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_213599.3(ANO5):c.304_308del (p.Lys102fs)

Version: 1.0

CA5922882

280322 (ClinVar)

Gene: ANO5 (HGNC:203859)
Condition: autosomal recessive limb-girdle muscular dystrophy (MONDO:0015152)
Inheritance Mode: Autosomal recessive inheritance
UUID: 066b273c-814e-4a7e-b828-1c0b24a725c2
Approved on: 2025/1/9
Published on: 2025/1/9

HGVS expressions

NM_213599.3(ANO5):c.304_308del (p.Lys102fs)
NM_213599.3:c.304_308del
NM_213599.3:c.304_308delAAAGA
NC_000011.10:g.22225993_22225997del
CM000673.2:g.22225993_22225997del
NC_000011.9:g.22247539_22247543del
CM000673.1:g.22247539_22247543del
NC_000011.8:g.22204115_22204119del
NG_015844.1:g.37818_37822del
ENST00000682266.1:c.-147_-143del
ENST00000682341.1:c.262_266del
ENST00000682530.1:c.*236_*240del
ENST00000682684.1:n.683_687del
ENST00000683197.1:c.262_266del
ENST00000683411.1:c.-147_-143del
ENST00000683437.1:c.-147_-143del
ENST00000683613.1:n.1298_1302del
ENST00000683834.1:n.504_508del
ENST00000684663.1:c.259_263del
ENST00000324559.9:c.304_308del
ENST00000648804.1:n.869_873del
ENST00000324559.8:c.304_308del
NM_001142649.1:c.301_305del
NM_213599.2:c.304_308del
NM_001142649.2:c.301_305del

Pathogenic

Met criteria codes 3

PP4 PM2_Supporting PVS1

Not Met criteria codes 1

PM3

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 ANO5 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_213599.3: c.304_308del p.(Lys102ValfsTer2) variant in ANO5 is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 6/22, leading to nonsense mediated decay in a gene in which loss of function is an established disease mechanism (PVS1). This variant has been detected in at least one individual with progressive limb girdle muscle weakness, where it was confirmed in trans with a second frameshift variant (PMID: 27862037; PP4). The filtering allele frequency of this variant is 0.000034729 (the upper threshold of the 95% CI of 28/1105382 exome chromosomes) in the European (non-Finnish) population in gnomAD v4.1.0, which is lower than the VCEP threshold (0.0001) for PM2_Supporting, meeting this criterion (PM2_Supporting). 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 (LGMD VCEP specifications version 1.0.0; 01/09/2025): PVS1, PP4, PM2_Supporting.

Met criteria codes

PP4	✔	At least one patient with this variant displayed progressive weakness, dystrophic features on biopsy, and elevated CK levels, which is highly specific for LGMD2L (PP4_Supporting, PMID: 27862037).
PM2_Supporting	✔	The filtering allele frequency of this variant is 0.000034729 (the upper threshold of the 95% CI of 28/1105382 exome chromosomes) in the European (non-Finnish) population in gnomAD v4.1.0, which is lower than the VCEP threshold (0.0001) for PM2_Supporting, meeting this criterion (PM2_Supporting).
PVS1	✔	The c.304_308del (p.Lys102ValfsTer2) variant in ANO5 is a frameshift variant predicted to cause a premature stop codon in biologically-relevant-exon 6/22 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).

Not Met criteria codes

PM3	✖	PM3 points not applied here as they are not needed to meet the pathogenic classification and this curation was used to bring the in trans variant from VUS to Pathogenic.

Curation History

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