

Variant: NM_000070.3(CAPN3):c.2290del (p.Asp764fs)

Version: 1.0

CA10606870 [↗](#)

497201 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 4977f95d-5881-4fad-8cc4-c3eba12331d8

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HGVS expressions

- NM_000070.3:c.2290del
- NM_000070.3(CAPN3):c.2290del (p.Asp764fs)
- NC_000015.10:g.42410910del
- CM000677.2:g.42410910del
- NC_000015.9:g.42703108del
- CM000677.1:g.42703108del
- NC_000015.8:g.40490400del
- NG_008660.1:g.67808del
- ENST00000337571.9:c.295del
- ENST00000349748.8:c.2014del
- ENST00000357568.8:c.2272del
- ENST00000397163.8:c.2290del
- ENST00000397204.9:c.295del
- ENST00000466222.7:n.735del
- ENST00000466369.5:n.2781del
- ENST00000495723.1:n.3161del
- ENST00000549793.5:n.2503del
- ENST00000562199.2:c.294del
- ENST00000567817.6:c.79del
- ENST00000568153.2:c.156del
- ENST00000569136.6:c.295del
- ENST00000638141.2:n.2029del
- ENST00000673646.1:c.854del
- ENST00000673684.1:n.272del
- ENST00000673692.1:c.295del
- ENST00000673705.1:c.833del
- ENST00000673743.1:c.193del
- ENST00000673750.1:c.295del
- ENST00000673771.1:c.295del
- ENST00000673774.1:n.1423del
- ENST00000673839.1:c.295del
- ENST00000673851.1:c.295del
- ENST00000673854.1:n.5712del
- ENST00000673886.1:c.295del
- ENST00000673890.1:c.295del
- ENST00000673928.1:c.295del
- ENST00000673936.1:c.295del

	ENST00000673939.1:c.*84del ENST00000673950.1:n.564del ENST00000673978.1:c.433del ENST00000673987.1:c.*84del ENST00000674011.1:c.*84del ENST00000674018.1:c.295del ENST00000674027.1:n.441del ENST00000674041.1:c.295del ENST00000674052.1:c.514del ENST00000674093.1:c.295del ENST00000674119.1:c.295del ENST00000674135.1:c.472del ENST00000674139.1:c.295del ENST00000674146.1:c.295del ENST00000674149.1:c.295del ENST00000318023.11:c.2146del ENST00000337571.8:c.295del ENST00000349748.7:c.2014del ENST00000356316.7:c.295del ENST00000357568.7:c.2272del ENST00000397163.7:c.2290del ENST00000397200.8:c.754del ENST00000397204.8:c.295del ENST00000466222.6:n.1213del ENST00000561817.5:c.295del ENST00000562199.1:n.294del ENST00000564503.5:c.333del ENST00000565274.5:c.468del ENST00000565559.5:c.472del ENST00000567817.5:c.106del ENST00000568153.1:c.27del ENST00000569136.5:c.295del ENST00000569827.5:c.622del NM_000070.2:c.2290del NM_024344.1:c.2272del NM_173087.1:c.2014del NM_173088.1:c.754del NM_173089.1:c.295del NM_173090.1:c.295del NM_024344.2:c.2272del NM_173087.2:c.2014del NM_173088.2:c.754del NM_173089.2:c.295del NM_173090.2:c.295del
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Pathogenic

Met criteria codes 4

- PM2_Supporting
- PP4
- PM3_Strong
- PVS1

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.2290del p.(Asp764ThrfsTer12) variant in CAPN3 is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 22/24, 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 three patients with features consistent with LGMD, including in a homozygous state in one patient without reported familial consanguinity (0.5 pts, PMID: 31671740, LOVD Individual #00416186) and confirmed in trans with a pathogenic variant in two patients (c.2362_2363delinsTCATCT p.(Arg788SerfsTer14), 1.0 pt x2, LOVD Individual #00214755; ClinVar SCV002227607.3 personal data communication) (PM3_Strong). At least one patient with this variant and a second presumed diagnostic variant in CAPN3 had a clinical diagnosis of LGMD (LOVD Individual #00214755; PP4). The highest minor allele frequency of this variant is 0.00004472 (2/44722 exome chromosomes) for the Admixed American population in gnomAD v4.1.0, 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; 05/03/2025): PVS1, PM3_Strong, PP4, PM2_Supporting.

Met criteria codes

PM2_Supporting			The highest minor allele frequency of this variant is 0.00004472 (2/44722 exome chromosomes) for the Admixed American population in gnomAD v4.1.0, 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 and a second presumed diagnostic variant in CAPN3 had a clinical diagnosis of LGMD (LOVD Individual #00214755; PP4).
PM3_Strong			This variant has been reported in at least three patients with features consistent with LGMD, including in a homozygous state in one patient without reported familial consanguinity (0.5 pts, PMID: 31671740, LOVD Individual #00416186) and confirmed in trans with a pathogenic variant in two patients (c.2362_2363delinsTCATCT p.(Arg788SerfsTer14), 1.0 pt x2, LOVD Individual #00214755; ClinVar SCV002227607.3 personal data communication) (PM3_Strong).
PVS1			The NM_000070.3: c.2290del p.(Asp764ThrfsTer12) variant in CAPN3 is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 22/24, leading to nonsense mediated decay in a gene in which loss of function is an established disease mechanism (PVS1).

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