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Variant: NM_001130987.2(DYSF):c.5150G>A (p.Cys1717Tyr)

Version: 1.0

CA10606239

288830 (ClinVar)

Gene: DYSF (HGNC:8291)
Condition: autosomal recessive limb-girdle muscular dystrophy (MONDO:0015152)
Inheritance Mode: Autosomal recessive inheritance
UUID: 5fe761fc-f0bf-4671-aeed-39b5cf55c5cb
Approved on: 2026/1/23
Published on: 2026/2/17

HGVS expressions

NM_001130987.2:c.5150G>A
NM_001130987.2(DYSF):c.5150G>A (p.Cys1717Tyr)
NC_000002.12:g.71664414G>A
CM000664.2:g.71664414G>A
NC_000002.11:g.71891544G>A
CM000664.1:g.71891544G>A
NC_000002.10:g.71745052G>A
NG_008694.1:g.215792G>A
ENST00000698057.1:c.2564G>A
ENST00000698058.1:c.1781G>A
ENST00000698059.1:c.1889G>A
ENST00000258104.8:c.5033G>A
ENST00000410020.8:c.5150G>A
ENST00000258104.7:c.5033G>A
ENST00000394120.6:c.5036G>A
ENST00000409366.5:c.5099G>A
ENST00000409582.7:c.5147G>A
ENST00000409651.5:c.5129G>A
ENST00000409744.5:c.5057G>A
ENST00000409762.5:c.5084G>A
ENST00000410020.7:c.5150G>A
ENST00000410041.1:c.5087G>A
ENST00000413539.6:c.5126G>A
ENST00000429174.6:c.5096G>A
ENST00000479049.6:n.1918G>A
NM_001130455.1:c.5036G>A
NM_001130976.1:c.4991G>A
NM_001130977.1:c.5054G>A
NM_001130978.1:c.5096G>A
NM_001130979.1:c.5126G>A
NM_001130980.1:c.5084G>A
NM_001130981.1:c.5147G>A
NM_001130982.1:c.5129G>A
NM_001130983.1:c.5099G>A
NM_001130984.1:c.5057G>A
NM_001130985.1:c.5087G>A
NM_001130986.1:c.4994G>A

NM_001130987.1:c.5150G>A
NM_003494.3:c.5033G>A
NM_001130455.2:c.5036G>A
NM_001130976.2:c.4991G>A
NM_001130977.2:c.5054G>A
NM_001130978.2:c.5096G>A
NM_001130979.2:c.5126G>A
NM_001130980.2:c.5084G>A
NM_001130981.2:c.5147G>A
NM_001130982.2:c.5129G>A
NM_001130983.2:c.5099G>A
NM_001130984.2:c.5057G>A
NM_001130985.2:c.5087G>A
NM_001130986.2:c.4994G>A
NM_003494.4:c.5033G>A

Pathogenic

Met criteria codes 5

PM3 PM5 PP4_Strong PM2_Supporting PP3

Not Met criteria codes 1

PS3

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.5033G>A variant in DYSF, which is also known as NM_001130987.2: c.5150G>A p.(Cys1717Tyr), is a missense variant predicted to cause substitution of cysteine to tyrosine at amino acid 1678, p.(Cys1678Tyr). This variant has been observed in three individuals with suspected LGMD, two in a homozygous state including one with confirmed consanguinity (0.75 pts, PMID: 17994539, 36012197) and one with a pathogenic variant in unknown phase (NM_003494.4: c.1053+1G>A, 0.5 pts, PMID: 30564623, LOVD Individual #00221638) (PM3). At least one individual with two presumably diagnostic variants and suspected LGMD had absent dysferlin expression in muscle, which is highly specific for DYSF-related LGMD (PMID: 17994539, PP4_Strong). This variant is absent in gnomAD v4.1.0 (PM2_Supporting). The computational predictor REVEL gives a score of 0.96, which is above the LGMD VCEP threshold of ≥0.70 (PP3). In addition, two other missense variants at the same codon, NM_003494.4: c.5033G>C p.(Cys1678Ser) and c.5032T>C p.(Cys1678Arg), have been classified as at least likely pathogenic by the ClinGen LGMD VCEP (PM5). In summary, this variant is classified as Pathogenic for autosomal recessive limb girdle muscular dystrophy based on the ACMG/AMP criteria applied, as specified by the ClinGen LGMD VCEP (specifications v2.0.0; 01/23/2026): PM3, PM5, PP4_Strong, PP3, PM2_Supporting.

Met criteria codes

PM3	✔	This variant has been observed in three individuals with suspected LGMD, two in a homozygous state including one with confirmed consanguinity (0.75 pts, PMID: 17994539, 36012197) and one with a pathogenic variant in unknown phase (c.1053+1G>A, 0.5 pts, PMID: 30564623, LOVD Individual #00221638) (PM3).

PM5	ℹ	✔	Two other missense variants at the same codon, c.5033G>C p.(Cys1678Ser) and c.5032T>C p.(Cys1678Arg), have been classified as at least likely pathogenic by the ClinGen LGMD VCEP (PM5). Both are LP without PM5 application. Splice AI<0.5 for all variants
PP4_Strong	ℹ	✔	At least one individual with two presumably diagnostic variants and suspected LGMD had absent dysferlin expression in muscle, which is highly specific for DYSF-related LGMD (PMID: 17994539, PP4_Strong).
PM2_Supporting	ℹ	✔	This variant is absent in gnomAD v4.1.0 (PM2_Supporting).
PP3	ℹ	✔	The computational predictor REVEL gives a score of 0.96, which is above the LGMD VCEP threshold of ≥0.70 (PP3). Splice AI: 0.08

Not Met criteria codes

PS3	ℹ	✖	Not in Tominaga et al. study. No functional studies.

Curation History

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