

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

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## 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

|                       |                                                                                   |                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|-----------------------|-----------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>PM3_Strong</b>     |    |    | 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).                                                                                   |
| <b>PP4_Strong</b>     |  |  | 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).                                                                                                                                                                                                                                                                                                                                                                                                          |
| <b>PVS1</b>           |  |  | 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. |
| <b>PM2_Supporting</b> |  |  | 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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| Showing 1 to 1 of 1 rows                                                                                                                                                                                                                                                                                                          |  |
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