The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_001130987.2(DYSF):c.5195G>A (p.Arg1732Gln)

Version: 1.0

CA351294

242527 (ClinVar)

Gene: DYSF (HGNC:8291)
Condition: autosomal recessive limb-girdle muscular dystrophy (MONDO:0015152)
Inheritance Mode: Autosomal recessive inheritance
UUID: 1bf4c8e3-f7c5-487d-9bdf-978457839cd4
Approved on: 2026/1/23
Published on: 2026/2/17

HGVS expressions

NM_001130987.2:c.5195G>A
NM_001130987.2(DYSF):c.5195G>A (p.Arg1732Gln)
NC_000002.12:g.71665182G>A
CM000664.2:g.71665182G>A
NC_000002.11:g.71892312G>A
CM000664.1:g.71892312G>A
NC_000002.10:g.71745820G>A
NG_008694.1:g.216560G>A
ENST00000698057.1:c.2609G>A
ENST00000698058.1:c.1826G>A
ENST00000698059.1:c.1934G>A
ENST00000258104.8:c.5078G>A
ENST00000410020.8:c.5195G>A
ENST00000258104.7:c.5078G>A
ENST00000394120.6:c.5081G>A
ENST00000409366.5:c.5144G>A
ENST00000409582.7:c.5192G>A
ENST00000409651.5:c.5174G>A
ENST00000409744.5:c.5102G>A
ENST00000409762.5:c.5129G>A
ENST00000410020.7:c.5195G>A
ENST00000410041.1:c.5132G>A
ENST00000413539.6:c.5171G>A
ENST00000429174.6:c.5141G>A
ENST00000479049.6:n.1963G>A
NM_001130455.1:c.5081G>A
NM_001130976.1:c.5036G>A
NM_001130977.1:c.5099G>A
NM_001130978.1:c.5141G>A
NM_001130979.1:c.5171G>A
NM_001130980.1:c.5129G>A
NM_001130981.1:c.5192G>A
NM_001130982.1:c.5174G>A
NM_001130983.1:c.5144G>A
NM_001130984.1:c.5102G>A
NM_001130985.1:c.5132G>A
NM_001130986.1:c.5039G>A

NM_001130987.1:c.5195G>A
NM_003494.3:c.5078G>A
NM_001130455.2:c.5081G>A
NM_001130976.2:c.5036G>A
NM_001130977.2:c.5099G>A
NM_001130978.2:c.5141G>A
NM_001130979.2:c.5171G>A
NM_001130980.2:c.5129G>A
NM_001130981.2:c.5192G>A
NM_001130982.2:c.5174G>A
NM_001130983.2:c.5144G>A
NM_001130984.2:c.5102G>A
NM_001130985.2:c.5132G>A
NM_001130986.2:c.5039G>A
NM_003494.4:c.5078G>A

Pathogenic

Met criteria codes 5

PM3 PM5 PP4_Strong PP3 PM2_Supporting

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.5078G>A variant in DYSF, which is also known as NM_001130987.2: c.5195G>A (p.Arg1732Gln), is a missense variant predicted to cause substitution of arginine by glutamine at amino acid 1693, p.(Arg1693Gln). This variant has been reported in at least six individuals with features overlapping LGMD (PMID: 26060040, 25868377, 27066573, 32400077, Jain Foundation Dysferlin Registry), including in a homozygous state without reported consanguinity in two individuals (0.5 pts each, PMID: 27066573, Jain Foundation Dysferlin Registry) (PM3). At least one patient with this variant and another presumed diagnostic DYSF variant had clinical features of LGMD and absent dysferlin expression in muscle biopsy, which is highly specific for DYSF-related LGMD (PMID: 25868377; PP4_Strong). The filtering allele frequency of this variant is 0.000010036 (upper threshold of the 95% CI of 6/1180040 European (non-Finnish) chromosomes) in gnomAD v4.1.0, which is less than the ClinGen LGMD VCEP threshold (<0.0001) (PM2_Supporting). The computational predictor REVEL gives a score of 0.93, which is above the LGMD VCEP threshold of ≥0.70, evidence that correlates with impact to DYSF function (PP3). In addition, another missense variant at the same codon, NM_003494.4: c.5077C>T p.(Arg1693Trp), has been classified as pathogenic by the ClinGen LGMD VCEP (PM5). 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 (specifications v2.0.0; 01/23/2026): PM3, PP4_Strong, PP3, PM2_Supporting, PM5.

Met criteria codes

PM3 ✔

This variant has been reported in at least six individuals with features overlapping LGMD (PMID: 26060040, 25868377, 27066573, 32400077, Jain Foundation Dysferlin Registry), including in a homozygous state without reported consanguinity in two individuals (0.5 pts each, PMID: 27066573, Jain Foundation Dysferlin Registry) (PM3).

PM5	✔	Another missense variant at the same codon, c.5077C>T p.(Arg1693Trp), has been classified as pathogenic by the ClinGen LGMD VCEP (PM5). PP3 met for both variants; Splice AI=0.00 for both variants.
PP4_Strong	✔	At least one patient with this variant and another presumed diagnostic DYSF variant had clinical features of LGMD and absent dysferlin expression in muscle biopsy, which is highly specific for DYSF-related LGMD (PMID: 25868377; PP4_Strong).
PP3	✔	The computational predictor REVEL gives a score of 0.93, which is above the LGMD VCEP threshold of ≥0.70, evidence that correlates with impact to DYSF function (PP3). Splice AI: 0.00
PM2_Supporting	✔	The filtering allele frequency of this variant is 0.000010036 (upper threshold of the 95% CI of 6/1180040 European (non-Finnish) chromosomes) in gnomAD v4.1.0, which is less than the ClinGen LGMD VCEP threshold (<0.0001) (PM2_Supporting).

Not Met criteria codes

PS3	✖	Not in Tominaga et al. study and no other functional studies.

Curation History

Showing 1 to 1 of 1 rows

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.

ClinGen Terms of Use.
⌑ Powered by BCM's Genboree.