

Variant: NM_001130987.2(DYSF):c.4614del (p.Phe1538fs)

Version: 1.0

CA10604426 [↗](#)

283205 (ClinVar) [↗](#)

Gene: DYSF ([HGNC:8291](#))

Condition: autosomal recessive limb-girdle muscular dystrophy
([MONDO:0015152](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: 92218107-5d89-4b5b-aa95-12f1ebffe88c

Approved on: 2025/1/8

Published on: 2025/1/8

HGVS expressions

- NM_001130987.2:c.4614del
- NM_001130987.2(DYSF):c.4614del (p.Phe1538fs)
- NC_000002.12:g.71644051del
- CM000664.2:g.71644051del
- NC_000002.11:g.71871181del
- CM000664.1:g.71871181del
- NC_000002.10:g.71724689del
- NG_008694.1:g.195429del
- ENST00000698057.1:c.2028del
- ENST00000698058.1:c.1245del
- ENST00000698059.1:c.1353del
- ENST00000258104.8:c.4497del
- ENST00000410020.8:c.4614del
- ENST00000258104.7:c.4497del
- ENST00000394120.6:c.4500del
- ENST00000409366.5:c.4563del
- ENST00000409582.7:c.4611del
- ENST00000409651.5:c.4593del
- ENST00000409744.5:c.4521del
- ENST00000409762.5:c.4548del
- ENST00000410020.7:c.4614del
- ENST00000410041.1:c.4551del
- ENST00000413539.6:c.4590del
- ENST00000429174.6:c.4560del
- ENST00000479049.6:n.1382del
- NM_001130455.1:c.4500del
- NM_001130976.1:c.4455del
- NM_001130977.1:c.4518del
- NM_001130978.1:c.4560del
- NM_001130979.1:c.4590del
- NM_001130980.1:c.4548del
- NM_001130981.1:c.4611del
- NM_001130982.1:c.4593del
- NM_001130983.1:c.4563del
- NM_001130984.1:c.4521del
- NM_001130985.1:c.4551del
- NM_001130986.1:c.4458del

NM_001130987.1:c.4614del
NM_003494.3:c.4497del
NM_001130455.2:c.4500del
NM_001130976.2:c.4455del
NM_001130977.2:c.4518del
NM_001130978.2:c.4560del
NM_001130979.2:c.4590del
NM_001130980.2:c.4548del
NM_001130981.2:c.4611del
NM_001130982.2:c.4593del
NM_001130983.2:c.4563del
NM_001130984.2:c.4521del
NM_001130985.2:c.4551del
NM_001130986.2:c.4458del
NM_003494.4:c.4497del

Pathogenic

Met criteria codes 5

- PVS1
- PM2_Supporting
- PP1
- PM3_Strong
- PP4_Strong

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.4497del p.(Phe1499LeufsTer4) variant in DYSF, which is also known as NM_001130987.2: c.4614del p.(Phe1538LeufsTer4), is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 41/55 leading to nonsense mediated decay in a gene in which loss of function is an established disease mechanism (PVS1). In the literature, this variant has also been described as c.4870delT. This variant has been detected in at least eight unrelated individuals with limb girdle muscular dystrophy (PMID: 23243261, 12796534, 17070050, 27647186, 26088049, 17614318). Among these individuals, it was identified in a homozygous state in three patients (1.0 pts, PMID: 26088049, 17614318, 12796534) and in trans with a pathogenic variant in at least one patient (c.2643+1G>A, 1.0 pt, PMID: 23243261) (PM3_Strong). At least one patient with this variant displayed progressive limb-girdle muscle weakness and absent dysferlin protein expression, which is highly specific for DYSF-associated LGMD (PP4_Strong, PMID: 27647186, 17070050). The variant was also reported to co-segregate with the disease in three affected family members from one family (PMID: 17614318) (PP1, capped with PP4_Strong). This variant is absent from gnomAD v2.1.1 and v3.1.2 (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; 01/08/2025): PVS1, PM3_Strong, PP4_Strong, PP1, PM2_Supporting.

Met criteria codes

PVS1



The NM_003494.4: c.4497del p.(Phe1499LeufsTer4) variant in DYSF, which is also known as NM_001130987.2: c.4614del p.(Phe1538LeufsTer4), is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 41/55 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).

PM2_Supporting			This variant is absent from gnomAD v2.1.1 and v3.1.2 (PM2_Supporting).
PP1			The variant was also reported to co-segregate with the disease in three affected family members from one family (PMID: 17614318) (PP1). (capped with PP4_Strong)
PM3_Strong			This variant has been detected in at least eight unrelated individuals with limb girdle muscular dystrophy (PMID: 23243261, 12796534, 17070050, 27647186, 26088049, 17614318). Among these individuals, it was identified in a homozygous state in three patients (1.0 pts, PMID: 26088049, 17614318, 12796534) and in trans with a pathogenic variant in at least one patient (c.2643+1G>A, 1.0 pt, PMID: 23243261) (PM3_Strong).
PP4_Strong			At least one patient with this variant displayed progressive limb-girdle muscle weakness and absent dysferlin protein expression, which is highly specific for DYSF-associated LGMD (PP4_Strong, PMID: 27647186, 17070050).

Curation History



 

 

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