

Variant: NM_000070.3(CAPN3):c.2362_2363delinsTCATCT
(p.Arg788fs)

Version: 1.0

CA127307 [↗](#)

17618 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 44debeb9-70da-4b9b-8bfc-7f1e2861589c

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HGVS expressions

NM_000070.3:c.2362_2363delinsTCATCT
NM_000070.3(CAPN3):c.2362_2363delinsTCATCT (p.Arg788fs)
NC_000015.10:g.42410982_42410983delinsTCATCT
CM000677.2:g.42410982_42410983delinsTCATCT
NC_000015.9:g.42703180_42703181delinsTCATCT
CM000677.1:g.42703180_42703181delinsTCATCT
NC_000015.8:g.40490472_40490473delinsTCATCT
NG_008660.1:g.67880_67881delinsTCATCT
ENST00000337571.9:c.367_368delinsTCATCT
ENST00000349748.8:c.2086_2087delinsTCATCT
ENST00000357568.8:c.2344_2345delinsTCATCT
ENST00000397163.8:c.2362_2363delinsTCATCT
ENST00000397204.9:c.367_368delinsTCATCT
ENST00000466222.7:n.751+56_751+57delinsTCATCT
ENST00000466369.5:n.2853_2854delinsTCATCT
ENST00000495723.1:n.3233_3234delinsTCATCT
ENST00000549793.5:n.2575_2576delinsTCATCT
ENST00000562199.2:c.366_367delinsTCATCT
ENST00000567817.6:c.151_152delinsTCATCT
ENST00000568153.2:c.228_229delinsTCATCT
ENST00000569136.6:c.367_368delinsTCATCT
ENST00000638141.2:n.2101_2102delinsTCATCT
ENST00000673646.1:c.926_927delinsTCATCT
ENST00000673684.1:n.344_345delinsTCATCT
ENST00000673692.1:c.367_368delinsTCATCT
ENST00000673705.1:c.905_906delinsTCATCT
ENST00000673743.1:c.265_266delinsTCATCT
ENST00000673750.1:c.367_368delinsTCATCT
ENST00000673771.1:c.367_368delinsTCATCT
ENST00000673774.1:n.1495_1496delinsTCATCT
ENST00000673839.1:c.367_368delinsTCATCT
ENST00000673851.1:c.367_368delinsTCATCT
ENST00000673854.1:n.5784_5785delinsTCATCT
ENST00000673886.1:c.367_368delinsTCATCT
ENST00000673890.1:c.367_368delinsTCATCT

ENST00000673928.1:c.367_368delinsTCATCT
ENST00000673936.1:c.367_368delinsTCATCT
ENST00000673939.1:c.*100+56_*100+57delinsTCATCT
ENST00000673950.1:n.636_637delinsTCATCT
ENST00000673978.1:c.505_506delinsTCATCT
ENST00000673987.1:c.*100+56_*100+57delinsTCATCT
ENST00000674011.1:c.*156_*157delinsTCATCT
ENST00000674018.1:c.367_368delinsTCATCT
ENST00000674027.1:n.513_514delinsTCATCT
ENST00000674041.1:c.367_368delinsTCATCT
ENST00000674052.1:c.586_587delinsTCATCT
ENST00000674093.1:c.367_368delinsTCATCT
ENST00000674119.1:c.367_368delinsTCATCT
ENST00000674135.1:c.544_545delinsTCATCT
ENST00000674139.1:c.367_368delinsTCATCT
ENST00000674146.1:c.367_368delinsTCATCT
ENST00000674149.1:c.367_368delinsTCATCT
ENST00000318023.11:c.2218_2219delinsTCATCT
ENST00000337571.8:c.367_368delinsTCATCT
ENST00000349748.7:c.2086_2087delinsTCATCT
ENST00000356316.7:c.367_368delinsTCATCT
ENST00000357568.7:c.2344_2345delinsTCATCT
ENST00000397163.7:c.2362_2363delinsTCATCT
ENST00000397200.8:c.826_827delinsTCATCT
ENST00000397204.8:c.367_368delinsTCATCT
ENST00000466222.6:n.1285_1286delinsTCATCT
ENST00000561817.5:c.367_368delinsTCATCT
ENST00000562199.1:n.366_367delinsTCATCT
ENST00000564503.5:c.405_406delinsTCATCT
ENST00000565274.5:c.540_541delinsTCATCT
ENST00000567817.5:c.178_179delinsTCATCT
ENST00000568153.1:c.99_100delinsTCATCT
ENST00000569136.5:c.367_368delinsTCATCT
ENST00000569827.5:c.694_695delinsTCATCT
NM_000070.2:c.2362_2363delinsTCATCT
NM_024344.1:c.2344_2345delinsTCATCT
NM_173087.1:c.2086_2087delinsTCATCT
NM_173088.1:c.826_827delinsTCATCT
NM_173089.1:c.367_368delinsTCATCT
NM_173090.1:c.367_368delinsTCATCT
NM_024344.2:c.2344_2345delinsTCATCT
NM_173087.2:c.2086_2087delinsTCATCT
NM_173088.2:c.826_827delinsTCATCT
NM_173089.2:c.367_368delinsTCATCT
NM_173090.2:c.367_368delinsTCATCT

Pathogenic

Met criteria codes 5

- PVS1_Moderate
- PM2_Supporting
- PP1
- PM3_Strong
- PP4_Strong

Evidence Links 0

Expert Panel

Limb Girdle Muscular Dystrophy VCEP

Criteria Specification Information

Evidence submitted by expert panel

Limb Girdle Muscular Dystrophy VCEP

The NM_000070.3: c.2362_2363delinsTCATCT p.(Arg788SerfsTer14) variant in CAPN3 is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 23/24 that may cause loss of function of the protein, however, it is predicted to escape nonsense mediated decay and remove <10% of the protein (PVS1_Moderate). This variant has been detected in at least 30 individuals with limb girdle muscular dystrophy, including in a homozygous state in one patient (0.5 pts, PMID: 18337726), in trans with a pathogenic variant in at least one patient (c.643_663del p.(Ser215_Gly221del), 1.0 pt, PMID: 9150160), and in unknown phase with a pathogenic variant (c.223dup p.(Tyr75LeufsTer5), 0.5 pts, PMID: 30564623, LOVD Individual #00220184) (PM3_Strong). At least one patient with this variant displayed a clinical suspicion of limb girdle muscular dystrophy and absent expression of calpain-3, which is highly specific for CAPN3-related LGMD (PP4_Strong; PMID: 18337726). The variant has also been reported to segregate with LGMD in one affected family member (PP1; PMID: 9150160). 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_Moderate, PM3_Strong, PP4_Strong, PP1, PM2_Supporting.

Met criteria codes

PVS1_Moderate			The NM_000070.3: c.2362_2363delinsTCATCT p.(Arg788SerfsTer14) variant in CAPN3 is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 23/24 that may cause loss of function of the protein, however, it is predicted to escape nonsense mediated decay and remove <10% of the protein (PVS1_Moderate).
PM2_Supporting			This variant is absent from gnomAD v2.1.1 and v3.1.2 (PM2_Supporting).
PP1			The variant has also been reported to segregate with LGMD in one affected family member (PP1; PMID: 9150160).
PM3_Strong			This variant has been detected in at least 30 individuals with limb girdle muscular dystrophy, including in a homozygous state in one patient (0.5 pts, PMID: 18337726), in trans with a pathogenic variant in at least one patient (c.643_663del p.(Ser215_Gly221del), 1.0 pt, PMID: 9150160), and in unknown phase with a pathogenic variant (c.223dup p.(Tyr75LeufsTer5), 0.5 pts, PMID: 30564623, LOVD Individual #00220184) (PM3_Strong).
PP4_Strong			At least one patient with this variant displayed a clinical suspicion of limb girdle muscular dystrophy and absent expression of calpain-3, which is highly specific for CAPN3-related LGMD (PP4_Strong; PMID: 18337726).

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