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Variant: NM_001130987.2(DYSF):c.2426C>G (p.Pro809Arg)

Version: 1.0

CA222139

6671 (ClinVar)

Gene: DYSF (HGNC:8291)
Condition: limb-girdle muscular dystrophy (MONDO:0016971)
Inheritance Mode: Autosomal recessive inheritance
UUID: 2366548f-6ee9-4d1a-96a0-c9352c48ed67
Approved on: 2026/4/30
Published on: 2026/5/7

HGVS expressions

NM_001130987.2(DYSF):c.2426C>G (p.Pro809Arg)
NM_001130987.2:c.2426C>G
NC_000002.12:g.71564074C>G
CM000664.2:g.71564074C>G
NC_000002.11:g.71791204C>G
CM000664.1:g.71791204C>G
NC_000002.10:g.71644712C>G
NG_008694.1:g.115452C>G
ENST00000258104.8:c.2372C>G
ENST00000410020.8:c.2426C>G
ENST00000258104.7:c.2372C>G
ENST00000394120.6:c.2375C>G
ENST00000409366.5:c.2375C>G
ENST00000409582.7:c.2423C>G
ENST00000409651.5:c.2468C>G
ENST00000409744.5:c.2333C>G
ENST00000409762.5:c.2423C>G
ENST00000410020.7:c.2426C>G
ENST00000410041.1:c.2426C>G
ENST00000413539.6:c.2465C>G
ENST00000429174.6:c.2372C>G
NM_001130455.1:c.2375C>G
NM_001130976.1:c.2330C>G
NM_001130977.1:c.2330C>G
NM_001130978.1:c.2372C>G
NM_001130979.1:c.2465C>G
NM_001130980.1:c.2423C>G
NM_001130981.1:c.2423C>G
NM_001130982.1:c.2468C>G
NM_001130983.1:c.2375C>G
NM_001130984.1:c.2333C>G
NM_001130985.1:c.2426C>G
NM_001130986.1:c.2333C>G
NM_001130987.1:c.2426C>G
NM_003494.3:c.2372C>G
NM_001130455.2:c.2375C>G
NM_001130976.2:c.2330C>G

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

Likely Pathogenic

Met criteria codes 5

PP1 PP3 PM3 PM2_Supporting PP4_Strong

Not Met criteria codes 3

PS1 PS3 PM5

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>G variant in DYSF, which is also known as NM_001130987.2: c.2426C>G p.(Pro809Arg), is a missense variant predicted to cause substitution of proline by arginine at amino acid position 809, p.(Pro791Arg). This variant has been detected in a homozygous state in at least five seemingly unrelated individuals with features consistent with limb girdle muscular dystrophy (1 pt; PMID: 30564623, 16996541, 10196377; PM3). It has also been reported in unconfirmed phase with a VUS in an individual with undetectable dysferlin protein expression (Jain Foundation Dysferlin Registry internal data communication). At least one patient with this variant in a homozygous state displayed progressive limb girdle muscle weakness and significantly reduced DYSF protein expression, which is highly specific for DYSF-related LGMD (PP4_Strong; PMID: 16996541, 10196377). This variant was also shown to co-segregate with autosomal recessive LGMD in at least 10 affected family members from three Canadian Indigenous families sharing the same haplotype, suggesting it is a founder variant in that population (PMID: 10196377; PP1_Supporting, capped with PP4_Strong). This variant is absent from gnomAD v4.1.0. (PM2_Supporting). The computational predictor REVEL gives a score of 0.902, which meets the VCEP threshold of ≥0.70, evidence that correlates with impact to DYSF function (PP3). In summary, this variant meets the criteria to be classified as Likely 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, PP1, PM2_Supporting, PP3.

Met criteria codes

PP1	✔	This variant has also been reported to co-segregate with autosomal recessive LGMD in at least 10 affected family members from three Canadian Indigenous families sharing the same haplotype (PMID: 10196377; PP1_Supporting, capped with PP4_Strong).
PP3	✔	

The computational predictor REVEL gives a score of 0.902, which meets the VCEP threshold of ≥0.70, evidence that correlates with impact to DYSF function. (PP3) SpliceAI 0

PM3	✔	This variant has been detected in a homozygous state in at least 5 seemingly unrelated individuals with features consistent with limb girdle muscular dystrophy (1 pt; PMID: 30564623, 16996541, 10196377; PM3). Haplotype analysis indicates this variant is a founder variant in a Canadian Indigenous population. It has also been reported in unconfirmed phase with a VUS in an individual with undetectable dysferlin protein expression (Jain Foundation Dysferlin Registry internal data communication). no non-homozygous cases in LOVD, no other lit identified Need compound het cases to upgrade but only one identified has unscoreable VUS
PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0. (PM2_Supporting)
PP4_Strong	✔	At least one patient with this variant in a homozygous state displayed progressive limb girdle muscle weakness and significantly reduced DYSF protein expression, which is highly specific for DYSF-related LGMD (PP4_Strong; PMID: 16996541, 10196377).

Not Met criteria codes

PS1	✖	No other nucleotide changes resulting in the same amino acid change reported.
PS3	✖	not evaluated in Tominaga et al.
PM5	✖	This variant is being curated to support the classification of another missense change at the same position, c.2372C>T p.(Pro791Leu), which is provisionally classified as VUS. 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)

Curation History

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