

Variant: NM_001130987.2(DYSF):c.110_111del (p.Lys37fs)

Version: 1.0

CA222121 [↗](#)

94263 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: f9fd6c8e-5ebe-4281-bce7-80b0b3f51d11

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HGVS expressions

NM_001130987.2(DYSF):c.110_111del (p.Lys37fs)
NM_001130987.2:c.110_111del
NC_000002.12:g.71480901_71480902del
CM000664.2:g.71480901_71480902del
NC_000002.11:g.71708031_71708032del
CM000664.1:g.71708031_71708032del
NC_000002.10:g.71561539_71561540del
NG_008694.1:g.32279_32280del
ENST00000258104.8:c.107_108del
ENST00000410020.8:c.110_111del
ENST00000258104.7:c.107_108del
ENST00000394120.6:c.110_111del
ENST00000409366.5:c.110_111del
ENST00000409582.7:c.107_108del
ENST00000409651.5:c.110_111del
ENST00000409744.5:c.110_111del
ENST00000409762.5:c.107_108del
ENST00000410020.7:c.110_111del
ENST00000410041.1:c.110_111del
ENST00000413539.6:c.107_108del
ENST00000429174.6:c.107_108del
NM_001130455.1:c.110_111del
NM_001130976.1:c.107_108del
NM_001130977.1:c.107_108del
NM_001130978.1:c.107_108del
NM_001130979.1:c.107_108del
NM_001130980.1:c.107_108del
NM_001130981.1:c.107_108del
NM_001130982.1:c.110_111del
NM_001130983.1:c.110_111del
NM_001130984.1:c.110_111del
NM_001130985.1:c.110_111del
NM_001130986.1:c.110_111del
NM_001130987.1:c.110_111del
NM_003494.3:c.107_108del
NM_001130455.2:c.110_111del
NM_001130976.2:c.107_108del

NM_001130977.2:c.107_108del
NM_001130978.2:c.107_108del
NM_001130979.2:c.107_108del
NM_001130980.2:c.107_108del
NM_001130981.2:c.107_108del
NM_001130982.2:c.110_111del
NM_001130983.2:c.110_111del
NM_001130984.2:c.110_111del
NM_001130985.2:c.110_111del
NM_001130986.2:c.110_111del
NM_003494.4:c.107_108del

Pathogenic

Met criteria codes 5

- PM2_Supporting
- PVS1
- PP4_Moderate
- PM3_Supporting
- PP1_Moderate

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.107_108del p.(Lys36SerfsTer12) variant in DYSF, which is also known as NM_001130987.2: c.110_111del p.(Lys37SerfsTer12), is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 2/55, 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 four individuals with features consistent with LGMD (PMID: 19528035, 18853459; ClinVar SCV004229601.1 internal data communication), including in unknown phase with a pathogenic variant (NM_003494.4: c.2643+1G>A, 0.5 pts, ClinVar SCV004229601.1 internal data communication) (PM3_Supporting). This variant has been reported to co-segregate with autosomal recessive LGMD in two affected family members from two families (PMID: 18853459, 19528035; PP1_Moderate). In addition, at least one patient with this variant and a second presumed diagnostic DYSF variant displayed progressive limb girdle muscle weakness and severely reduced or absent dysferlin protein expression in skeletal muscle, which is highly specific for DYSF-related LGMD (PMID: 18853459, 17698709; PP4_Moderate, capped with PP1_Moderate). The filtering allele frequency of this variant in gnomAD v4.1.0 exomes is 0.000016374 (the lower threshold of the 95% CI of 11/1111948 European (non-Finnish) chromosomes), which is lower than the LGMD VCEP threshold (<0.0001) for PM2_Supporting, meeting 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, PP1_Moderate, PP4_Moderate, PM2_Supporting.

Met criteria codes

PM2_Supporting  

The filtering allele frequency of this variant in gnomAD v4.1.0 exomes is 0.000016374 (the lower threshold of the 95% CI of 11/1111948 European (non-Finnish) chromosomes), which is lower than the LGMD VCEP threshold (<0.0001) for PM2_Supporting, meeting this criterion.

PVS1			The NM_003494.4:c.107_108del p.(Lys36SerfsTer12) variant in DYSF, which is also known as NM_001130987.2: c.110_111del p.(Lys37SerfsTer12), is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 2/55, leading to nonsense mediated decay in a gene in which loss of function is an established disease mechanism (PVS1).
PP4_Moderate			At least one patient with this variant and a second presumed diagnostic DYSF variant displayed progressive limb girdle muscle weakness and severely reduced or absent dysferlin protein expression in skeletal muscle, which is highly specific for DYSF-related LGMD (PMID: 18853459, 17698709; PP4_Moderate, capped with PP1_Moderate).
PM3_Supporting			This variant has been identified in at least four individuals with features consistent with LGMD (PMID: 19528035, 18853459; ClinVar SCV001214479.6 internal data communication), including in unknown phase with a pathogenic variant (NM_003494.4: c.2643+1G>A, 0.5 pts, ClinVar SCV001214479.6 internal data communication) (PM3_Supporting). c.2643+1G>A is classified as P independently of this case, LabCorp SCV001214479.6 6/21/2025: Second submission (DYSF):c.2697+1G>A , SCV004229601.1, unknow phase and known pathogenic and published variant. (Quest). Patient in 30's with LGMD symptoms. (0.5 pts not added to the summary yet). c.107_108del is not in gnomAD v2, so co-occurrence cannot be evaluated
PP1_Moderate			This variant has been reported to co-segregate with autosomal recessive LGMD in two affected family members from two families (PMID: 18853459, 19528035; PP1_Moderate).

Curation History 		
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