

Variant: NM_001130987.2(DYSF):c.3762del (p.Asp1255fs)

Version: 1.0

CA1706701 [↗](#)

813985 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 6847a91a-a62b-40fc-a763-5b96fa251ddb

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HGVS expressions

- NM_001130987.2:c.3762del
NM_001130987.2(DYSF):c.3762del (p.Asp1255fs)
NC_000002.12:g.71600707del
CM000664.2:g.71600707del
NC_000002.11:g.71827837del
CM000664.1:g.71827837del
NC_000002.10:g.71681345del
NG_008694.1:g.152085del
ENST00000698057.1:c.1134del
ENST00000698058.1:c.351del
ENST00000698059.1:c.351del
ENST00000258104.8:c.3708del
ENST00000410020.8:c.3762del
ENST00000258104.7:c.3708del
ENST00000394120.6:c.3711del
ENST00000409366.5:c.3711del
ENST00000409582.7:c.3759del
ENST00000409651.5:c.3804del
ENST00000409744.5:c.3669del
ENST00000409762.5:c.3759del
ENST00000410020.7:c.3762del
ENST00000410041.1:c.3762del
ENST00000413539.6:c.3801del
ENST00000429174.6:c.3708del
ENST00000475076.5:n.536del
ENST00000479049.6:n.593del
ENST00000493767.1:n.429del
NM_001130455.1:c.3711del
NM_001130976.1:c.3666del
NM_001130977.1:c.3666del
NM_001130978.1:c.3708del
NM_001130979.1:c.3801del
NM_001130980.1:c.3759del
NM_001130981.1:c.3759del
NM_001130982.1:c.3804del
NM_001130983.1:c.3711del
NM_001130984.1:c.3669del

NM_001130985.1:c.3762del
NM_001130986.1:c.3669del
NM_001130987.1:c.3762del
NM_003494.3:c.3708del
NM_001130455.2:c.3711del
NM_001130976.2:c.3666del
NM_001130977.2:c.3666del
NM_001130978.2:c.3708del
NM_001130979.2:c.3801del
NM_001130980.2:c.3759del
NM_001130981.2:c.3759del
NM_001130982.2:c.3804del
NM_001130983.2:c.3711del
NM_001130984.2:c.3669del
NM_001130985.2:c.3762del
NM_001130986.2:c.3669del
NM_003494.4:c.3708del

Pathogenic

Met criteria codes 4

PP4_Strong

PM2_Supporting

PVS1

PM3_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.3708delA p.(Asp1237ThrfsTer24) variant in DYSF, which is also known as NM_001130987.2: c.3762del p.(Asp1255ThrfsTer24), is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 34/55, leading to nonsense mediated decay in a gene in which loss of function is an established disease mechanism (PVS1). This variant has been detected in at least three unrelated individuals with limb girdle muscular dystrophy, including in a homozygous state in two patients (1.0 pts, PMID: 25046369, 30919934) and in trans with a pathogenic variant in at least one patient (c.1662C>T p.(Arg555Trp), 1.0 pt, PMID: 19015158) (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: 19015158). 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, PM2_Supporting.

Met criteria codes

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: 19015158).

PM2_Supporting			This variant is absent from gnomAD v2.1.1 and v3.1.2 (PM2_Supporting).
PVS1			The NM_003494.4: c.3708delA p.(Asp1237ThrfsTer24) variant in DYSF, which is also known as NM_001130987.2: c.3762del p.(Asp1255ThrfsTer24), is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 34/55 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).
PM3_Strong			This variant has been detected in at least three unrelated individuals with limb girdle muscular dystrophy, including in a homozygous state in two patients (1.0 pts, PMID: 25046369, 30919934) and in trans with a pathogenic variant in at least one patient (c.1662C>T p.(Arg555Trp), 1.0 pt, PMID: 19015158) (PM3_Strong).

Curation History 		
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