

Variant: NM_001130987.2(DYSF):c.4989del (p.Glu1663fs)

Version: 1.0

CA533262859 [↗](#)

1300185 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 14f74d3c-69bd-4b31-8825-d8129650e299

Approved on: 2025/8/14

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HGVS expressions

- NM_001130987.2:c.4989del
- NM_001130987.2(DYSF):c.4989del (p.Glu1663fs)
- NC_000002.12:g.71660637del
- CM000664.2:g.71660637del
- NC_000002.11:g.71887767del
- CM000664.1:g.71887767del
- NC_000002.10:g.71741275del
- NG_008694.1:g.212015del
- ENST00000698057.1:c.2403del
- ENST00000698058.1:c.1620del
- ENST00000698059.1:c.1728del
- ENST00000258104.8:c.4872del
- ENST00000410020.8:c.4989del
- ENST00000258104.7:c.4872del
- ENST00000394120.6:c.4875del
- ENST00000409366.5:c.4938del
- ENST00000409582.7:c.4986del
- ENST00000409651.5:c.4968del
- ENST00000409744.5:c.4896del
- ENST00000409762.5:c.4923del
- ENST00000410020.7:c.4989del
- ENST00000410041.1:c.4926del
- ENST00000413539.6:c.4965del
- ENST00000429174.6:c.4935del
- ENST00000479049.6:n.1757del
- NM_001130455.1:c.4875del
- NM_001130976.1:c.4830del
- NM_001130977.1:c.4893del
- NM_001130978.1:c.4935del
- NM_001130979.1:c.4965del
- NM_001130980.1:c.4923del
- NM_001130981.1:c.4986del
- NM_001130982.1:c.4968del
- NM_001130983.1:c.4938del
- NM_001130984.1:c.4896del
- NM_001130985.1:c.4926del
- NM_001130986.1:c.4833del

NM_001130987.1:c.4989del
NM_003494.3:c.4872del
NM_001130455.2:c.4875del
NM_001130976.2:c.4830del
NM_001130977.2:c.4893del
NM_001130978.2:c.4935del
NM_001130979.2:c.4965del
NM_001130980.2:c.4923del
NM_001130981.2:c.4986del
NM_001130982.2:c.4968del
NM_001130983.2:c.4938del
NM_001130984.2:c.4896del
NM_001130985.2:c.4926del
NM_001130986.2:c.4833del
NM_003494.4:c.4872del

Pathogenic

Met criteria codes 4

- PVS1
- PM2_Supporting
- PM3
- 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.4872delG p.(Glu1624AspfsTer10) variant in DYSF, which is also known as NM_001130987.2: c.4989del (p.Glu1663AspfsTer10), is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 45/55, 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 at least 13 unrelated patients with phenotypes consistent with LGMD in a homozygous state in all individuals, with reported consanguinity in at least one family (1.0 pt, PMID: 10825360, 35723113, 17698709) (PM3). Many of these families were Jewish and from Libya. At least one of these individuals displayed muscle weakness and reduced or absent dysferlin protein expression in skeletal muscle, which is highly specific for DYSF-associated LGMD (PMID: 17698709; PP4_Strong). The highest population frequency of this variant in gnomAD v4.1.0 is 0.00001335 in the African/African American population (1/74922 chromosomes), which is less than the ClinGen LGMD VCEP threshold (≤ 0.0001) (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; 08/14/2025): PVS1, PP4_Strong, PM3, PM2_Supporting.

Met criteria codes

PVS1



The NM_003494.4: c.4872del p.(Glu1624AspfsTer10) variant in DYSF, which is also known as NM_001130987.2: c.4989del (p.Glu1663AspfsTer10), is a frameshift variant predicted to cause a premature stop codon in biologically

relevant exon 45/55, leading to nonsense mediated decay in a gene in which loss of function is an established disease mechanism (PVS1). deletion is in exon 44 but premature stop is in exon 45

PM2_Supporting			The highest population frequency of this variant in gnomAD v4.1.0 is 0.00001335 in the African/African American population (1/74922 chromosomes), which is less than the ClinGen LGMD VCEP threshold (≤ 0.0001) (PM2_Supporting). Criterion also met if FAF used: 0.000009455 (the upper threshold of the 95% CI of 5/1111868 European (non-Finnish) exome chromosomes)
PM3			This variant has been reported in at least 13 unrelated patients with phenotypes consistent with LGMD and was identified in a homozygous state in all individuals, with reported consanguinity in at least one family (1.0 pt, PMID: 10825360, 35723113, 17698709) (PM3). Many of these families were Jewish and from Libya.
PP4_Strong			At least one of these individuals displayed muscle weakness and reduced or absent dysferlin protein expression in skeletal muscle, which is highly specific for DYSF-associated LGMD (PMID: 17698709; PP4_Strong).

Curation History



 

 

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