAPN3):c.967G>T (p.Glu323Ter)

Version: 1.0

CA7511203

620114 (ClinVar)

Gene: CAPN3 (HGNC:825)
Condition: autosomal recessive limb-girdle muscular dystrophy (MONDO:0015152)
Inheritance Mode: Autosomal recessive inheritance
UUID: 99a108aa-1418-4d66-b6c8-dfbc94a73c7b
Approved on: 2025/1/9
Published on: 2025/1/9

HGVS expressions

NM_000070.3:c.967G>T
NM_000070.3(CAPN3):c.967G>T (p.Glu323Ter)
NC_000015.10:g.42392660G>T
CM000677.2:g.42392660G>T
NC_000015.9:g.42684858G>T
CM000677.1:g.42684858G>T
NC_000015.8:g.40472150G>T
NG_008660.1:g.49558G>T
ENST00000349748.8:c.823G>T
ENST00000357568.8:c.967G>T
ENST00000397163.8:c.967G>T
ENST00000466369.5:n.1476G>T
ENST00000483208.5:n.1198G>T
ENST00000495723.1:n.1198G>T
ENST00000549793.5:n.1198G>T
ENST00000638141.2:n.838G>T
ENST00000673705.1:c.71-4140G>T
ENST00000318023.11:c.823G>T
ENST00000349748.7:c.823G>T
ENST00000357568.7:c.967G>T
ENST00000397163.7:c.967G>T
NM_000070.2:c.967G>T
NM_024344.1:c.967G>T
NM_173087.1:c.823G>T
NM_024344.2:c.967G>T
NM_173087.2:c.823G>T

Pathogenic

Met criteria codes 4

PM2_Supporting PP4 PVS1 PM3

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.967G>T p.(Glu323Ter) variant in CAPN3, which is also known as p.(Glu323del), 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 trans with a likely pathogenic or pathogenic variant in an individual with limb girdle muscular dystrophy (c.146G>A p.(Arg49His), 1.0 pt, PMID: 17318636) (PM3). At least one patient with this variant displayed progressive limb girdle muscle weakness or a clinical suspicion of LGMD (PMID: 17318636; PP4). The highest population minor allele frequency in gnomAD v2.1.1 is 0.000008802 (1/113610 exome alleles) in the European (non-Finnish) population, which is lower 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 in gnomAD v2.1.1 is 0.000008802 (1/113610 exome alleles) in European (non-Finnish) population, which is lower than the LGMD VCEP threshold (<0.0001) for PM2_Supporting, meeting this criterion (PM2_Supporting).
PP4	✔	At least one patient with this variant displayed progressive limb girdle muscle weakness or a clinical suspicion of LGMD (PMID: 17318636; PP4).
PVS1	✔	The NM_000070.3: c.967G>T p.(Glu323Ter)) 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 (PVS1).
PM3	✔	This variant has been detected in trans with a likely pathogenic or pathogenic variant in an individual with limb girdle muscular dystrophy (c.146G>A p.(Arg49His), 1.0 pt, PMID: 17318636) (PM3).

Curation History

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