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Variant: NM_001130987.2(DYSF):c.5830C>T (p.Arg1944Ter)

Version: 1.0

CA118412

6676 (ClinVar)

Gene: DYSF (HGNC:8291)
Condition: autosomal recessive limb-girdle muscular dystrophy (MONDO:0015152)
Inheritance Mode: Autosomal recessive inheritance
UUID: b4eed7af-a90e-4888-a97f-1ba06b302740
Approved on: 2026/1/23
Published on: 2026/2/17

HGVS expressions

NM_001130987.2(DYSF):c.5830C>T (p.Arg1944Ter)
NM_001130987.2:c.5830C>T
NC_000002.12:g.71674242C>T
CM000664.2:g.71674242C>T
NC_000002.11:g.71901372C>T
CM000664.1:g.71901372C>T
NC_000002.10:g.71754880C>T
NG_008694.1:g.225620C>T
ENST00000698057.1:c.3244C>T
ENST00000698058.1:c.2461C>T
ENST00000698059.1:c.2569C>T
ENST00000258104.8:c.5713C>T
ENST00000410020.8:c.5830C>T
ENST00000258104.7:c.5713C>T
ENST00000394120.6:c.5716C>T
ENST00000409366.5:c.5779C>T
ENST00000409582.7:c.5827C>T
ENST00000409651.5:c.5809C>T
ENST00000409744.5:c.5737C>T
ENST00000409762.5:c.5764C>T
ENST00000410020.7:c.5830C>T
ENST00000410041.1:c.5767C>T
ENST00000413539.6:c.5806C>T
ENST00000429174.6:c.5776C>T
ENST00000479049.6:n.2598C>T
NM_001130455.1:c.5716C>T
NM_001130976.1:c.5671C>T
NM_001130977.1:c.5734C>T
NM_001130978.1:c.5776C>T
NM_001130979.1:c.5806C>T
NM_001130980.1:c.5764C>T
NM_001130981.1:c.5827C>T
NM_001130982.1:c.5809C>T
NM_001130983.1:c.5779C>T
NM_001130984.1:c.5737C>T
NM_001130985.1:c.5767C>T
NM_001130986.1:c.5674C>T

NM_001130987.1:c.5830C>T
NM_003494.3:c.5713C>T
NM_001130455.2:c.5716C>T
NM_001130976.2:c.5671C>T
NM_001130977.2:c.5734C>T
NM_001130978.2:c.5776C>T
NM_001130979.2:c.5806C>T
NM_001130980.2:c.5764C>T
NM_001130981.2:c.5827C>T
NM_001130982.2:c.5809C>T
NM_001130983.2:c.5779C>T
NM_001130984.2:c.5737C>T
NM_001130985.2:c.5767C>T
NM_001130986.2:c.5674C>T
NM_003494.4:c.5713C>T

Pathogenic

Met criteria codes 4

PM3_Strong PP4_Strong PVS1 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.5713C>T p.(Arg1905Ter) variant in DYSF, which is also known as NM_001130987.2: c.5830C>T p.(Arg1944Ter), is a nonsense variant predicted to cause a premature stop codon in exon 51/55, leading to nonsense mediated decay in a gene in which loss of function is a known mechanism of disease (PVS1). There is also a chance for missplicing (SpliceAI delta score 0.23 for acceptor loss and 0.21 for donor loss), but exon skipping would be expected to introduce a frameshift and nonsense mediated decay. Across a selection of the available literature, this variant has been reported in at least seven individuals with suspected LGMD (PMID: 27602406, 33927379, 39548682), including in a homozygous state in at least two individuals with no reported familial consanguinity (1.0 pt, PMID: 39548682, LOVD individuals #00219410 and #00220156) and four with a second pathogenic variant in unknown phase (c.2779del p.(Ala927LeufsTer21), 0.5 pts, and c.3517dup p.(Ser1173PhefsTer2), 0.5 pts, PMID: 33927379; c.1392dupA p.(Asp465ArgfsTer9), 0.5 pts, and c.1481-1G>A, 0.5 pts, PMID: 27602406) (PM3_Strong). At least one patient with this variant and a second presumed diagnostic DYSF variant had suspected LGMD and absent dysferlin protein expression in blood monocytes, which is highly specific for DYSF-associated LGMD (PMID: 27602406; PP4_Strong). The filtering allele frequency for this variant is 0.000043167 in gnomAD v4.1.0 (the upper bound of the 95% CI of 39/1180060 European (non-Finnish) chromosomes), which is lower than the LGMD VCEP threshold for PM2_Supporting, 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 (specifications v2.0.0; 01/23/2026): PVS1, PP4_Strong, PM3_Strong, PM2_Supporting.

Met criteria codes

PM3_Strong		✔	Across a selection of the available literature, this variant has been reported in at least seven individuals with suspected LGMD including in a homozygous state in at least two individuals with no reported familial consanguinity (1.0 pt, PMID: 39548682, LOVD individuals #00219410 and #00220156) and four with a second pathogenic variant in unknown phase (c.2779del p.(Ala927LeufsTer21), 0.5 pts, and c.3517dup p.(Ser1173PhefsTer2), 0.5 pts, PMID: 33927379; c.1392dupA p.(Asp465ArgfsTer9), 0.5 pts, and c.1481-1G>A, 0.5 pts, PMID: 27602406) (PM3_Strong).
PP4_Strong		✔	At least one patient with this variant and a second presumed diagnostic DYSF variant had suspected LGMD and absent dysferlin protein expression in blood monocytes, which is highly specific for DYSF-associated LGMD (PMID: 27602406; PP4_Strong).
PVS1		✔	The NM_003494.4: c.5713C>T p.(Arg1905Ter) variant in DYSF, which is also known as NM_001130987.2: c.5830C>T p.(Arg1944Ter), is a nonsense variant predicted to cause a premature stop codon in exon 51/55, leading to nonsense mediated decay in a gene in which loss of function is a known mechanism of disease (PVS1). There is also a chance for missplicing (SpliceAI delta score 0.23 for acceptor loss and 0.21 for donor loss), but exon skipping would be expected to introduce a frameshift and nonsense mediated decay. Splice AI (acceptor loss 0.23; donor loss=0.21) Ref scores are 0.98 and 0.99, respectively. Alt scores are 0.75 and 0.78.
PM2_Supporting		✔	The filtering allele frequency for this variant is 0.000043167 in gnomAD v4.1.0 (the upper bound of the 95% CI of 39/1180060 European (non-Finnish) chromosomes), which is lower than the LGMD VCEP threshold for PM2_Supporting, meeting this criterion (PM2_Supporting).

Curation History

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