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Variant: NM_000070.3(CAPN3):c.2393C>A (p.Ala798Glu)

Version: 1.0

CA220348

92414 (ClinVar)

Gene: CAPN3 (HGNC:825)
Condition: autosomal recessive limb-girdle muscular dystrophy (MONDO:0015152)
Inheritance Mode: Autosomal recessive inheritance
UUID: ce4d1700-8d2f-43d4-b2db-a351e5aaa75d
Approved on: 2026/2/18
Published on: 2026/4/9

HGVS expressions

NM_000070.3:c.2393C>A
NM_000070.3(CAPN3):c.2393C>A (p.Ala798Glu)
NC_000015.10:g.42411299C>A
CM000677.2:g.42411299C>A
NC_000015.9:g.42703497C>A
CM000677.1:g.42703497C>A
NC_000015.8:g.40490789C>A
NG_008660.1:g.68197C>A
ENST00000337571.9:c.398C>A
ENST00000349748.8:c.2117C>A
ENST00000357568.8:c.2375C>A
ENST00000397163.8:c.2393C>A
ENST00000397204.9:c.398C>A
ENST00000466222.7:n.764C>A
ENST00000466369.5:n.2884C>A
ENST00000495723.1:n.3264C>A
ENST00000549793.5:n.2606C>A
ENST00000562199.2:c.397C>A
ENST00000567817.6:c.182C>A
ENST00000568153.2:c.259C>A
ENST00000569136.6:c.398C>A
ENST00000638141.2:n.2132C>A
ENST00000673646.1:c.957C>A
ENST00000673684.1:n.375C>A
ENST00000673692.1:c.398C>A
ENST00000673705.1:c.1222C>A
ENST00000673743.1:c.296C>A
ENST00000673750.1:c.398C>A
ENST00000673771.1:c.398C>A
ENST00000673774.1:n.1526C>A
ENST00000673839.1:c.398C>A
ENST00000673851.1:c.398C>A
ENST00000673854.1:n.5815C>A
ENST00000673886.1:c.398C>A
ENST00000673890.1:c.398C>A
ENST00000673928.1:c.398C>A
ENST00000673936.1:c.398C>A

ENST00000673939.1:c.*113C>A
ENST00000673950.1:n.667C>A
ENST00000673978.1:c.536C>A
ENST00000673987.1:c.*113C>A
ENST00000674011.1:c.*187C>A
ENST00000674018.1:c.398C>A
ENST00000674027.1:n.544C>A
ENST00000674041.1:c.398C>A
ENST00000674052.1:c.617C>A
ENST00000674093.1:c.398C>A
ENST00000674119.1:c.398C>A
ENST00000674135.1:c.575C>A
ENST00000674139.1:c.398C>A
ENST00000674146.1:c.398C>A
ENST00000674149.1:c.398C>A
ENST00000318023.11:c.2249C>A
ENST00000337571.8:c.398C>A
ENST00000349748.7:c.2117C>A
ENST00000356316.7:c.398C>A
ENST00000357568.7:c.2375C>A
ENST00000397163.7:c.2393C>A
ENST00000397200.8:c.857C>A
ENST00000397204.8:c.398C>A
ENST00000466222.6:n.1316C>A
ENST00000561817.5:c.398C>A
ENST00000564503.5:c.436C>A
ENST00000565274.5:c.571C>A
ENST00000567817.5:c.209C>A
ENST00000568153.1:c.130C>A
ENST00000569136.5:c.398C>A
ENST00000569827.5:c.725C>A
NM_000070.2:c.2393C>A
NM_024344.1:c.2375C>A
NM_173087.1:c.2117C>A
NM_173088.1:c.857C>A
NM_173089.1:c.398C>A
NM_173090.1:c.398C>A
NM_024344.2:c.2375C>A
NM_173087.2:c.2117C>A
NM_173088.2:c.857C>A
NM_173089.2:c.398C>A
NM_173090.2:c.398C>A

Pathogenic

Met criteria codes 2

PP4_Strong PM3_Very Strong

Not Met criteria codes 5

PP3 PM2 BA1 BS1 BP4

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 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.2393C>A variant in CAPN3 is a missense variant predicted to cause substitution of alanine by glutamic acid at amino acid 798, p.(Ala798Glu). This variant has been detected in at least 10 individuals with features consistent with limb girdle muscular dystrophy (PMID: 38794994, 37526466, 31555977, 19556129, 30919934), including in a homozygous state without reported consanguinity in one patient (0.5 pts, PMID: 31555977), in unconfirmed phase with a pathogenic variant in two patients (c.598_612del p.(Phe200_Leu204del), 0.5pts, PMID: 38794994; c.550del p.(Thr184ArgfsTer36), 0.5 pts, PMID: 38794994), and confirmed in trans with a pathogenic variant in four patients (c.550del p.(Thr184Argfs36),1 pt, PMID: 37526466; c.1194-9A>G,1 pt, PMID: 37526466; c.1621C>T p.(Arg541Trp), 1 pt, PMID: 19556129; c.2362_2363delinsTCATCT p.(Arg788SerfsTer14),1 pt, PMID: 30919934) (PM3_Very Strong). At least one patient with this variant and a second presumed diagnostic CAPN3 variant displayed progressive limb girdle muscle weakness and absent calpain-3 protein expression, which is highly specific for CAPN3-related LGMD (PP4_Strong; PMID: 18055493, 19556129). The upper bound of the 95% confidence interval of the Grpmax variant allele frequency in gnomAD v4.1.0 is 0.0002868 (308/1179972 European (non-Finnish) exome and genome chromosomes), which is greater than the ClinGen LGMD VCEP threshold <0.0001 for PM2_Supporting (criterion not met). The computational predictor REVEL gives a score of 0.687, which is less than the Clingen LGMD VCEP threshold of ≥0.7. 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 (specifications version 2.0.0; 02/18/2026): PM3_VeryStrong, PP4_Strong.

Met criteria codes

PP4_Strong	✔	At least one patient with this variant and a second presumed diagnostic CAPN3 variant displayed progressive limb girdle muscle weakness and absent calpain-3 protein expression, which is highly specific for CAPN3-related LGMD (PP4_Strong; PMID: 18055493, 19556129).
PM3_Very Strong	✔	This variant has been detected in at least 10 individuals with features consistent with limb girdle muscular dystrophy (PMID: 38794994, 37526466, 31555977, 19556129, 30919934), including in a homozygous state without reported consanguinity in one patient (0.5 pts, PMID: 31555977), in unconfirmed phase with a pathogenic variant in two patients (c.598_612del p.(Phe200_Leu204del), 0.5pts, PMID: 38794994; c.550del p.(Thr184ArgfsTer36), 0.5 pts, PMID: 38794994), and confirmed in trans with a pathogenic variant in four patients (c.550del p.(Thr184Argfs36),1 pt, PMID: 37526466; c.1194-9A>G,1 pt, PMID: 37526466; c.1621C>T p.(Arg541Trp), 1 pt, PMID: 19556129; c.2362_2363delinsTCATCT p.(Arg788SerfsTer14),1 pt, PMID: 30919934) (PM3_Very Strong).

Not Met criteria codes

PP3	✖	The computational predictor REVEL gives a score of 0.687, which is less than the Clingen LGMD VCEP threshold of ≥0.7.
PM2	✖	The upper bound of the 95% confidence interval of the Grpmax variant allele frequency in gnomAD v4.1.0 is 0.0002868 (308/1179972 European (non-Finnish) exome and genome chromosomes), which is greater than the ClinGen LGMD VCEP threshold <0.0001 for PM2_Supporting (criterion not met).
BA1	✖	

No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

BS1	✖	The filtering allele frequency of this variant is 0.0002367 (the lower threshold of the 95% CI of 308/1179972 exomes and genome chromosomes) in the European (non-Finnish) population in gnomAD v4.1.0, which is less than the ClinGen LGMD VCEP threshold >0.001 for BS1.
BP4	✖	The computational predictor REVEL gives a score of 0.687, which is greater than the Clingen LGMD VCEP threshold of ≥0.1.

Curation History

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See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_000070.3(CAPN3):c.2393C>A (p.Al...	Pathogenic	Autosomal Recessive Limb-Girdle Muscular Dystrophy	2026-04-09	1.0	ClinGen Limb Girdle Muscular Dystrophy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for CAPN3 Version 2.0.0	CAPN3

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