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Variant: NM_001130987.2(DYSF):c.4822C>T (p.Gln1608Ter)

Version: 1.0

CA347219737

813970 (ClinVar)

Gene: DYSF (HGNC:8291)
Condition: autosomal recessive limb-girdle muscular dystrophy (MONDO:0015152)
Inheritance Mode: Autosomal recessive inheritance
UUID: 6cf55584-a4b4-44b8-ad57-fe65325e2f97
Approved on: 2025/8/14
Published on: 2025/9/5

HGVS expressions

NM_001130987.2:c.4822C>T
NM_001130987.2(DYSF):c.4822C>T (p.Gln1608Ter)
NC_000002.12:g.71658944C>T
CM000664.2:g.71658944C>T
NC_000002.11:g.71886074C>T
CM000664.1:g.71886074C>T
NC_000002.10:g.71739582C>T
NG_008694.1:g.210322C>T
ENST00000698057.1:c.2236C>T
ENST00000698058.1:c.1453C>T
ENST00000698059.1:c.1561C>T
ENST00000258104.8:c.4705C>T
ENST00000410020.8:c.4822C>T
ENST00000258104.7:c.4705C>T
ENST00000394120.6:c.4708C>T
ENST00000409366.5:c.4771C>T
ENST00000409582.7:c.4819C>T
ENST00000409651.5:c.4801C>T
ENST00000409744.5:c.4729C>T
ENST00000409762.5:c.4756C>T
ENST00000410020.7:c.4822C>T
ENST00000410041.1:c.4759C>T
ENST00000413539.6:c.4798C>T
ENST00000429174.6:c.4768C>T
ENST00000479049.6:n.1590C>T
NM_001130455.1:c.4708C>T
NM_001130976.1:c.4663C>T
NM_001130977.1:c.4726C>T
NM_001130978.1:c.4768C>T
NM_001130979.1:c.4798C>T
NM_001130980.1:c.4756C>T
NM_001130981.1:c.4819C>T
NM_001130982.1:c.4801C>T
NM_001130983.1:c.4771C>T
NM_001130984.1:c.4729C>T
NM_001130985.1:c.4759C>T
NM_001130986.1:c.4666C>T

NM_001130987.1:c.4822C>T
NM_003494.3:c.4705C>T
NM_001130455.2:c.4708C>T
NM_001130976.2:c.4663C>T
NM_001130977.2:c.4726C>T
NM_001130978.2:c.4768C>T
NM_001130979.2:c.4798C>T
NM_001130980.2:c.4756C>T
NM_001130981.2:c.4819C>T
NM_001130982.2:c.4801C>T
NM_001130983.2:c.4771C>T
NM_001130984.2:c.4729C>T
NM_001130985.2:c.4759C>T
NM_001130986.2:c.4666C>T
NM_003494.4:c.4705C>T

Pathogenic

Met criteria codes 4

PVS1 PM3 PP4 PM2_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.4705C>T p.(Gln1569Ter) variant in DYSF, which is also known as NM_001130987.2: c.4822C>T (p.Gln1608Ter), is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 43/55, 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 two individuals with clinically suspected limb-girdle muscular dystrophy (LGMD), both of whom had the same second variant, NM_003494.4: c.5804C>T p.(Pro1935Leu), which is classified as Pathogenic by the LGMD VCEP. In one case, the variants were confirmed in trans (1.0 pt, ClinVar SCV001164498.1 internal data communication), whereas in the other the variants were in unknown phase (0.5 pts, GRASP-LGMD Consortium internal data communication) (PM3, PP4). 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; 08/14/2025): PVS1, PM2_Supporting, PM3, PP4.

Met criteria codes

PVS1	ℹ	✔	The NM_003494.4: c.4705C>T p.(Gln1569Ter) variant in DYSF, which is also known as NM_001130987.2: c.4822C>T (p.Gln1608Ter), is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 43/55, 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 two individuals with suspected limb-girdle muscular dystrophy (LGMD), both of whom had the same second variant, NM_003494.4: c.5804C>T p.(Pro1935Leu), which is classified as Pathogenic by the LGMD VCEP. In one case, the variants were confirmed in trans (1.0 pt, ClinVar SCV001164498.1 internal data communication), whereas in the other the variants were in unknown phase (0.5 pts, GRASP-LGMD Consortium internal data communication) (PM3, PP4). c.5804C>T p.(Pro1935Leu) can be classified as at least LP without counting these two observations with the curated variant: PM2_Supporting and PM3_Supporting, PP1, and PP4_Strong for other patients The ClinVar submission by the Broad Center for Mendelian Genomics, Broad Institute of MIT and Harvard was made before the GRASP participant received a diagnosis through testing at Invitae (now Labcorp), so we are confident these are distinct individuals.
PP4		✔	At least one patient with this variant and a second presumed diagnostic DYSF variant had a clinical suspicion of LGMD (PP4).
PM2_Supporting		✔	This variant is absent from gnomAD v4.1.0 (PM2_Supporting).

Curation History

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