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Variant: NM_001130987.2(DYSF):c.706C>T (p.Arg236Ter)

Version: 1.0

CA222201

94352 (ClinVar)

Gene: DYSF (HGNC:8291)
Condition: autosomal recessive limb-girdle muscular dystrophy (MONDO:0015152)
Inheritance Mode: Autosomal recessive inheritance
UUID: 06a5fc8e-22fb-48db-8541-4b6ae194596f
Approved on: 2025/7/8
Published on: 2025/8/14

HGVS expressions

NM_001130987.2(DYSF):c.706C>T (p.Arg236Ter)
NM_001130987.2:c.706C>T
NC_000002.12:g.71513868C>T
CM000664.2:g.71513868C>T
NC_000002.11:g.71740998C>T
CM000664.1:g.71740998C>T
NC_000002.10:g.71594506C>T
NG_008694.1:g.65246C>T
ENST00000258104.8:c.610C>T
ENST00000410020.8:c.706C>T
ENST00000258104.7:c.610C>T
ENST00000394120.6:c.613C>T
ENST00000409366.5:c.613C>T
ENST00000409582.7:c.703C>T
ENST00000409651.5:c.706C>T
ENST00000409744.5:c.613C>T
ENST00000409762.5:c.703C>T
ENST00000410020.7:c.706C>T
ENST00000410041.1:c.706C>T
ENST00000413539.6:c.703C>T
ENST00000429174.6:c.610C>T
NM_001130455.1:c.613C>T
NM_001130976.1:c.610C>T
NM_001130977.1:c.610C>T
NM_001130978.1:c.610C>T
NM_001130979.1:c.703C>T
NM_001130980.1:c.703C>T
NM_001130981.1:c.703C>T
NM_001130982.1:c.706C>T
NM_001130983.1:c.613C>T
NM_001130984.1:c.613C>T
NM_001130985.1:c.706C>T
NM_001130986.1:c.613C>T
NM_001130987.1:c.706C>T
NM_003494.3:c.610C>T
NM_001130455.2:c.613C>T
NM_001130976.2:c.610C>T

NM_001130977.2:c.610C>T
NM_001130978.2:c.610C>T
NM_001130979.2:c.703C>T
NM_001130980.2:c.703C>T
NM_001130981.2:c.703C>T
NM_001130982.2:c.706C>T
NM_001130983.2:c.613C>T
NM_001130984.2:c.613C>T
NM_001130985.2:c.706C>T
NM_001130986.2:c.613C>T
NM_003494.4:c.610C>T

Pathogenic

Met criteria codes 4

PM2_Supporting PVS1 PM3 PP4_Strong

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 DYSF 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_003494.4: c.610C>T p.(Arg204Ter) variant in DYSF, which is also known as NM_001130987.2: c.706C>T p.(Arg236Ter), is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 6/55, leading to nonsense mediated decay in a gene in which loss of function is an established disease mechanism (PVS1). This variant has been identified in at least two patients with clinical features consistent with LGMD, including in a homozygous state in an individual from a consanguineous family (0.25 pts, PMID: 35422632) and in trans with a pathogenic variant (NM_003494.4: c.855+1del, 1.0 pt, PMID: 18853459) (PM3). At least one of these patients had a clinical diagnosis of LGMD (Miyoshi myopathy) and severely reduced dysferlin protein expression in skeletal muscle, which is highly specific for DYSF-related LGMD (PP4_Strong; PMID: 18853459). The filtering allele frequency of this variant in gnomAD v4.1.0 exomes is 0.00006973 (the upper threshold of the 95% CI of 3/1111878 European (non-Finnish) chromosomes), which is less than the ClinGen LGMD VCEP threshold (≤0.0001) (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; 07/08/2025): PVS1, PM3, PP4_Strong, PM2_Supporting.

Met criteria codes

PM2_Supporting	✔	The filtering allele frequency of this variant in gnomAD v4.1.0 exomes is 0.00006973 (the upper threshold of the 95% CI of 3/1111878 European (non-Finnish) chromosomes), which is less than the ClinGen LGMD VCEP threshold (≤0.0001) (PM2_Supporting).
PVS1	✔	The NM_003494.4: c.610C>T p.(Arg204Ter) variant in DYSF, which is also known as NM_001130987.2: c.706C>T p.(Arg236Ter), is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 6/55, leading to nonsense mediated decay in a gene in which loss of function is an established disease mechanism (PVS1).

PM3		✔	This variant has been identified in at least two patients with clinical features consistent with LGMD, including in a homozygous state in an individual from a consanguineous family (0.25 pts, PMID: 35422632) and in trans with a pathogenic variant (NM_003494.4: c.855+1del, 1.0 pt, PMID: 18853459) (PM3). c.855+1del is independently classified as P
PP4_Strong		✔	At least one patient with this variant and a second presumed diagnostic DYSF variant had a clinical diagnosis of LGMD (Miyoshi myopathy) and severely reduced dysferlin protein expression in skeletal muscle, which is highly specific for DYSF-related LGMD (PP4_Strong; PMID: 18853459).

Curation History

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