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Variant: NM_001130987.2(DYSF):c.5210C>G (p.Pro1737Arg)

Version: 1.0

CA1707292

567124 (ClinVar)

Gene: DYSF (HGNC:8291)
Condition: autosomal recessive limb-girdle muscular dystrophy (MONDO:0015152)
Inheritance Mode: Autosomal recessive inheritance
UUID: d8445323-1604-42aa-a076-e8e266797546
Approved on: 2026/1/23
Published on: 2026/2/17

HGVS expressions

NM_001130987.2:c.5210C>G
NM_001130987.2(DYSF):c.5210C>G (p.Pro1737Arg)
NC_000002.12:g.71665197C>G
CM000664.2:g.71665197C>G
NC_000002.11:g.71892327C>G
CM000664.1:g.71892327C>G
NC_000002.10:g.71745835C>G
NG_008694.1:g.216575C>G
ENST00000698057.1:c.2624C>G
ENST00000698058.1:c.1841C>G
ENST00000698059.1:c.1949C>G
ENST00000258104.8:c.5093C>G
ENST00000410020.8:c.5210C>G
ENST00000258104.7:c.5093C>G
ENST00000394120.6:c.5096C>G
ENST00000409366.5:c.5159C>G
ENST00000409582.7:c.5207C>G
ENST00000409651.5:c.5189C>G
ENST00000409744.5:c.5117C>G
ENST00000409762.5:c.5144C>G
ENST00000410020.7:c.5210C>G
ENST00000410041.1:c.5147C>G
ENST00000413539.6:c.5186C>G
ENST00000429174.6:c.5156C>G
ENST00000479049.6:n.1978C>G
NM_001130455.1:c.5096C>G
NM_001130976.1:c.5051C>G
NM_001130977.1:c.5114C>G
NM_001130978.1:c.5156C>G
NM_001130979.1:c.5186C>G
NM_001130980.1:c.5144C>G
NM_001130981.1:c.5207C>G
NM_001130982.1:c.5189C>G
NM_001130983.1:c.5159C>G
NM_001130984.1:c.5117C>G
NM_001130985.1:c.5147C>G
NM_001130986.1:c.5054C>G

NM_001130987.1:c.5210C>G
NM_003494.3:c.5093C>G
NM_001130455.2:c.5096C>G
NM_001130976.2:c.5051C>G
NM_001130977.2:c.5114C>G
NM_001130978.2:c.5156C>G
NM_001130979.2:c.5186C>G
NM_001130980.2:c.5144C>G
NM_001130981.2:c.5207C>G
NM_001130982.2:c.5189C>G
NM_001130983.2:c.5159C>G
NM_001130984.2:c.5117C>G
NM_001130985.2:c.5147C>G
NM_001130986.2:c.5054C>G
NM_003494.4:c.5093C>G

Likely Pathogenic

Met criteria codes 6

PM3_Supporting PP1 PP3 PP4 PM2_Supporting PM5_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.5093C>G variant in DYSF, which is also known as NM_001130987.2: c.5210C>G p.(Pro1737Arg), is a missense variant predicted to cause substitution of proline to arginine at amino acid 1698, p.(Pro1698Arg). This variant has been observed in three individuals with LGMD, including two siblings in a homozygous state with reported consanguinity (0.25 pts, ClinVar SCV000814671.7 internal data communication; PP1) and one with a pathogenic variant in unknown phase (NM_003494.4: c.265C>T p.(Arg89Ter), 0.5 pts, PMID: 38582400) (PM3_Supporting; PP4). The highest allele frequency for this variant in gnomAD v4.1.0 is 0.00001098 (1/91080 South Asian chromosomes), which is less than the ClinGen LGMD VCEP threshold (<0.0001) (PM2_Supporting). The computational predictor REVEL gives a score of 0.91, which is above the LGMD VCEP threshold of ≥0.70 (PP3). In addition, another missense variant at the same codon, NM_003494.4: c.5093C>T p.(Pro1698Leu), has been classified as likely pathogenic by the ClinGen LGMD VCEP (PM5_Supporting). In summary, this variant is 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 (specifications v2.0.0; 01/23/2026): PM3_Supporting, PP4, PP3, PM2_Supporting, PM5_Supporting, PP1.

Met criteria codes

PM3_Supporting	✔	This variant has been observed in three individuals with LGMD, including two siblings in a homozygous state with reported consanguinity (0.25 pts, ClinVar SCV000814671.7 internal data communication; PP1) and one with a pathogenic variant in unknown phase (c.265C>T p.(Arg89Ter), 0.5 pts, PMID: 38582400) (PM3_Supporting; PP4).

PP1	ℹ	✔	Siblings diagnosed with LGMD. Both had this variant in a homozygous state (ClinVar SCV000814671.7 internal data communication).
PP3	ℹ	✔	The computational predictor REVEL gives a score of 0.91, which is above the LGMD VCEP threshold of ≥0.70 (PP3). Splice AI: 0.00
PP4	ℹ	✔	This variant has been observed in three individuals with LGMD with two presumably diagnostic variants (ClinVar SCV000814671.7 internal data communication; PMID: 38582400) (PP4).
PM2_Supporting	ℹ	✔	The highest allele frequency for this variant in gnomAD v4.1.0 is 0.00001098 (1/91080 South Asian chromosomes), which is less than the ClinGen LGMD VCEP threshold (<0.0001) (PM2_Supporting).
PM5_Supporting	ℹ	✔	Another missense variant at the same codon, c.5093C>T p.(Pro1698Leu), has been classified as likely pathogenic by the ClinGen LGMD VCEP without the use of PM5 (PM5_Supporting). splice AI<0.5 for both variants In addition, there is another variant, p.(Pro1698Ser), that looks like it will not go above VUS (not curated).

Not Met criteria codes

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

Curation History

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