The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000070.3(CAPN3):c.219del (p.Leu74fs)

Version: 1.0

CA2499222909

1072479 (ClinVar)

Gene: CAPN3 (HGNC:825)
Condition: autosomal recessive limb-girdle muscular dystrophy (MONDO:0015152)
Inheritance Mode: Autosomal recessive inheritance
UUID: 2b7e9311-a423-41bc-bcfa-6db58a5cda0d
Approved on: 2025/1/7
Published on: 2025/1/7

HGVS expressions

NM_000070.3(CAPN3):c.219del (p.Leu74fs)
NM_000070.3:c.219del
NC_000015.10:g.42360024del
CM000677.2:g.42360024del
NC_000015.9:g.42652222del
CM000677.1:g.42652222del
NC_000015.8:g.40439514del
NG_008660.1:g.16922del
ENST00000349748.8:c.219del
ENST00000357568.8:c.219del
ENST00000397163.8:c.219del
ENST00000466369.5:n.540+5571del
ENST00000483208.5:n.540+5571del
ENST00000495723.1:n.540+5571del
ENST00000549793.5:n.540+5571del
ENST00000318023.11:c.219del
ENST00000349748.7:c.219del
ENST00000357568.7:c.219del
ENST00000397163.7:c.219del
NM_000070.2:c.219del
NM_024344.1:c.219del
NM_173087.1:c.219del
NM_024344.2:c.219del
NM_173087.2:c.219del

Likely Pathogenic

Met criteria codes 2

PM2_Supporting PVS1

Not Met criteria codes 15

PP2 PP3 BA1 PM1 PM5 PM4 BS1 BS3 PS1 PS3 BP5 BP7 BP4 BP3 BP1

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 1.0.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Limb Girdle Muscular Dystrophy VCEP

The NM_000070.3: c.219del p.(Leu74PhefsTer53) variant in CAPN3 is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 2/24 leading to nonsense mediated decay in a gene in which loss of function is an established disease mechanism (PVS1). 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 Likely 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; 01/07/2025): PVS1, PM2_Supporting.

Met criteria codes

PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1 and v3.1.2 (PM2_Supporting).
PVS1	✔	The NM_000070.3:c.219del p.(Leu74PhefsTer53) variant in CAPN3 is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 2/24 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).

Not Met criteria codes

PP2	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM5	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM4	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

PS3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP5		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP7		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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