

Variant: NM_001130987.2(DYSF):c.2426C>T (p.Pro809Leu)

Version: 1.0

CA49742304 [↗](#)

566085 (ClinVar) [↗](#)

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

Condition: limb-girdle muscular dystrophy ([MONDO:0016971](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: f3a996a4-fbe5-4ea1-afbf-d481d523ba99

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HGVS expressions

NM_001130987.2(DYSF):c.2426C>T (p.Pro809Leu)

NM_001130987.2:c.2426C>T

NC_000002.12:g.71564074C>T

CM000664.2:g.71564074C>T

NC_000002.11:g.71791204C>T

CM000664.1:g.71791204C>T

NC_000002.10:g.71644712C>T

NG_008694.1:g.115452C>T

ENST00000258104.8:c.2372C>T

ENST00000410020.8:c.2426C>T

ENST00000258104.7:c.2372C>T

ENST00000394120.6:c.2375C>T

ENST00000409366.5:c.2375C>T

ENST00000409582.7:c.2423C>T

ENST00000409651.5:c.2468C>T

ENST00000409744.5:c.2333C>T

ENST00000409762.5:c.2423C>T

ENST00000410020.7:c.2426C>T

ENST00000410041.1:c.2426C>T

ENST00000413539.6:c.2465C>T

ENST00000429174.6:c.2372C>T

NM_001130455.1:c.2375C>T

NM_001130976.1:c.2330C>T

NM_001130977.1:c.2330C>T

NM_001130978.1:c.2372C>T

NM_001130979.1:c.2465C>T

NM_001130980.1:c.2423C>T

NM_001130981.1:c.2423C>T

NM_001130982.1:c.2468C>T

NM_001130983.1:c.2375C>T

NM_001130984.1:c.2333C>T

NM_001130985.1:c.2426C>T

NM_001130986.1:c.2333C>T

NM_001130987.1:c.2426C>T

NM_003494.3:c.2372C>T

NM_001130455.2:c.2375C>T

NM_001130976.2:c.2330C>T

NM_001130977.2:c.2330C>T
NM_001130978.2:c.2372C>T
NM_001130979.2:c.2465C>T
NM_001130980.2:c.2423C>T
NM_001130981.2:c.2423C>T
NM_001130982.2:c.2468C>T
NM_001130983.2:c.2375C>T
NM_001130984.2:c.2333C>T
NM_001130985.2:c.2426C>T
NM_001130986.2:c.2333C>T
NM_003494.4:c.2372C>T

Uncertain Significance

Met criteria codes 3

PP3 PM2_Supporting
PM5_Supporting

Not Met criteria codes 3

PS3 PP4 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.2372C>T variant in DYSF, which is also known as NM_001130987.2: c.2426C>T p.(Pro809Leu) is a missense variant expected to cause the substitution of proline for leucine at amino acid 791, p.(Pro791Leu). To our knowledge, this variant has not been reported in association with limb girdle muscular dystrophy. The upper bound of the 95% confidence interval of the Grpmax variant allele frequency in gnomAD v4.1.0 is 0.000014 (10/1180030 European (non-Finnish) chromosomes), which is less than the LGMD VCEP threshold (0.0001), meeting this criterion (PM2_Supporting). The computational predictor REVEL gives a score of 0.86, which exceeds the threshold of ≥ 0.70 , evidence that correlates with impact to DYSF function. In addition, another missense variant at this position, NM_003494.4: c.2372C>G p.(Pro791Arg), has been classified as likely pathogenic for limb girdle muscular dystrophy by the LGMD VCEP (PM5_Supporting). In summary, at this time there is insufficient evidence to classify this variant as pathogenic or benign, and it remains a variant of uncertain significance 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; 04/30/2026): PM2_Supporting, PP3, PM5_Supporting.

Met criteria codes

PP3			The computational predictor REVEL gives a score of 0.86, which exceeds the threshold of ≥ 0.70 , evidence that correlates with impact to DYSF function.
PM2_Supporting			The upper bound of the 95% confidence interval of the Grpmax variant allele frequency in gnomAD v4.1.0 is 0.000014 (10/1180030 European (non-Finnish) chromosomes), which is less than the LGMD VCEP threshold (0.0001), meeting this criterion (PM2_Supporting).

PM5_Supporting			Another missense variant at this position, NM_003494.4: c.2372C>G p.(Pro791Arg), has been classified as likely pathogenic for limb girdle muscular dystrophy by the LGMD VCEP (PM5_Supporting). PP3 applies to both variants neither variant is predicted to affect splicing do not affect first or last amino acid of an exon c.2372C>A p.(Pro791Gln) not in LOVD, not in Dysferlin Registry, LP by Labcorp Genetics (formerly Invitae), Labcorp in ClinVar but no literature citations (looks to be based on PM5 for c.2372C>G p.(Pro791Arg)
Not Met criteria codes			
PS3			not evaluated in Tominaga et al.
PP4			To our knowledge, this variant has not been reported in association with limb girdle muscular dystrophy.
PM3			To our knowledge, this variant has not been reported in association with limb girdle muscular dystrophy. not in LOVD no literature identified not in Dysferlin Registry

Curation History 			
    			
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