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.1867C>T (p.Gln623Ter)

Version: 1.0

CA253901

6665 (ClinVar)

Gene: DYSF (HGNC:8291)
Condition: autosomal recessive limb-girdle muscular dystrophy (MONDO:0015152)
Inheritance Mode: Autosomal recessive inheritance
UUID: 976d5508-20a4-411e-b250-1c0288ee17ab
Approved on: 2025/12/29
Published on: 2026/1/12

HGVS expressions

NM_001130987.2(DYSF):c.1867C>T (p.Gln623Ter)
NM_001130987.2:c.1867C>T
NC_000002.12:g.71553071C>T
CM000664.2:g.71553071C>T
NC_000002.11:g.71780201C>T
CM000664.1:g.71780201C>T
NC_000002.10:g.71633709C>T
NG_008694.1:g.104449C>T
ENST00000258104.8:c.1813C>T
ENST00000410020.8:c.1867C>T
ENST00000258104.7:c.1813C>T
ENST00000394120.6:c.1816C>T
ENST00000409366.5:c.1816C>T
ENST00000409582.7:c.1864C>T
ENST00000409651.5:c.1909C>T
ENST00000409744.5:c.1774C>T
ENST00000409762.5:c.1864C>T
ENST00000410020.7:c.1867C>T
ENST00000410041.1:c.1867C>T
ENST00000413539.6:c.1906C>T
ENST00000429174.6:c.1813C>T
NM_001130455.1:c.1816C>T
NM_001130976.1:c.1771C>T
NM_001130977.1:c.1771C>T
NM_001130978.1:c.1813C>T
NM_001130979.1:c.1906C>T
NM_001130980.1:c.1864C>T
NM_001130981.1:c.1864C>T
NM_001130982.1:c.1909C>T
NM_001130983.1:c.1816C>T
NM_001130984.1:c.1774C>T
NM_001130985.1:c.1867C>T
NM_001130986.1:c.1774C>T
NM_001130987.1:c.1867C>T
NM_003494.3:c.1813C>T
NM_001130455.2:c.1816C>T
NM_001130976.2:c.1771C>T

NM_001130977.2:c.1771C>T
NM_001130978.2:c.1813C>T
NM_001130979.2:c.1906C>T
NM_001130980.2:c.1864C>T
NM_001130981.2:c.1864C>T
NM_001130982.2:c.1909C>T
NM_001130983.2:c.1816C>T
NM_001130984.2:c.1774C>T
NM_001130985.2:c.1867C>T
NM_001130986.2:c.1774C>T
NM_003494.4:c.1813C>T

Pathogenic

Met criteria codes 4

PM2_Supporting | PVS1 | PP4_Strong | PM3_Supporting

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.1813C>T p.(Gln605Ter) variant in DYSF, which is also known as NM_001130987.2: c.1867C>T (p.Gln623Ter), is a stop-gained variant expected to introduce a premature stop codon in exon 20/55, leading to nonsense mediated decay in a gene in which loss of function is a known disease mechanism (PVS1). This variant has been reported in at least three patients with features consistent with LGMD or dysferlinopathy (PMID: 9731526, 17129727, 17828519, 33715265), including in a homozygous state without reported familial consanguinity (0.5 pts, PMID: 9731526) (PM3_Supporting). At least one patient with this variant and a second presumed diagnostic DYSF variant exhibited both progressive limb girdle muscle weakness and absent or significantly reduced dysferlin protein expression in skeletal muscle or blood monocytes, which is highly specific for DYSF-related LGMD (PMID: 33715265; PP4_Strong). This variant is absent from gnomAD v4.1.0 (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 2.0.0; 12/29/2025): PVS1, PM3_Supporting, PP4_Strong, PM2_Supporting.

Met criteria codes

PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0 (PM2_Supporting).
PVS1	✔	The NM_003494.4: c.1813C>T p.(Gln605Ter) variant in DYSF, which is also known as NM_001130987.2: c.1867C>T (p.Gln623Ter), is a stop-gained variant expected to introduce a premature stop codon in exon 20/55, leading to nonsense mediated decay in a gene in which loss of function is a known disease mechanism (PVS1). SpliceAI 0.01
PP4_Strong	✔	

At least one patient with this variant and a second presumed diagnostic DYSF variant exhibited both progressive limb girdle muscle weakness and absent or significantly reduced dysferlin protein expression in skeletal muscle or blood monocytes, which is highly specific for DYSF-related LGMD (PMID: 33715265; PP4_Strong).

PM3_Supporting ✔

This variant has been reported in at least three patients with features consistent with LGMD or dysferlinopathy (PMID: 9731526, 17129727, 17828519, 33715265), including in a homozygous state without reported familial consanguinity (0.5 pts, PMID: 9731526) (PM3_Supporting).

Curation History

Showing 1 to 1 of 1 rows

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