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Variant: NM_213599.3(ANO5):c.148C>T (p.Arg50Ter)

Version: 1.0

CA379924765

468825 (ClinVar)

Gene: ANO5 (HGNC:203859)
Condition: autosomal recessive limb-girdle muscular dystrophy (MONDO:0015152)
Inheritance Mode: Autosomal recessive inheritance
UUID: 6efeb5b0-da16-48e2-8a9c-b824a6aebdae
Approved on: 2025/1/7
Published on: 2025/1/7

HGVS expressions

NM_213599.3(ANO5):c.148C>T (p.Arg50Ter)
NM_213599.3:c.148C>T
NC_000011.10:g.22218255C>T
CM000673.2:g.22218255C>T
NC_000011.9:g.22239801C>T
CM000673.1:g.22239801C>T
NC_000011.8:g.22196377C>T
NG_015844.1:g.30080C>T
ENST00000682084.1:n.3322C>T
ENST00000682266.1:c.-270-2842C>T
ENST00000682341.1:c.139-2842C>T
ENST00000682530.1:c.136-488C>T
ENST00000682684.1:n.560-2842C>T
ENST00000683197.1:c.139-2842C>T
ENST00000683411.1:c.-270-2842C>T
ENST00000683437.1:c.-270-2842C>T
ENST00000683834.1:n.381-2842C>T
ENST00000683897.1:n.425-2842C>T
ENST00000684365.1:n.550-2842C>T
ENST00000684663.1:c.136-2842C>T
ENST00000324559.9:c.148C>T
ENST00000648804.1:n.670-331C>T
ENST00000324559.8:c.148C>T
NM_001142649.1:c.145C>T
NM_213599.2:c.148C>T
NM_001142649.2:c.145C>T

Pathogenic

Met criteria codes 4

PVS1 PM2_Supporting PM3 PP4

Not Met criteria codes 14

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

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*

Evidence Links 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.148C>T p.(Arg50Ter) variant in ANO5 is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 4/22 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 two individuals with LGMD, including confirmed in trans with a pathogenic or likely pathogenic variant (c.191dup, 1.0 pt, PMID: 23041008) (PM3). At least one patient with this variant displayed progressive limb girdle muscle weakness (PMID: 28403181; PP4). This variant is absent from gnomAD v3.1.2 and v2.1.1 (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; 01/07/2025): PVS1, PM3, PP4, PM2_Supporting.

Met criteria codes

PVS1	✔	The c.148C>T (p.Arg50Ter) variant in ANO5 is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 4/22 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).
PM2_Supporting	✔	This variant is absent from gnomAD v3.1.2 and v2.1.1 (PM2_Supporting).
PM3	✔	This variant has been detected in at least 2 individuals with autosomal recessive limb-girdle muscular dystrophy. Of those individuals, one was compound heterozygous for the variant and a pathogenic or likely pathogenic variant confirmed in trans by molecular methods (PM3, PMID: 23041008).
PP4	✔	At least one patient with this variant displayed progressive muscle weakness, which is highly specific for autosomal recessive limb-girdle muscular dystrophy (PP4, PMID:28403181).

Not Met criteria codes

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
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
PS1	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS3	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1	ℹ	✖	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	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM4	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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