

Variant: NM_000070.3(CAPN3):c.2134C>T (p.Leu712Phe)

Version: 1.0

CA241878 [↗](#)

195450 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: dee1b669-400a-4ed1-930d-64adb51d4ceb

Approved on: 2026/4/29

Published on: 2026/5/7

HGVS expressions

NM_000070.3(CAPN3):c.2134C>T (p.Leu712Phe)

NM_000070.3:c.2134C>T

NC_000015.10:g.42410446C>T

CM000677.2:g.42410446C>T

NC_000015.9:g.42702644C>T

CM000677.1:g.42702644C>T

NC_000015.8:g.40489936C>T

NG_008660.1:g.67344C>T

ENST00000337571.9:c.139C>T

ENST00000349748.8:c.1858C>T

ENST00000357568.8:c.2116C>T

ENST00000397163.8:c.2134C>T

ENST00000397204.9:c.139C>T

ENST00000466222.7:n.399C>T

ENST00000466369.5:n.2625C>T

ENST00000495723.1:n.3005C>T

ENST00000549793.5:n.2347C>T

ENST00000562199.2:c.138C>T

ENST00000569136.6:c.139C>T

ENST00000638141.2:n.1873C>T

ENST00000673646.1:c.698C>T

ENST00000673684.1:n.116C>T

ENST00000673687.1:n.643C>T

ENST00000673692.1:c.139C>T

ENST00000673705.1:c.511-142C>T

ENST00000673743.1:c.37C>T

ENST00000673750.1:c.139C>T

ENST00000673771.1:c.139C>T

ENST00000673774.1:n.1267C>T

ENST00000673839.1:c.139C>T

ENST00000673851.1:c.139C>T

ENST00000673854.1:n.5556C>T

ENST00000673886.1:c.139C>T

ENST00000673890.1:c.139C>T

ENST00000673893.1:c.337C>T

ENST00000673928.1:c.139C>T

ENST00000673936.1:c.139C>T

ENST00000673939.1:c.139C>T
ENST00000673950.1:n.408C>T
ENST00000673978.1:c.277C>T
ENST00000673987.1:c.139C>T
ENST00000674011.1:c.139C>T
ENST00000674018.1:c.139C>T
ENST00000674027.1:n.194C>T
ENST00000674041.1:c.139C>T
ENST00000674052.1:c.358C>T
ENST00000674093.1:c.139C>T
ENST00000674119.1:c.139C>T
ENST00000674135.1:c.316C>T
ENST00000674139.1:c.139C>T
ENST00000674146.1:c.139C>T
ENST00000674149.1:c.139C>T
ENST00000318023.11:c.1990C>T
ENST00000337571.8:c.139C>T
ENST00000349748.7:c.1858C>T
ENST00000356316.7:c.139C>T
ENST00000357568.7:c.2116C>T
ENST00000397163.7:c.2134C>T
ENST00000397200.8:c.598C>T
ENST00000397204.8:c.139C>T
ENST00000466222.6:n.1057C>T
ENST00000561817.5:c.139C>T
ENST00000562199.1:n.138C>T
ENST00000564503.5:c.231C>T
ENST00000565274.5:c.366C>T
ENST00000565559.5:c.316C>T
ENST00000569136.5:c.139C>T
ENST00000569827.5:c.466C>T
NM_000070.2:c.2134C>T
NM_024344.1:c.2116C>T
NM_173087.1:c.1858C>T
NM_173088.1:c.598C>T
NM_173089.1:c.139C>T
NM_173090.1:c.139C>T
NM_024344.2:c.2116C>T
NM_173087.2:c.1858C>T
NM_173088.2:c.598C>T
NM_173089.2:c.139C>T
NM_173090.2:c.139C>T

Likely Pathogenic

Met criteria codes 5

- PM3_Strong
- PP1_Moderate
- PP3
- PP4
- PM2_Supporting

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

Evidence submitted by expert panel

Limb Girdle Muscular Dystrophy VCEP

The NM_000070.3: c.2134C>T variant in CAPN3 is a missense variant predicted to cause the substitution of leucine by phenylalanine at amino acid position 712, p.(Leu712Phe). The variant has been detected in at least six patients with LGMD2A (PMID: 17562833, 26886200, 30919934; GRASP-LGMD Consortium internal data communication), including in a homozygous state without consanguinity in 3 unrelated patients (1.0 pt; PMID: 17562833, 26886200, 30919934). In a fourth patient, the variant was confirmed in trans with a pathogenic CAPN3 variant (c.1981del, p.(Ile661Ter), 1.0 pt) (PMID: 17562833, 26886200, 30919934) (PM3_Strong). At least one patient with this variant displayed a progressive limb girdle pattern of muscle weakness (PP4). This variant was also observed to segregate with autosomal recessive LGMD in three affected family members from one family (PMID: 17562833; PP1_Moderate). The upper bound of the 95% confidence interval of the Grpmax variant allele frequency in gnomAD v4.1.0 is 0.000007757 (4/1180004 European (non-Finnish) chromosomes), which is less than the ClinGen LGMD VCEP threshold (≤ 0.0001) (PM2_Supporting). The computational predictor REVEL gives a score of 0.855, which is above the threshold of 0.70 (PP3). In summary, this variant meets the criteria to be classified as Likely Pathogenic for autosomal recessive limb girdle muscular dystrophy based on the ACMG/AMP criteria applied, as specified by the ClinGen LGMD VCEP (specifications v2.0.0; 04/29/2026): PM3_Strong, PP4, PP1_Moderate, PM2_Supporting, PP3.

Met criteria codes

PM3_Strong			The variant has been detected in at least six patients with LGMD2A (PMID: 17562833, 26886200, 30919934; GRASP-LGMD Consortium internal data communication), including in a homozygous state without consanguinity in 3 unrelated patients (1.0 pt; PMID: 17562833, 26886200, 30919934). In a fourth patient, the variant was confirmed in trans with a pathogenic CAPN3 variant (c.1981del, p.(Ile661Ter), 1.0 pt) (PMID: 17562833, 26886200, 30919934) (PM3_Strong).
PP1_Moderate			This variant was observed to segregate with autosomal recessive LGMD in three affected family members from one family (PMID: 17562833; PP1_Moderate).
PP3			The computational predictor Revel gives a score of 0.855, which is above the threshold of 0.70 (PP3). SpliceAI: 0.0100
PP4			At least one patient with this variant displayed progressive limb girdle pattern of muscle weakness (PP4).
PM2_Supporting			The upper bound of the 95% confidence interval of the Grpmax variant allele frequency in gnomAD v4.1.0 is 0.000007757 (4/1180004 European (non-Finnish) chromosomes), which is less than the ClinGen LGMD VCEP threshold (≤ 0.0001) (PM2_Supporting).

▾

▾

Showing 1 to 1 of 1 rows

--

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.