

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

PS1

PS3

BA1

PP2

PP3

PM1

PM5

PM4

BS1

BS3

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**

|                       |                                                                                   |                                                                                   |                                                                                                                                                                                                                                                                                       |
|-----------------------|-----------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>PM2_Supporting</b> |  |  | This variant is absent from gnomAD v2.1.1 and v3.1.2 (PM2_Supporting).                                                                                                                                                                                                                |
| <b>PVS1</b>           |  |  | 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**

|            |                                                                                     |                                                                                     |                                                                                                                            |
|------------|-------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| <b>PS1</b> |    |    | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| <b>PS3</b> |   |   | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| <b>BA1</b> |  |  | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| <b>PP2</b> |                                                                                     |  | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| <b>PP3</b> |  |  | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| <b>PM1</b> |                                                                                     |  | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| <b>PM5</b> |  |  | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| <b>PM4</b> |  |  | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| <b>BS1</b> |  |  | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |

|            |                                                                                   |   |                                                                                                                            |
|------------|-----------------------------------------------------------------------------------|---|----------------------------------------------------------------------------------------------------------------------------|
| <b>BS3</b> |                                                                                   | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| <b>BP5</b> |                                                                                   | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| <b>BP7</b> |  | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| <b>BP4</b> |  | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| <b>BP3</b> |                                                                                   | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| <b>BP1</b> |                                                                                   | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |

| Curation History  |  |  |
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