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_001130987.2(DYSF):c.4282C>T (p.Gln1428Ter)

Version: 1.0

CA1706954

285153 (ClinVar)

Gene: DYSF (HGNC:8291)
Condition: autosomal recessive limb-girdle muscular dystrophy (MONDO:0015152)
Inheritance Mode: Autosomal recessive inheritance
UUID: aab3c348-66cf-4f14-b09e-6878ec67455d
Approved on: 2025/9/30
Published on: 2025/10/9

HGVS expressions

NM_001130987.2(DYSF):c.4282C>T (p.Gln1428Ter)
NM_001130987.2:c.4282C>T
NC_000002.12:g.71612701C>T
CM000664.2:g.71612701C>T
NC_000002.11:g.71839831C>T
CM000664.1:g.71839831C>T
NC_000002.10:g.71693339C>T
NG_008694.1:g.164079C>T
ENST00000698057.1:c.1696C>T
ENST00000698058.1:c.913C>T
ENST00000698059.1:c.871C>T
ENST00000258104.8:c.4228C>T
ENST00000410020.8:c.4282C>T
ENST00000258104.7:c.4228C>T
ENST00000394120.6:c.4231C>T
ENST00000409366.5:c.4231C>T
ENST00000409582.7:c.4279C>T
ENST00000409651.5:c.4324C>T
ENST00000409744.5:c.4189C>T
ENST00000409762.5:c.4279C>T
ENST00000410020.7:c.4282C>T
ENST00000410041.1:c.4282C>T
ENST00000413539.6:c.4321C>T
ENST00000429174.6:c.4228C>T
ENST00000468173.1:n.464C>T
ENST00000479049.6:n.1113C>T
ENST00000487180.5:n.447C>T
ENST00000494501.5:n.526C>T
NM_001130455.1:c.4231C>T
NM_001130976.1:c.4186C>T
NM_001130977.1:c.4186C>T
NM_001130978.1:c.4228C>T
NM_001130979.1:c.4321C>T
NM_001130980.1:c.4279C>T
NM_001130981.1:c.4279C>T
NM_001130982.1:c.4324C>T
NM_001130983.1:c.4231C>T

NM_001130984.1:c.4189C>T
NM_001130985.1:c.4282C>T
NM_001130986.1:c.4189C>T
NM_001130987.1:c.4282C>T
NM_003494.3:c.4228C>T
NM_001130455.2:c.4231C>T
NM_001130976.2:c.4186C>T
NM_001130977.2:c.4186C>T
NM_001130978.2:c.4228C>T
NM_001130979.2:c.4321C>T
NM_001130980.2:c.4279C>T
NM_001130981.2:c.4279C>T
NM_001130982.2:c.4324C>T
NM_001130983.2:c.4231C>T
NM_001130984.2:c.4189C>T
NM_001130985.2:c.4282C>T
NM_001130986.2:c.4189C>T
NM_003494.4:c.4228C>T

Pathogenic

Met criteria codes 4

PM3_Supporting PP1 PP4 PVS1

Not Met criteria codes 1

PM2

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 2.0.0*

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Limb Girdle Muscular Dystrophy VCEP

The NM_003494.4: c.4228C>T p.(Gln1410Ter) variant in DYSF, which is also known as NM_001130987.2: c.4282C>T (p.Gln1428Ter), is a nonsense variant predicted to introduce a premature stop codon in exon 39/55, leading to nonsense mediated decay in a gene in which loss of function is an established disease mechanism (PVS1). This variant has been observed in four individuals with features of LGMD from two families (PMID: 35047756, 34624274). In a consanguineous family from Jordan, it was identified in a homozygous state in two affected siblings (PMID: 35047756; PP1). In the affected child of one of the homozygous individuals, it was also identified in unconfirmed phase with a pathogenic variant (NM_003494.4: c.4022T>C p.(Leu1341Pro), 0.5 pts; PM3_Supporting). At least one patient with this variant and a second presumed diagnostic DYSF allele displayed progressive proximal muscle weakness or had a clinical diagnosis of LGMD (PMID: 35047756, 34624274; PP4). The filtering allele frequency for this variant is 0.0001752 in gnomAD v4.1.0 (the upper bound of the 95% confidence interval of 5/60012 Admixed American alleles), which is higher than the VCEP threshold of 0.0001 for PM2_Supporting (criterion not met). 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; 09/30/2025): PVS1, PP1, PM3_Supporting, PP4.

Met criteria codes

PM3_Supporting		✔	This variant has been observed in four individuals with features of LGMD from two families (PMID: 35047756, 34624274). In a consanguineous family from Jordan, it was identified in a homozygous state in two affected siblings (PMID: 35047756; PP1). In the affected child of one of the homozygous individuals, it was also identified in unconfirmed phase with a pathogenic variant (NM_003494.4: c.4022T>C p.(Leu1341Pro), 0.5 pts; PM3_Supporting).
PP1		✔	This variant was shown to co-segregate with autosomal recessive LGMD in one affected family member (PMID: 34624274, PP1).
PP4		✔	At least one patient with this variant and a second presumed diagnostic DYSF allele displayed progressive proximal muscle weakness or had a clinical diagnosis of LGMD (PMID: 35047756, 34624274; PP4).
PVS1		✔	The NM_003494.4: c.4228C>T p.(Gln1410Ter) variant in DYSF, which is also known as NM_001130987.2: c.4282C>T (p.Gln1428Ter), is a nonsense variant predicted to introduce a premature stop codon in exon 39/55, leading to nonsense mediated decay in a gene in which loss of function is an established disease mechanism (PVS1).

Not Met criteria codes

PM2		✖	The filtering allele frequency for this variant is 0.0001752 in gnomAD v4.1.0 (the upper bound of the 95% confidence interval of 5/60012 Admixed American alleles), which is higher than the VCEP threshold of 0.0001 for PM2_Supporting (criterion 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.