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.1838del (p.Lys613fs)

Version: 1.0

CA489885447

554906 (ClinVar)

Gene: CAPN3 (HGNC:825)
Condition: autosomal recessive limb-girdle muscular dystrophy (MONDO:0015152)
Inheritance Mode: Autosomal recessive inheritance
UUID: 2e9a54c0-2e50-435c-a657-df050e1fec2b
Approved on: 2025/1/9
Published on: 2025/1/9

HGVS expressions

NM_000070.3:c.1838del
NM_000070.3(CAPN3):c.1838del (p.Lys613fs)
NC_000015.10:g.42408248del
CM000677.2:g.42408248del
NC_000015.9:g.42700446del
CM000677.1:g.42700446del
NC_000015.8:g.40487738del
NG_008660.1:g.65146del
ENST00000337571.9:c.-81-1055del
ENST00000349748.8:c.1639-1055del
ENST00000357568.8:c.1820del
ENST00000397163.8:c.1838del
ENST00000397204.9:c.-81-1055del
ENST00000466369.5:n.2329del
ENST00000495723.1:n.2709del
ENST00000549793.5:n.2051del
ENST00000565173.2:n.212del
ENST00000569136.6:c.-158del
ENST00000638141.2:n.1654-1055del
ENST00000673646.1:c.402del
ENST00000673692.1:c.-3-1539del
ENST00000673705.1:c.310-1055del
ENST00000673743.1:c.-179+108del
ENST00000673750.1:c.-158del
ENST00000673771.1:c.-158del
ENST00000673839.1:c.-302del
ENST00000673851.1:c.-158del
ENST00000673854.1:n.4282del
ENST00000673886.1:c.-158del
ENST00000673890.1:c.-158del
ENST00000673928.1:c.-82+108del
ENST00000673936.1:c.-158del
ENST00000673939.1:c.-81-1055del
ENST00000673978.1:c.-324del
ENST00000673987.1:c.-158del
ENST00000674011.1:c.-158del
ENST00000674012.1:n.113del

ENST00000674018.1:c.-158del
ENST00000674041.1:c.-81-1055del
ENST00000674052.1:c.62del
ENST00000674064.1:n.217del
ENST00000674093.1:c.-81-1055del
ENST00000674119.1:c.-81-1055del
ENST00000674135.1:c.-94del
ENST00000674139.1:c.-158del
ENST00000674140.1:n.989del
ENST00000674146.1:c.-158del
ENST00000674149.1:c.-158del
ENST00000318023.11:c.1694del
ENST00000337571.8:c.-81-1055del
ENST00000349748.7:c.1639-1055del
ENST00000356316.7:c.-90-1046del
ENST00000357568.7:c.1820del
ENST00000397163.7:c.1838del
ENST00000397200.8:c.302del
ENST00000397204.8:c.-81-1055del
ENST00000561817.5:c.-81-1055del
ENST00000565173.1:n.167del
ENST00000565274.5:c.50del
ENST00000565559.5:c.-94del
ENST00000567071.5:c.297del
ENST00000569136.5:c.-158del
ENST00000569827.5:c.247-1055del
NM_000070.2:c.1838del
NM_024344.1:c.1820del
NM_173087.1:c.1639-1055del
NM_173088.1:c.302del
NM_173089.1:c.-81-1055del
NM_173090.1:c.-81-1055del
NM_024344.2:c.1820del
NM_173087.2:c.1639-1055del
NM_173088.2:c.302del
NM_173089.2:c.-81-1055del
NM_173090.2:c.-81-1055del

Pathogenic

Met criteria codes 4

PVS1 PM3 PM2 PP4

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.1838del p.(Lys613ArgfsTer49) variant in CAPN3 is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 17/24, 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 three individuals with features of limb girdle muscular dystrophy (PMID: 16607617, 18055493, ClinVar SCV000953543.3 internal data communication), including confirmed in trans with a pathogenic variant (c.1079G>A p.(Trp360Ter), 1.0 pt, ClinVar SCV000953543.3 internal data communication) (PM3). At least one patient with this variant was clinically suspected to have limb girdle muscular dystrophy or showed progressive limb girdle muscle weakness (PP4). This variant is absent from gnomAD v2.1.1 and v3.1.2 (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

PVS1	✔	The NM_000070.3: c.1838del p.(Lys613ArgfsTer49) variant in CAPN3 is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 17/24 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 at least three individuals with features of calpainopathy (PMID: 16607617, 18055493, SCV000953543.3), including confirmed in trans with a pathogenic variant (c.1079G>A p.(Trp360Ter), 1.0 pt, SCV000953543.3) (PM3).
PM2	✔	This variant is absent from gnomAD v2.1.1 and v3.1.2 (PM2_Supporting).
PP4	✔	At least one patient with this variant was clinically suspected to have limb girdle muscular dystrophy or showed progressive limb girdle muscle weakness (PP4).

Curation History

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