

Variant: NM_001130987.2(DYSF):c.1225C>T (p.Arg409Ter)

Version: 1.0

CA1705654 [↗](#)

265487 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 07b0d7cb-9a41-40f0-a2a3-3665888ce2f6

Approved on: 2026/5/1

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HGVS expressions

NM_001130987.2(DYSF):c.1225C>T (p.Arg409Ter)
NM_001130987.2:c.1225C>T
NC_000002.12:g.71526295C>T
CM000664.2:g.71526295C>T
NC_000002.11:g.71753425C>T
CM000664.1:g.71753425C>T
NC_000002.10:g.71606933C>T
NG_008694.1:g.77673C>T
ENST00000258104.8:c.1129C>T
ENST00000410020.8:c.1225C>T
ENST00000258104.7:c.1129C>T
ENST00000394120.6:c.1132C>T
ENST00000409366.5:c.1132C>T
ENST00000409582.7:c.1222C>T
ENST00000409651.5:c.1225C>T
ENST00000409744.5:c.1132C>T
ENST00000409762.5:c.1222C>T
ENST00000410020.7:c.1225C>T
ENST00000410041.1:c.1225C>T
ENST00000413539.6:c.1222C>T
ENST00000429174.6:c.1129C>T
NM_001130455.1:c.1132C>T
NM_001130976.1:c.1129C>T
NM_001130977.1:c.1129C>T
NM_001130978.1:c.1129C>T
NM_001130979.1:c.1222C>T
NM_001130980.1:c.1222C>T
NM_001130981.1:c.1222C>T
NM_001130982.1:c.1225C>T
NM_001130983.1:c.1132C>T
NM_001130984.1:c.1132C>T
NM_001130985.1:c.1225C>T
NM_001130986.1:c.1132C>T
NM_001130987.1:c.1225C>T
NM_003494.3:c.1129C>T
NM_001130455.2:c.1132C>T
NM_001130976.2:c.1129C>T

NM_001130977.2:c.1129C>T
NM_001130978.2:c.1129C>T
NM_001130979.2:c.1222C>T
NM_001130980.2:c.1222C>T
NM_001130981.2:c.1222C>T
NM_001130982.2:c.1225C>T
NM_001130983.2:c.1132C>T
NM_001130984.2:c.1132C>T
NM_001130985.2:c.1225C>T
NM_001130986.2:c.1132C>T
NM_003494.4:c.1129C>T

Pathogenic

Met criteria codes 2

PP4_Strong PVS1

Not Met criteria codes 3

PP1 PM3 PM2

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.1129C>T p.(Arg377Ter) variant in DYSF, which is also known as NM_001130987.2: c.1225C>T p.(Arg409Ter), is a nonsense variant that introduces a premature stop codon in exon 12/55, 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 three unrelated individuals with LGMD (PMID: 33250842, 22297152; ClinVar SCV004292580.2 internal data communication), including in unconfirmed phase with a presumed diagnostic variant in two patients and in a homozygous state in one patient with possible familial consanguinity (0.25 pts, PMID: 33250842). At least one patient homozygous for this variant showed both progressive proximal muscle weakness and absent dysferlin expression in skeletal muscle, which is highly specific for DYSF-associated LGMD (PMID: 33250842; PP4_Strong). The upper bound of the 95% confidence interval of the Grpmax variant allele frequency is 0.00017529 in gnomAD v4.1.0 (5/60010 Admixed American alleles), which is greater than the threshold for PM2_Supporting (criterion not met). 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 LGMD VCEP (specifications v2.0.0; 05/01/2026): PVS1, PP4_Strong.

Met criteria codes

PP4_Strong			At least one patient homozygous for this variant showed both progressive proximal muscle weakness and absent dysferlin expression in skeletal muscle, which is highly specific for DYSF-associated LGMD (PMID: 33250842; PP4_Strong).
PVS1			The NM_003494.4: c.1129C>T p.(Arg377Ter) variant in DYSF, which is also known as NM_001130987.2: c.1225C>T p.(Arg409Ter), is a nonsense variant that introduces a premature stop codon in exon 12/55, leading to nonsense mediated decay in a gene in which loss of function is an established disease mechanism (PVS1).

Not Met criteria codes

PP1			Likely one affected family member with the same genotype, but phase not confirmed (ClinVar SCV004292580.2 internal data communication).
PM3			This variant has been reported in at least three unrelated individuals with LGMD (PMID: 33250842, 22297152; ClinVar SCV004292580.2 internal data communication), including in unconfirmed phase with a presumed diagnostic variant in two patients and in a homozygous state in one patient with possible familial consanguinity (0.25 pts, PMID: 33250842). LOVD DYSF_000796: 2 single hits in Nallamilli et al. additional weight from PM3 not need for P classification
PM2			The upper bound of the 95% confidence interval of the Grpmax variant allele frequency is 0.00017529 in gnomAD v4.1.0 (5/60010 Admixed American alleles), which is greater than the threshold for PM2_Supporting (criterion not met).

Curation History

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