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Variant: NM_001130987.2(DYSF):c.5420G>A (p.Arg1807Gln)

Version: 1.0

CA1707357

282624 (ClinVar)

Gene: DYSF (HGNC:8291)
Condition: autosomal recessive limb-girdle muscular dystrophy (MONDO:0015152)
Inheritance Mode: Autosomal recessive inheritance
UUID: 71f89ba6-5f38-4520-af34-1d6d2549ec04
Approved on: 2026/4/30
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HGVS expressions

NM_001130987.2(DYSF):c.5420G>A (p.Arg1807Gln)
NM_001130987.2:c.5420G>A
NC_000002.12:g.71667478G>A
CM000664.2:g.71667478G>A
NC_000002.11:g.71894608G>A
CM000664.1:g.71894608G>A
NC_000002.10:g.71748116G>A
NG_008694.1:g.218856G>A
ENST00000698057.1:c.2834G>A
ENST00000698058.1:c.2051G>A
ENST00000698059.1:c.2159G>A
ENST00000258104.8:c.5303G>A
ENST00000410020.8:c.5420G>A
ENST00000258104.7:c.5303G>A
ENST00000394120.6:c.5306G>A
ENST00000409366.5:c.5369G>A
ENST00000409582.7:c.5417G>A
ENST00000409651.5:c.5399G>A
ENST00000409744.5:c.5327G>A
ENST00000409762.5:c.5354G>A
ENST00000410020.7:c.5420G>A
ENST00000410041.1:c.5357G>A
ENST00000413539.6:c.5396G>A
ENST00000429174.6:c.5366G>A
ENST00000479049.6:n.2188G>A
NM_001130455.1:c.5306G>A
NM_001130976.1:c.5261G>A
NM_001130977.1:c.5324G>A
NM_001130978.1:c.5366G>A
NM_001130979.1:c.5396G>A
NM_001130980.1:c.5354G>A
NM_001130981.1:c.5417G>A
NM_001130982.1:c.5399G>A
NM_001130983.1:c.5369G>A
NM_001130984.1:c.5327G>A
NM_001130985.1:c.5357G>A
NM_001130986.1:c.5264G>A

NM_001130987.1:c.5420G>A
NM_003494.3:c.5303G>A
NM_001130455.2:c.5306G>A
NM_001130976.2:c.5261G>A
NM_001130977.2:c.5324G>A
NM_001130978.2:c.5366G>A
NM_001130979.2:c.5396G>A
NM_001130980.2:c.5354G>A
NM_001130981.2:c.5417G>A
NM_001130982.2:c.5399G>A
NM_001130983.2:c.5369G>A
NM_001130984.2:c.5327G>A
NM_001130985.2:c.5357G>A
NM_001130986.2:c.5264G>A
NM_003494.4:c.5303G>A

Pathogenic

Met criteria codes 5

PM3 PM5 PP4_Strong PP3 PM2_Supporting

Not Met criteria codes 4

BA1 BS1 PS1 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.5303G>A variant in DYSF, which is also known as NM_001130987.2(DYSF):c.5420G>A p.(Arg1807Gln), is a missense variant predicted to cause the substitution of arginine for glutamine at amino acid position 1768, p.(Arg1768Gln). This variant has been identified in at least three individuals with features consistent with LGMD, including in a homozygous state without reported consanguinity in one patient (0.5 pts, PMID: 33927379, LOVD Individual #00327538) and confirmed in trans with a pathogenic variant in one patient (NM_003494.4: c.1284+2T>C, 1.0 pt, PMID: 32751317) (PM3). In the third patient, it was reported in unknown phase with two other DYSF missense variants (Jain Foundation Dysferlin Registry internal data communication). The homozygous patient was referred for diagnostic sequencing of DYSF by a neurologist due to a clinical suspicion of dysferlinopathy. Absent dysferlin expression in skeletal muscle was also confirmed in this individual (PMID: 33927379, LOVD Individual #00327538; PP4_Strong). The upper bound of the 95% confidence interval of the Grpmax variant allele frequency in gnomAD v4.1.0 is 0.000074234 (72/1180030 European (non-Finnish chromosomes), which is lower than the LGMD VCEP threshold (<0.0001) (PM2_Supporting). The REVEL score of this variant is 0.843, which is above the threshold (≥0.7), evidence that correlates with impact on DYSF function (PP3). In addition, another missense change at the same position, NM_003494.4: c.5302C>T p.(Arg1768Trp), is classified as pathogenic for limb girdle muscular dystrophy by the 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 (LGMD VCEP specifications version 2.0.0; 04/30/2026): PM3, PP4_Strong, PM2_Supporting, PP3, PM5.

Met criteria codes

PM3	✔	This variant has been identified in at least three individuals with features consistent with LGMD, including in a homozygous state without reported consanguinity in one patient (0.5 pts, PMID: 33927379, LOVD Individual #00327538) and confirmed in trans with a pathogenic variant in one patient (NM_003494.4: c.1284+2T>C, 1.0 pt, PMID: 32751317) (PM3). In the third patient, it was reported in unknown phase with two other DYSF missense variants (Jain Foundation Dysferlin Registry internal data communication).
PM5	✔	Another missense change at the same position, NM_003494.4: c.5302C>T p.(Arg1768Trp), is classified as pathogenic for limb girdle muscular dystrophy by the LGMD VCEP (PM5). c.5302C>T p.(Arg1768Trp) is approved at P by the VCEP without use of PM5: PM3, PP4_Strong, PP1, PS3_Moderate, PP3 PP3 applies to both the curated variant and the comparison variant neither are predicted to effect splicing do not affect first or last residue of an exon other variants at this position: c.5303G>T p.(Arg1768Leu) LOVD Individual #00313713 / Fam47Pat1 from Magri et al. (2015) with c.2200_2204del p.(Thr734Profs*18)
PP4_Strong	✔	This variant was reported in a homozygous state in an individual referred for diagnostic sequencing of DYSF by a neurologist due to a clinical suspicion of dysferlinopathy. Absent dysferlin expression in skeletal muscle was also confirmed in this individual (PMID: 33927379, LOVD Individual #00327538; PP4_Strong).
PP3	✔	The REVEL score of this variant is 0.843, which is above the threshold (≥0.7), evidence that correlates with impact on DYSF function (PP3). SpliceAI 0
PM2_Supporting	✔	The upper bound of the 95% confidence interval of the Grpmax variant allele frequency in gnomAD v4.1.0 is 0.000074234 (72/1180030 European (non-Finnish chromosomes), which is lower than the LGMD VCEP threshold (<0.0001) (PM2_Supporting).

Not Met criteria codes

BA1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS1	✖	No other pathogenic variant was found to lead to the same amino acid change (PS1 Not Met).
PS3	✖	Arg1768Gln not evaluated in Tominaga et al. (2022)

Curation History

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