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Variant: NM_001130987.2(DYSF):c.3274_3275del (p.Leu1092fs)

Version: 1.0

CA915944059

653601 (ClinVar)

Gene: DYSF (HGNC:8291)
Condition: autosomal recessive limb-girdle muscular dystrophy (MONDO:0015152)
Inheritance Mode: Autosomal recessive inheritance
UUID: 48fd8804-58c8-4e55-9780-9306c6a60864
Approved on: 2025/1/9
Published on: 2025/1/9

HGVS expressions

NM_001130987.2(DYSF):c.3274_3275del (p.Leu1092fs)
NM_001130987.2:c.3274_3275del
NC_000002.12:g.71574243_71574244del
CM000664.2:g.71574243_71574244del
NC_000002.11:g.71801373_71801374del
CM000664.1:g.71801373_71801374del
NC_000002.10:g.71654881_71654882del
NG_008694.1:g.125621_125622del
ENST00000698057.1:c.646_647del
ENST00000258104.8:c.3220_3221del
ENST00000410020.8:c.3274_3275del
ENST00000258104.7:c.3220_3221del
ENST00000394120.6:c.3223_3224del
ENST00000409366.5:c.3223_3224del
ENST00000409582.7:c.3271_3272del
ENST00000409651.5:c.3316_3317del
ENST00000409744.5:c.3181_3182del
ENST00000409762.5:c.3271_3272del
ENST00000410020.7:c.3274_3275del
ENST00000410041.1:c.3274_3275del
ENST00000413539.6:c.3313_3314del
ENST00000429174.6:c.3220_3221del
NM_001130455.1:c.3223_3224del
NM_001130976.1:c.3178_3179del
NM_001130977.1:c.3178_3179del
NM_001130978.1:c.3220_3221del
NM_001130979.1:c.3313_3314del
NM_001130980.1:c.3271_3272del
NM_001130981.1:c.3271_3272del
NM_001130982.1:c.3316_3317del
NM_001130983.1:c.3223_3224del
NM_001130984.1:c.3181_3182del
NM_001130985.1:c.3274_3275del
NM_001130986.1:c.3181_3182del
NM_001130987.1:c.3274_3275del

NM_003494.3:c.3220_3221del
NM_001130455.2:c.3223_3224del
NM_001130976.2:c.3178_3179del
NM_001130977.2:c.3178_3179del
NM_001130978.2:c.3220_3221del
NM_001130979.2:c.3313_3314del
NM_001130980.2:c.3271_3272del
NM_001130981.2:c.3271_3272del
NM_001130982.2:c.3316_3317del
NM_001130983.2:c.3223_3224del
NM_001130984.2:c.3181_3182del
NM_001130985.2:c.3274_3275del
NM_001130986.2:c.3181_3182del
NM_003494.4:c.3220_3221del

Pathogenic

Met criteria codes 4

PM3 PP4_Strong PVS1 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 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.3220_3221delCT p.(Leu1074PheTer39) variant in DYSF, which is also known as NM_001130987.2: c.3274_3275del p.(Leu1092PhefsTer39), is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 30/55, leading to nonsense mediated decay in a gene in which loss of function is an established disease mechanism (PVS1). This variant has been detected in trans with a pathogenic variant in at least one patient with LGMD (c.1662C>T p.(Arg555Trp), 1.0 pt, PMID: 25591676) (PM3). At least one patient with this variant displayed progressive limb girdle muscle weakness and absent dysferlin protein expression, which is highly specific for DYSF-associated LGMD (PP4_Strong, PMID: 25591676). This variant is absent from gnomAD v2.1.1 and v3.1.2 (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; 01/09/2025): PVS1, PM3, PP4_Strong, PM2_Supporting.

Met criteria codes

PM3	✔	This variant has been detected in trans with a pathogenic variant in at least one patient with LGMD (c.1662C>T p.(Arg555Trp), 1.0 pt, PMID: 25591676) (PM3).
PP4_Strong	✔	At least one patient with this variant displayed progressive limb-girdle muscle weakness and absent dysferlin protein expression, which is highly specific for DYSF-associated LGMD (PP4_Strong, PMID: 25591676).

PVS1		✔	The NM_003494.4: c.3220_3221delCT p.(Leu1074PheTer39) variant in DYSF, which is also known as NM_001130987.2: c.3274_3275del p.(Leu1092PhefsTer39), is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 30/55 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).
PM2_Supporting		✔	This variant is absent from gnomAD v2.1.1 and v3.1.2 (PM2_Supporting).

Curation History

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