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Variant: NM_000070.3(CAPN3):c.620A>C (p.Lys207Thr)

Version: 1.0

CA10605119

285460 (ClinVar)

Gene: CAPN3 (HGNC:825)
Condition: autosomal recessive limb-girdle muscular dystrophy (MONDO:0015152)
Inheritance Mode: Autosomal recessive inheritance
UUID: f5e69e5c-ee57-4869-8164-d438c5214ae9
Approved on: 2026/4/28
Published on: 2026/5/7

HGVS expressions

NM_000070.3(CAPN3):c.620A>C (p.Lys207Thr)
NM_000070.3:c.620A>C
NC_000015.10:g.42387874A>C
CM000677.2:g.42387874A>C
NC_000015.9:g.42680072A>C
CM000677.1:g.42680072A>C
NC_000015.8:g.40467364A>C
NG_008660.1:g.44772A>C
ENST00000349748.8:c.620A>C
ENST00000357568.8:c.620A>C
ENST00000397163.8:c.620A>C
ENST00000466369.5:n.1129A>C
ENST00000483208.5:n.851A>C
ENST00000495723.1:n.851A>C
ENST00000549793.5:n.851A>C
ENST00000638141.2:n.635A>C
ENST00000673705.1:c.70+3322A>C
ENST00000318023.11:c.620A>C
ENST00000349748.7:c.620A>C
ENST00000357568.7:c.620A>C
ENST00000397163.7:c.620A>C
NM_000070.2:c.620A>C
NM_024344.1:c.620A>C
NM_173087.1:c.620A>C
NM_024344.2:c.620A>C
NM_173087.2:c.620A>C

Likely Pathogenic

Met criteria codes 4

PP3 PP4 PM3_Strong 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*

Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Limb Girdle Muscular Dystrophy VCEP

The NM_000070.3: c.620A>C variant in CAPN3 is a missense variant predicted to cause the substitution of lysine by threonine at amino acid position 207, p.(Lys207Thr). This variant has been identified with a second CAPN3 variant in at least five patients with LGMD, including in unknown phase with a pathogenic variant in four unrelated individuals (c.1746-20C>G, 2.0 pts) and confirmed in trans with a variant not yet curated by the VCEP and considered VUS (PMID: 16141003, 18055493, 30564623, 26404900; LOVD CAPN3_000227; GRASP-LGMD Consortium internal data communication) (PM3_Strong). At least one of these patients displayed progressive limb girdle muscle weakness (PP4). The highest minor allele frequency of this variant is 0.000001695 (2/1180038 chromosomes) in the European (non-Finnish) population in gnomAD v4.1.1, which is less than the LGMD VCEP threshold for PM2_Supporting (0.0001), meeting this criterion (PM2_Supporting). The computational predictor REVEL gives a score of 0.98, which is above the LGMD VCEP threshold of 0.70, evidence that correlates with impact to CAPN3 function (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; 04/28/2026): PM3_Strong, PP4, PM2_Supporting, PP3.

Met criteria codes

PP3	✔	The computational predictor REVEL gives a score of 0.98, which is above the LGMD VCEP threshold of 0.70, evidence that correlates with impact to CAPN3 function (PP3). SpliceAI: 0.00
PP4	✔	At least one patient with this variant displayed progressive limb girdle muscle weakness (PP4).
PM3_Strong	✔	This variant has been identified with a second CAPN3 variant in at least five patients with LGMD, including in unknown phase with a pathogenic variant in four unrelated individuals (c.1746-20C>G, 2.0 pts) and confirmed in trans with a variant not yet curated by the VCEP and considered VUS (PMID: 16141003, 18055493, 30564623, 26404900; LOVD CAPN3_000227; GRASP-LGMD Consortium internal data communication) (PM3_Strong). 2 cases from Nallamilli 2018 with no second variant identified no other ClinVar data absent from gnomAD v2, so co-occurrence cannot be checked
PM2_Supporting	✔	The highest minor allele frequency of this variant is 0.000001695 (2/1180038 chromosomes) in the European (non-Finnish) population in gnomAD v4.1.1, which is less than the LGMD VCEP threshold for PM2_Supporting (0.0001), meeting this criterion (PM2_Supporting).

Curation History

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