

Variant: NM_001130987.2(DYSF):c.959dup (p.Asp320fs)

Version: 1.0

CA533254006 [↗](#)

2674961 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: b74affdc-5f90-46bf-b094-50f735774930

Approved on: 2025/7/29

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HGVS expressions

- NM_001130987.2:c.959dup
- NM_001130987.2(DYSF):c.959dup (p.Asp320fs)
- NC_000002.12:g.71516996dup
- CM000664.2:g.71516996dup
- NC_000002.11:g.71744126dup
- CM000664.1:g.71744126dup
- NC_000002.10:g.71597634dup
- NG_008694.1:g.68374dup
- ENST00000258104.8:c.863dup
- ENST00000410020.8:c.959dup
- ENST00000258104.7:c.863dup
- ENST00000394120.6:c.866dup
- ENST00000409366.5:c.866dup
- ENST00000409582.7:c.956dup
- ENST00000409651.5:c.959dup
- ENST00000409744.5:c.866dup
- ENST00000409762.5:c.956dup
- ENST00000410020.7:c.959dup
- ENST00000410041.1:c.959dup
- ENST00000413539.6:c.956dup
- ENST00000429174.6:c.863dup
- NM_001130455.1:c.866dup
- NM_001130976.1:c.863dup
- NM_001130977.1:c.863dup
- NM_001130978.1:c.863dup
- NM_001130979.1:c.956dup
- NM_001130980.1:c.956dup
- NM_001130981.1:c.956dup
- NM_001130982.1:c.959dup
- NM_001130983.1:c.866dup
- NM_001130984.1:c.866dup
- NM_001130985.1:c.959dup
- NM_001130986.1:c.866dup
- NM_001130987.1:c.959dup
- NM_003494.3:c.863dup
- NM_001130455.2:c.866dup
- NM_001130976.2:c.863dup

NM_001130977.2:c.863dup
NM_001130978.2:c.863dup
NM_001130979.2:c.956dup
NM_001130980.2:c.956dup
NM_001130981.2:c.956dup
NM_001130982.2:c.959dup
NM_001130983.2:c.866dup
NM_001130984.2:c.866dup
NM_001130985.2:c.959dup
NM_001130986.2:c.866dup
NM_003494.4:c.863dup

Pathogenic

Met criteria codes 3

PM3_Supporting

PM2_Supporting

PVS1

Not Met criteria codes 1

PP4

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.863dup p.(Asp288GlufsTer40) variant in DYSF, which is also known as NM_001130987.2: c.959dup p.(Asp320GlufsTer40), is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 11/55, leading to nonsense mediated decay in a gene in which loss of function is an established disease mechanism (PVS1). This variant has been identified in at least two individuals with dysferlinopathy (PMID: 36983702, 33715265, 14673575; LOVD DYSF_000186), including in unknown phase with a pathogenic variant (NM_003494.4: c.3031+2T>C, 0.5 pts, PMID: 36983702; PM3_Supporting). The filtering allele frequency of this variant in gnomAD v4.1.0 exomes is 0.000008232 (the upper threshold of the 95% CI of 4/1111996 European (non-Finnish) chromosomes), which is lower than the ClinGen LGMD VCEP threshold (<0.0001) for PM2_Supporting, and therefore meets 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 1.0.0; 07/29/2025): PVS1, PM3_Supporting, PM2_Supporting.

Met criteria codes

PM3_Supporting



This variant has been identified in at least two individuals with dysferlinopathy (PMID: 36983702, 33715265, 14673575; LOVD DYSF_000186), including in unknown phase with a pathogenic variant (NM_003494.4: c.3031+2T>C, 0.5 pts, PMID: 36983702; PM3_Supporting). c.3031+2T>C is independently classified as P and is not found in gnomAD v2 so cannot check co-occurrence

PM2_Supporting



The filtering allele frequency of this variant in gnomADv4.1.0 exomes is 0.000008232 (the upper threshold of the 95% CI of 4/1111996 European (non-Finnish) chromosomes), which is lower than the ClinGen LGMD VCEP threshold (<0.0001) for PM2_Supporting, and therefore meets this criterion (PM2_Supporting).

PVS1	 	The NM_003494.4: c.863dup p.(Asp288GlufsTer40) variant in DYSF, which is also known as NM_001130987.2: c.959dup p.(Asp320GlufsTer40), is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 11/55, leading to nonsense mediated decay in a gene in which loss of function is an established disease mechanism (PVS1).
Not Met criteria codes		
PP4	 	Cannot conclusively determine that one patient met genetic, clinical, and protein expression criteria. Cannot definitively confirm that Fernández-Eulate and Rufibach cases are the same individual, and cannot exclude possibility that in Fernández-Eulate case, protein expression was from family member. Walter case had only 1 presumed diagnostic variant identified.

Curation History 	
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Showing 1 to 1 of 1 rows	

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