The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_001130987.2(DYSF):c.1167del (p.Ser390fs)

Version: 1.0

CA10606659

290141 (ClinVar)

Gene: DYSF (HGNC:8291)
Condition: autosomal recessive limb-girdle muscular dystrophy (MONDO:0015152)
Inheritance Mode: Autosomal recessive inheritance
UUID: 75cd278c-1ee3-46ec-b86d-0516ab57e2ed
Approved on: 2025/10/6
Published on: 2025/11/11

HGVS expressions

NM_001130987.2(DYSF):c.1167del (p.Ser390fs)
NM_001130987.2:c.1167del
NC_000002.12:g.71526237del
CM000664.2:g.71526237del
NC_000002.11:g.71753367del
CM000664.1:g.71753367del
NC_000002.10:g.71606875del
NG_008694.1:g.77615del
ENST00000258104.8:c.1071del
ENST00000410020.8:c.1167del
ENST00000258104.7:c.1071del
ENST00000394120.6:c.1074del
ENST00000409366.5:c.1074del
ENST00000409582.7:c.1164del
ENST00000409651.5:c.1167del
ENST00000409744.5:c.1074del
ENST00000409762.5:c.1164del
ENST00000410020.7:c.1167del
ENST00000410041.1:c.1167del
ENST00000413539.6:c.1164del
ENST00000429174.6:c.1071del
NM_001130455.1:c.1074del
NM_001130976.1:c.1071del
NM_001130977.1:c.1071del
NM_001130978.1:c.1071del
NM_001130979.1:c.1164del
NM_001130980.1:c.1164del
NM_001130981.1:c.1164del
NM_001130982.1:c.1167del
NM_001130983.1:c.1074del
NM_001130984.1:c.1074del
NM_001130985.1:c.1167del
NM_001130986.1:c.1074del
NM_001130987.1:c.1167del
NM_003494.3:c.1071del
NM_001130455.2:c.1074del
NM_001130976.2:c.1071del

NM_001130977.2:c.1071del
NM_001130978.2:c.1071del
NM_001130979.2:c.1164del
NM_001130980.2:c.1164del
NM_001130981.2:c.1164del
NM_001130982.2:c.1167del
NM_001130983.2:c.1074del
NM_001130984.2:c.1074del
NM_001130985.2:c.1167del
NM_001130986.2:c.1074del
NM_003494.4:c.1071del

Pathogenic

Met criteria codes 4

PVS1 PP4_Strong PM3_Supporting 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.1071del p.(Ser358LeufsTer17) variant in DYSF, which is also known as NM_001130987.2: c.1167del (p.Ser390LeufsTer17), is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 12/55, leading to nonsense mediated decay in a gene in which loss of function is an established disease mechanism (PVS1). This variant has been reported in one individual with a pathogenic variant in unknown phase (NM_003494.4: c.5698_5699del p.(Ser1900GlnfsTer14), 0.5 pts, PMID: 36983702) (PM3_Supporting). This patient displayed progressive muscle weakness and disease range dysferlin expression in blood monocytes, which is highly specific for DYSF-related LGMD (PP4_Strong). This variant is absent from gnomAD v.4.1.0 (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; 10/06/2025): PVS1, PM3_Supporting, PP4_Strong, PM2_Supporting.

Met criteria codes

PVS1	✔	The NM_003494.4: c.1071del p.(Ser358LeufsTer17) variant in DYSF, which is also known as NM_001130987.2: c.1167del (p.Ser390LeufsTer17), is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 12/55 leading to nonsense mediated decay in a gene in which loss of function is an established disease mechanism (PVS1).
PP4_Strong	✔	This patient displayed progressive muscle weakness and disease range dysferlin expression in blood monocytes, which is highly specific for DYSF-related LGMD (PP4_Strong).

PM3_Supporting		✔	This variant has been reported in one individual with a pathogenic variant in unknown phase (NM_003494.4: c.5698_5699del p.(Ser1900GlnfsTer14), 0.5 pts, PMID: 36983702) (PM3_Supporting).
PM2_Supporting		✔	This variant is absent from gnomAD v.4.1.0 (PM2_Supporting).

Curation History

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