

Variant: NM_003494.4:c.1278dup

Version: 1.0

CA2580067902 [↗](#)

2116162 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 57aaac69-6e1d-48a6-bebe-af12a284019d

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HGVS expressions

NM_003494.4:c.1278dup

NC_000002.12:g.71528395dup

CM000664.2:g.71528395dup

NC_000002.11:g.71755525dup

CM000664.1:g.71755525dup

NC_000002.10:g.71609033dup

NG_008694.1:g.79773dup

ENST00000258104.8:c.1278dup

ENST00000410020.8:c.1374dup

ENST00000258104.7:c.1278dup

ENST00000394120.6:c.1281dup

ENST00000409366.5:c.1281dup

ENST00000409582.7:c.1371dup

ENST00000409651.5:c.1374dup

ENST00000409744.5:c.1281dup

ENST00000409762.5:c.1371dup

ENST00000410020.7:c.1374dup

ENST00000410041.1:c.1374dup

ENST00000413539.6:c.1371dup

ENST00000429174.6:c.1278dup

NM_001130455.1:c.1281dup

NM_001130976.1:c.1278dup

NM_001130977.1:c.1278dup

NM_001130978.1:c.1278dup

NM_001130979.1:c.1371dup

NM_001130980.1:c.1371dup

NM_001130981.1:c.1371dup

NM_001130982.1:c.1374dup

NM_001130983.1:c.1281dup

NM_001130984.1:c.1281dup

NM_001130985.1:c.1374dup

NM_001130986.1:c.1281dup

NM_001130987.1:c.1374dup

NM_003494.3:c.1278dup

NM_001130987.2:c.1374dup

NM_001130455.2:c.1281dup

NM_001130976.2:c.1278dup

NM_001130977.2:c.1278dup
NM_001130978.2:c.1278dup
NM_001130979.2:c.1371dup
NM_001130980.2:c.1371dup
NM_001130981.2:c.1371dup
NM_001130982.2:c.1374dup
NM_001130983.2:c.1281dup
NM_001130984.2:c.1281dup
NM_001130985.2:c.1374dup
NM_001130986.2:c.1281dup

Pathogenic

Met criteria codes 3

PVS1 PM2_Supporting PP4_Strong

Not Met criteria codes 1

PM3

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.1278dup p.(Lys427GlufsTer47) variant in DYSF, which is also known as NM_001130987.2: c.1374dup p.(Lys459GlufsTer47), is a duplication expected to cause a frameshift, premature stop codon, and nonsense-mediated decay in a gene for which loss of function is an established mechanism of disease (PVS1). This variant has been identified in one individual with progressive muscle weakness, elevated serum creatine kinase, and suspected Miyoshi myopathy as well as absent dysferlin expression by blood monocyte assay, where it was identified in unconfirmed phase with a second presumed diagnostic DYSF variant (ClinVar SCV002975439.1, Jain Foundation Dysferlin Registry internal data communication; PP4_Strong, PM3_Supporting not met). It is absent from gnomAD v.4.1.0, meeting the criteria for PM2_Supporting. In summary, this variant meets criteria to be classified as Pathogenic for autosomal recessive limb girdle muscular dystrophy based on the ACMG/AMP criteria applied, as specified by the LGMD VCEP (specifications v2.0.0; 04/30/2026): PVS1, PP4_Strong, PM2_Supporting.

Met criteria codes

PVS1



The NM_003494.4: c.1278dup p.(Lys427GlufsTer47) variant in DYSF, which is also known as NM_001130987.2: c.1374dup p.(Lys459GlufsTer47), is a duplication expected to cause a frameshift and premature stop codon, with nonsense-mediated decay expected in a gene for which loss of function is an established mechanism of disease (PVS1). SpliceAI: no Splice effect

PM2_Supporting



This variant is absent from gnomAD v.4.1.0, meeting the criteria for PM2_Supporting.

PP4_Strong



This variant has been identified in one individual with progressive muscle weakness, elevated serum creatine kinase, and suspected Miyoshi myopathy as well as absent dysferlin expression by blood monocyte assay, where it

was identified in unconfirmed phase with a second presumed diagnostic DYSF variant (ClinVar SCV002975439.1, Jain Foundation Dysferlin Registry internal data communication; PP4_Strong).

Not Met criteria codes

PM3		This variant has been identified in one individual with progressive muscle weakness, elevated serum creatine kinase, and suspected Miyoshi myopathy, where it was identified in unconfirmed phase with a second presumed diagnostic DYSF variant (ClinVar SCV002975439.1, Jain Foundation Dysferlin Registry internal data communication; PM3_Supporting not met). Labcorp Genetics (formerly Invitae), Labcorp Accession: SCV002975439.1: unconfirmed phase with c.5629T>C p.(Tyr1877His), which is VUS without evidence from this case (0 PM3 pts) this variant was curated to support the classification of c.5629T>C This case is also in the Dysferlin Registry, with monocyte assay data No other ClinVar submissions not in LOVD no lit
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Curation History

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