

Variant: NM_001130987.2(DYSF):c.797G>A (p.Gly266Glu)

Version: 1.0

CA275400 [↗](#)

198495 (ClinVar) [↗](#)

Gene: DYSF ([HGNC:8291](#))

Condition: autosomal recessive limb-girdle muscular dystrophy
([MONDO:0015152](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: 401b6f36-78f9-46e6-921f-3c797dbad5e3

Approved on: 2026/1/23

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HGVS expressions

NM_001130987.2:c.797G>A
NM_001130987.2(DYSF):c.797G>A (p.Gly266Glu)
NC_000002.12:g.71515660G>A
CM000664.2:g.71515660G>A
NC_000002.11:g.71742790G>A
CM000664.1:g.71742790G>A
NC_000002.10:g.71596298G>A
NG_008694.1:g.67038G>A
ENST00000258104.8:c.701G>A
ENST00000410020.8:c.797G>A
ENST00000258104.7:c.701G>A
ENST00000394120.6:c.704G>A
ENST00000409366.5:c.704G>A
ENST00000409582.7:c.794G>A
ENST00000409651.5:c.797G>A
ENST00000409744.5:c.704G>A
ENST00000409762.5:c.794G>A
ENST00000410020.7:c.797G>A
ENST00000410041.1:c.797G>A
ENST00000413539.6:c.794G>A
ENST00000429174.6:c.701G>A
NM_001130455.1:c.704G>A
NM_001130976.1:c.701G>A
NM_001130977.1:c.701G>A
NM_001130978.1:c.701G>A
NM_001130979.1:c.794G>A
NM_001130980.1:c.794G>A
NM_001130981.1:c.794G>A
NM_001130982.1:c.797G>A
NM_001130983.1:c.704G>A
NM_001130984.1:c.704G>A
NM_001130985.1:c.797G>A
NM_001130986.1:c.704G>A
NM_001130987.1:c.797G>A
NM_003494.3:c.701G>A
NM_001130455.2:c.704G>A
NM_001130976.2:c.701G>A

NM_001130977.2:c.701G>A
NM_001130978.2:c.701G>A
NM_001130979.2:c.794G>A
NM_001130980.2:c.794G>A
NM_001130981.2:c.794G>A
NM_001130982.2:c.797G>A
NM_001130983.2:c.704G>A
NM_001130984.2:c.704G>A
NM_001130985.2:c.797G>A
NM_001130986.2:c.704G>A
NM_003494.4:c.701G>A

Pathogenic

Met criteria codes 3

PS3_Moderate PP4_Strong
PM3_Strong

Not Met criteria codes 3

BP4 PP3 PM2

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.701G>A variant in DYSF, which is also known as NM_001130987.2: c.797G>A p.(Gly266Glu), is a missense variant predicted to cause substitution of glycine by glutamic acid at amino acid 234, p.(Gly234Glu). This variant has been reported in at least seven patients with features overlapping LGMD (PMID: 18853459, 22194990, 38357254, 30564623, Jain Foundation Registry internal data communication), including in unknown phase with a second pathogenic variant in four individuals (c.3137G>A p.(Arg1046His), 0.5 pts, c.1555G>A p.(Gly519Arg), 0.5 pts, PMID: 21522182, LOVD individuals #00220647 and #00220234, respectively; c.5979dupA p.(Glu1994ArgfsTer3), 0.5 pts, c.5429G>A p.(Arg1810Lys), 0.5 pts, Jain Foundation Dysferlin Registry internal data communication) (PM3_Strong). At least one of these patients with two presumed diagnostic variants and clinical features of LGMD had absent dysferlin expression in muscle or blood monocytes, which is highly specific for DYSF-related LGMD (PMID: 18853459, 22194990; PP4_Strong). The Grpmax allele frequency of this variant is 0.0001167 in gnomAD v4.1.0 (7/59982 Admixed American chromosomes), which is greater than the LGMD VCEP threshold (≤ 0.0001) (PM2_Supporting not met). Immunofluorescence and 2-A assays of dysferlin membrane localization in HEK293T cells showed the Gly234Glu protein did not reach the cell membrane, indicating an impact on protein function (PMID: 35028538) (PS3_Moderate). The computational predictor REVEL gives a score of 0.64 (PP3 and BP4 not met). 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; 01/23/2026): PM3_Strong, PP4_Strong, PS3_Moderate.

Met criteria codes

PS3_Moderate



Immunofluorescence and 2-A assays of dysferlin membrane localization in HEK293T cells showed the Gly234Glu protein did not reach the cell membrane, indicating an impact on protein function (PMID: 35028538) (PS3_Moderate).

PP4_Strong			At least one patient with two presumed diagnostic variants and clinical features of LGMD had absent dysferlin expression in muscle or blood monocytes, which is highly specific for DYSF-related LGMD (PMID: 18853459, 22194990; PP4_strong).
PM3_Strong			This variant has been reported in at least seven patients with features overlapping LGMD (PMID: 18853459, 22194990, 38357254, 30564623, Jain Foundation Registry internal data communication), including in unknown phase with a second pathogenic variant in four individuals (c.3137G>A p.(Arg1046His), 0.5 pts, c.1555G>A p.(Gly519Arg), 0.5 pts, PMID: 21522182, LOVD individuals #00220647 and #00220234, respectively; c.5979dupA p.(Glu1994ArgfsTer3), 0.5 pts, c.5429G>A p.(Arg1810Lys), 0.5 pts, Jain Foundation Registry internal data communication) (PM3_Strong).
Not Met criteria codes			
BP4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3			The computational predictor REVEL gives a score of 0.64 (PP3 and BP4 not met). Splice AI: 0.02
PM2			The Grpmax allele frequency of this variant is 0.0001167 in gnomAD v4.1.0 (7/59982 Admixed American chromosomes), which is greater than the LGMD VCEP threshold (≤ 0.0001) (PM2_Supporting not met).

Curation History 			
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