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.1733T>C (p.Phe578Ser)

Version: 1.0

CA232785

140553 (ClinVar)

Gene: ANO5 (HGNC:203859)
Condition: autosomal recessive limb-girdle muscular dystrophy (MONDO:0015152)
Inheritance Mode: Autosomal recessive inheritance
UUID: 4aaaaa8b-632d-4b0d-abb4-999289ba9ca5
Approved on: 2026/2/17
Published on: 2026/4/9

HGVS expressions

NM_213599.3(ANO5):c.1733T>C (p.Phe578Ser)
NM_213599.3:c.1733T>C
NC_000011.10:g.22262231T>C
CM000673.2:g.22262231T>C
NC_000011.9:g.22283777T>C
CM000673.1:g.22283777T>C
NC_000011.8:g.22240353T>C
NG_015844.1:g.74056T>C
ENST00000682266.1:c.1283T>C
ENST00000682341.1:c.1691T>C
ENST00000683197.1:c.1691T>C
ENST00000683411.1:c.1283T>C
ENST00000683437.1:c.1283T>C
ENST00000683613.1:n.2727T>C
ENST00000684663.1:c.1688T>C
ENST00000324559.9:c.1733T>C
ENST00000648804.1:n.2068T>C
ENST00000324559.8:c.1733T>C
NM_001142649.1:c.1730T>C
NM_213599.2:c.1733T>C
NM_001142649.2:c.1730T>C

Pathogenic

Met criteria codes 4

PM3_Very Strong | PP1 | PP3 | PP4

Not Met criteria codes 3

PM2 | BA1 | BS1

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 2.0.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Limb Girdle Muscular Dystrophy VCEP

The NM_213599.3: c.1733T>C variant in ANO5 is a missense variant predicted to cause a substitution of phenylalanine by serine at amino acid 578, p.(Phe578Ser). Among a selection of the available literature, this variant has been reported in at least 16 unrelated individuals with features consistent with LGMD or anoctaminopathy (PMID: 21186264, 22742934, 23041008, 23663589, 23670307, 25891276, 28187523, 30919934, 31069529, 31517061, 32978841, 34687219, 35563815, 37526466, 31069529, 38374194). In two unrelated patients without reported familial consanguinity, the variant was observed in a homozygous state (1.0 pt; PMID: 31069529, 38374194). Three patients were reported as compound heterozygous with the pathogenic variant c.191dup p.(Asn64LysfsTer15) confirmed in trans (1.0 pt x3 = 3.0 pts, PMID: 21186264, 23670307, 25891276), and two patients had the c.191dup variant in unknown phase (0.5 pt x2 = 1.0 pt, PMID: 32978841, 34687219). One patient was reported as compound heterozygous with the pathogenic variant c.1898+1G>A (1.0 pt, PMID: 28187523) (PM3_Very Strong). This variant has also been shown to co-segregate with autosomal recessive LGMD in at least two family members from one family (PMID: 25891276; PP1), and at least one patient with this variant and a second presumed diagnostic ANO5 allele displayed a progressive limb girdle pattern of muscle weakness (PMID: 21186264, 25891276, 31069529, 38374194; PP4). The highest population minor allele frequency for this variant is 0.000816 in gnomAD v4.1.10 (73/91068 South Asian chromosomes), which is higher than the VCEP threshold for PM2_Supporting (0.0001) (PM2_Supporting not met). The REVEL score is 0.75, which is above the LGMD VCEP threshold of ≥0.70, evidence that correlates with impact to ANO5 function (PP3). 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 2.0.0; 02/17/2026): PM3_Very Strong, PP4, PP1, PP3.

Met criteria codes

PM3_Very Strong	✔	Among a selection of the available literature, this variant has been reported in at least 16 unrelated individuals with features consistent with LGMD or anoctaminopathy (PMID:21186264, 22742934, 23041008, 23663589, 23670307, 25891276, 28187523, 30919934, 31069529, 31517061, 32978841, 34687219, 35563815, 37526466, 31069529, 38374194). Two patients had the VOI in a homozygous state without reported familial consanguinity (1.0 pt; PMID: 31069529, 38374194). Three patients were reported as compound heterozygous with the pathogenic variant c.191dup p.(Asn64LysfsTer15) confirmed in trans (1.0 pt x3 = 3.0 pts, PMID: 21186264, 23670307, 25891276) and unknown phase in two patients (0.5 pt x2 = 1.0 pt, PMID: 32978841, 34687219). One patient was reported as compound heterozygous with the pathogenic variant c.1898+1G>A (1.0 pt, PMID: 28187523) (PM3_Very Strong). c.191dup p.(Asn64LysfsTer15) is predicted on a different haplotype than the curated variant
PP1	✔	This variant has been shown to co-segregate with autosomal recessive LGMD in one family member (PMID: 25891276; PP1).
PP3	✔	The REVEL score is 0.75, which is above the LGMD VCEP threshold of ≥0.70, evidence that correlates with impact to ANO5 function (PP3).
PP4	✔	At least one patient with this variant and a second presumed diagnostic ANO5 allele displayed a progressive limb girdle pattern of muscle weakness (PMID: 21186264, 25891276, 31069529, 38374194; PP4).

Not Met criteria codes

PM2	✖	The highest population minor allele frequency for this variant is 0.000816 in gnomAD v4.1.10 (73/91068 South Asian chromosomes), which is higher than the VCEP threshold for PM2_Supporting (0.0001) (PM2_Supporting not met).

BA1		✖	The filtering allele frequency for this variant is 0.0006536 in gnomAD v.4.1.0 (the lower threshold of the 95% CI of 73/91068 South Asian chromosomes), which is less than the LGMD VCEP threshold for BA1 (BA1 not met).
BS1		✖	The filtering allele frequency for this variant is 0.0006536 in gnomAD v.4.1.0 (the lower threshold of the 95% CI of 73/91068 South Asian chromosomes), which is less than the LGMD VCEP threshold for BA1 (BS1 not met).

Curation History

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.

ClinGen Terms of Use.
¤ Powered by BCM's Genboree.