

Variant: NM_001130987.2(DYSF):c.1464C>A (p.Cys488Ter)

Version: 1.0

CA222125 [↗](#)

94269 (ClinVar) [↗](#)

Gene: DYSF ([HGNC:8291](#))
Condition: autosomal recessive limb-girdle muscular dystrophy ([MONDO:0015152](#))
Inheritance Mode: Autosomal recessive inheritance
UUID: 1dbc1db3-eac3-4c88-8822-a76ef45c89aa
Approved on: 2025/10/6
Published on: 2025/11/11

HGVS expressions

NM_001130987.2(DYSF):c.1464C>A (p.Cys488Ter)
NM_001130987.2:c.1464C>A
NC_000002.12:g.71535282C>A
CM000664.2:g.71535282C>A
NC_000002.11:g.71762412C>A
CM000664.1:g.71762412C>A
NC_000002.10:g.71615920C>A
NG_008694.1:g.86660C>A
ENST00000258104.8:c.1368C>A
ENST00000410020.8:c.1464C>A
ENST00000258104.7:c.1368C>A
ENST00000394120.6:c.1371C>A
ENST00000409366.5:c.1371C>A
ENST00000409582.7:c.1461C>A
ENST00000409651.5:c.1464C>A
ENST00000409744.5:c.1371C>A
ENST00000409762.5:c.1461C>A
ENST00000410020.7:c.1464C>A
ENST00000410041.1:c.1464C>A
ENST00000413539.6:c.1461C>A
ENST00000429174.6:c.1368C>A
NM_001130455.1:c.1371C>A
NM_001130976.1:c.1368C>A
NM_001130977.1:c.1368C>A
NM_001130978.1:c.1368C>A
NM_001130979.1:c.1461C>A
NM_001130980.1:c.1461C>A
NM_001130981.1:c.1461C>A
NM_001130982.1:c.1464C>A
NM_001130983.1:c.1371C>A
NM_001130984.1:c.1371C>A
NM_001130985.1:c.1464C>A
NM_001130986.1:c.1371C>A
NM_001130987.1:c.1464C>A
NM_003494.3:c.1368C>A
NM_001130455.2:c.1371C>A
NM_001130976.2:c.1368C>A

NM_001130977.2:c.1368C>A
NM_001130978.2:c.1368C>A
NM_001130979.2:c.1461C>A
NM_001130980.2:c.1461C>A
NM_001130981.2:c.1461C>A
NM_001130982.2:c.1464C>A
NM_001130983.2:c.1371C>A
NM_001130984.2:c.1371C>A
NM_001130985.2:c.1464C>A
NM_001130986.2:c.1371C>A
NM_003494.4:c.1368C>A

Pathogenic

Met criteria codes 4

PM2_Supporting

PP4_Strong

PVS1

PM3

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.1368C>A p.(Cys456Ter) variant in DYSF, which is also known as NM_001130987.2: c.1464C>A p.(Cys488Ter), is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 15/55, 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 five individuals with features consistent with dysferlinopathy (PMID: 33927379, 33610434, 36983702), including in a homozygous state without reported familial consanguinity in two individuals (1.0 pt, PMID: 33610434; LOVD Individual #00327594, #00326989) (PM3). At least one individual with this variant and a second presumed diagnostic DYSF variant displayed progressive muscle wasting and absent dysferlin protein expression in skeletal muscle or blood monocytes, which is highly specific for DYSF-related LGMD (PMID: 33610434, 36983702; PP4_Strong). In gnomAD v4.1.0, the upper bound of the 95% confidence interval of the Grpmax variant allele frequency is 0.000046991 (based on 43/1179974 European (non-Finnish) alleles), 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 2.0.0; 10/06/2025): PVS1, PM3, PM2_Supporting, PP4_Strong.

Met criteria codes

PM2_Supporting



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PP4_Strong



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specific for DYSF-related LGMD (PMID: 33610434, 36983702; PP4_Strong).

PVS1



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PM3



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Curation History [↗](#)

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