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.2266C>T (p.Gln756Ter)

Version: 1.0

CA347208953

1433815 (ClinVar)

Gene: DYSF (HGNC:8291)
Condition: autosomal recessive limb-girdle muscular dystrophy (MONDO:0015152)
Inheritance Mode: Autosomal recessive inheritance
UUID: 71a57ffa-8ae3-48e6-bdc5-8b296b89d91c
Approved on: 2025/7/23
Published on: 2025/8/14

HGVS expressions

NM_001130987.2:c.2266C>T
NM_001130987.2(DYSF):c.2266C>T (p.Gln756Ter)
NC_000002.12:g.71561801C>T
CM000664.2:g.71561801C>T
NC_000002.11:g.71788931C>T
CM000664.1:g.71788931C>T
NC_000002.10:g.71642439C>T
NG_008694.1:g.113179C>T
ENST00000258104.8:c.2212C>T
ENST00000410020.8:c.2266C>T
ENST00000258104.7:c.2212C>T
ENST00000394120.6:c.2215C>T
ENST00000409366.5:c.2215C>T
ENST00000409582.7:c.2263C>T
ENST00000409651.5:c.2308C>T
ENST00000409744.5:c.2173C>T
ENST00000409762.5:c.2263C>T
ENST00000410020.7:c.2266C>T
ENST00000410041.1:c.2266C>T
ENST00000413539.6:c.2305C>T
ENST00000429174.6:c.2212C>T
NM_001130455.1:c.2215C>T
NM_001130976.1:c.2170C>T
NM_001130977.1:c.2170C>T
NM_001130978.1:c.2212C>T
NM_001130979.1:c.2305C>T
NM_001130980.1:c.2263C>T
NM_001130981.1:c.2263C>T
NM_001130982.1:c.2308C>T
NM_001130983.1:c.2215C>T
NM_001130984.1:c.2173C>T
NM_001130985.1:c.2266C>T
NM_001130986.1:c.2173C>T
NM_001130987.1:c.2266C>T
NM_003494.3:c.2212C>T
NM_001130455.2:c.2215C>T
NM_001130976.2:c.2170C>T

NM_001130977.2:c.2170C>T
NM_001130978.2:c.2212C>T
NM_001130979.2:c.2305C>T
NM_001130980.2:c.2263C>T
NM_001130981.2:c.2263C>T
NM_001130982.2:c.2308C>T
NM_001130983.2:c.2215C>T
NM_001130984.2:c.2173C>T
NM_001130985.2:c.2266C>T
NM_001130986.2:c.2173C>T
NM_003494.4:c.2212C>T

Pathogenic

Met criteria codes 3

PP4 PVS1 PM2_Supporting

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 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.2212C>T p.(Gln738Ter) variant in DYSF, which is also known as NM_001130987.2: c.2266C>T p.(Gln756Ter), is a nonsense variant predicted to cause a premature stop codon in exon 23/55, leading to nonsense mediated decay in a gene in which loss of function is a known mechanism of disease (PVS1). This variant has been reported in a homozygous state in an individual with known familial consanguinity who displayed features of LGMD including proximal muscle weakness (0.25 pts, PMID: 39548682, LOVD individual #00391981) (PP4; PM3_Supporting not met). The highest allele frequency for this variant is 0.0000008474 in the European (non-Finnish) population of gnomAD v4.1.0 (1/1180024 chromosomes), which is less than the LGMD VCEP threshold for PM2_Supporting (0.0001), 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; 07/23/2025): PVS1, PP4, PM2_Supporting.

Met criteria codes

PP4	✔	This variant has been reported in a homozygous state in an individual who displayed features of LGMD including proximal muscle weakness (PMID: 39548682, LOVD individual #00391981) (PP4).
PVS1	✔	The NM_003494.4: c.2212C>T p.(Gln738Ter) variant in DYSF, which is also known as NM_001130987.2: c.2266C>T p.(Gln756Ter), is a nonsense variant predicted to cause a premature stop codon in exon 23/55, leading to nonsense mediated decay in a gene in which loss of function is a known mechanism of disease (PVS1).
PM2_Supporting	✔	

The highest allele frequency for this variant is 0.0000008474 in the European (non-Finnish) population of gnomAD v4.1.0 (1/1180024 chromosomes), which is less than the LGMD VCEP threshold for PM2_Supporting (0.0001), meeting this criterion (PM2_Supporting).

Not Met criteria codes

PM3	✖	This variant has been reported in a homozygous state in an individual with known familial consanguinity who displayed features of LGMD including proximal muscle weakness (0.25 pts, PMID: 39548682, LOVD individual #00391981) (PM3_Supporting not met). Additional individuals with this variant present in Dysferlin Registry, but details not requested given a Pathogenic classification reached.

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.