

Variant: NM_001130987.2(DYSF):c.1350del (p.Phe451fs)

Version: 1.0

CA1705706 [↗](#)

551669 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 4c9547ca-5c55-4e70-9c57-f110c35e4994

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HGVS expressions

NM_001130987.2(DYSF):c.1350del (p.Phe451fs)

NM_001130987.2:c.1350del

NC_000002.12:g.71528371del

CM000664.2:g.71528371del

NC_000002.11:g.71755501del

CM000664.1:g.71755501del

NC_000002.10:g.71609009del

NG_008694.1:g.79749del

ENST00000258104.8:c.1254del

ENST00000410020.8:c.1350del

ENST00000258104.7:c.1254del

ENST00000394120.6:c.1257del

ENST00000409366.5:c.1257del

ENST00000409582.7:c.1347del

ENST00000409651.5:c.1350del

ENST00000409744.5:c.1257del

ENST00000409762.5:c.1347del

ENST00000410020.7:c.1350del

ENST00000410041.1:c.1350del

ENST00000413539.6:c.1347del

ENST00000429174.6:c.1254del

NM_001130455.1:c.1257del

NM_001130976.1:c.1254del

NM_001130977.1:c.1254del

NM_001130978.1:c.1254del

NM_001130979.1:c.1347del

NM_001130980.1:c.1347del

NM_001130981.1:c.1347del

NM_001130982.1:c.1350del

NM_001130983.1:c.1257del

NM_001130984.1:c.1257del

NM_001130985.1:c.1350del

NM_001130986.1:c.1257del

NM_001130987.1:c.1350del

NM_003494.3:c.1254del

NM_001130455.2:c.1257del

NM_001130976.2:c.1254del

NM_001130977.2:c.1254del
NM_001130978.2:c.1254del
NM_001130979.2:c.1347del
NM_001130980.2:c.1347del
NM_001130981.2:c.1347del
NM_001130982.2:c.1350del
NM_001130983.2:c.1257del
NM_001130984.2:c.1257del
NM_001130985.2:c.1350del
NM_001130986.2:c.1257del
NM_003494.4:c.1254del

Pathogenic

Met criteria codes 4

- PM3_Supporting
- PP4_Strong
- PM2_Supporting
- PVS1

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.1254del p.(Phe419LeufsTer41) variant in DYSF, which is also known as NM_001130987.2: c.1350del p.(Phe451LeufsTer41), is a frameshift variant expected to introduce a premature stop codon in exon 15/55, leading to nonsense mediated decay in a gene in which loss of function is a known mechanism of disease (PVS1). In the literature, this variant has also been described as p.(Pro418ProfsTer123). This variant has been reported in at least three patients with features consistent with LGMD (PMID: 27647186, 26404900, 26404900), including in a homozygous state without reported familial consanguinity (0.5 pts, PMID: 17994539; PM3_Supporting). This homozygous individual had both progressive limb girdle muscle weakness and absent dysferlin expression in skeletal muscle via both immunohistochemistry and Western blot (PMID: 17994539; PP4_Strong). The highest population allele frequency for this variant is 8.475e-7 in gnomAD v4.1.0 (1/1180008 European (non-Finnish) alleles), which is less than the threshold of 0.0001 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 (LGMD VCEP specifications version 2.0.0; 09/17/2025): PVS1, PM3_Supporting, PP4_Strong, PM2_Supporting.

Met criteria codes

PM3_Supporting



This variant has been reported in at least three patients with features consistent with LGMD (PMID: 27647186, 26404900, 26404900), including in a homozygous state without reported familial consanguinity (0.5 pts, PMID: 17994539; PM3_Supporting).

PP4_Strong



This homozygous individual had both progressive limb girdle muscle weakness and absent dysferlin expression in skeletal muscle via both immunohistochemistry and Western blot (PMID: 17994539; PP4_Strong).

