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Variant: NM_001130987.2(DYSF):c.6155C>G (p.Pro2052Arg)

Version: 1.0

CA10607009

291078 (ClinVar)

Gene: DYSF (HGNC:8291)
Condition: autosomal recessive limb-girdle muscular dystrophy (MONDO:0015152)
Inheritance Mode: Autosomal recessive inheritance
UUID: 269e144b-4131-4ccc-ba25-b60cddc1be71
Approved on: 2025/6/10
Published on: 2025/7/8

HGVS expressions

NM_001130987.2:c.6155C>G
NM_001130987.2(DYSF):c.6155C>G (p.Pro2052Arg)
NC_000002.12:g.71681092C>G
CM000664.2:g.71681092C>G
NC_000002.11:g.71908222C>G
CM000664.1:g.71908222C>G
NC_000002.10:g.71761730C>G
NG_008694.1:g.232470C>G
ENST00000698057.1:c.3569C>G
ENST00000698058.1:c.2786C>G
ENST00000698059.1:c.2894C>G
ENST00000258104.8:c.6038C>G
ENST00000410020.8:c.6155C>G
ENST00000258104.7:c.6038C>G
ENST00000394120.6:c.6041C>G
ENST00000409366.5:c.6104C>G
ENST00000409582.7:c.6152C>G
ENST00000409651.5:c.6134C>G
ENST00000409744.5:c.6062C>G
ENST00000409762.5:c.6089C>G
ENST00000410020.7:c.6155C>G
ENST00000410041.1:c.6092C>G
ENST00000413539.6:c.6131C>G
ENST00000429174.6:c.6101C>G
ENST00000479049.6:n.2923C>G
NM_001130455.1:c.6041C>G
NM_001130976.1:c.5996C>G
NM_001130977.1:c.6059C>G
NM_001130978.1:c.6101C>G
NM_001130979.1:c.6131C>G
NM_001130980.1:c.6089C>G
NM_001130981.1:c.6152C>G
NM_001130982.1:c.6134C>G
NM_001130983.1:c.6104C>G
NM_001130984.1:c.6062C>G
NM_001130985.1:c.6092C>G
NM_001130986.1:c.5999C>G

NM_001130987.1:c.6155C>G
NM_003494.3:c.6038C>G
NM_001130455.2:c.6041C>G
NM_001130976.2:c.5996C>G
NM_001130977.2:c.6059C>G
NM_001130978.2:c.6101C>G
NM_001130979.2:c.6131C>G
NM_001130980.2:c.6089C>G
NM_001130981.2:c.6152C>G
NM_001130982.2:c.6134C>G
NM_001130983.2:c.6104C>G
NM_001130984.2:c.6062C>G
NM_001130985.2:c.6092C>G
NM_001130986.2:c.5999C>G
NM_003494.4:c.6038C>G

Likely Pathogenic

Met criteria codes 4

PM3_Supporting PP4_Strong PM2_Supporting PP3

Not Met criteria codes 1

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 1.0.0*

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Limb Girdle Muscular Dystrophy VCEP

The NM_003494.4: c.6038C>G variant in DYSF, which is also known as NM_001130987.2: c.6155C>G p.(Pro2052Arg), is a missense variant predicted to cause substitution of proline by arginine at amino acid 2013, p.(Pro2013Arg). This variant has been reported in unknown phase with a pathogenic variant in at least one individual with LGMD (NM_003494.4: c.3137G>A p.(Arg1064His), 0.5 pts, PMID: 36983702, 30564623; LOVD Individual #00221252) (PM3_Supporting). This individual displayed progressive limb girdle muscle weakness and disease range dysferlin expression by blood monocyte assay, which is highly specific for DYSF-related LGMD (PP4_Strong). This variant is absent from gnomAD v4.1.0 (PM2_Supporting). The computational predictor REVEL gives a score of 0.83, which is above the LGMD VCEP threshold of 0.70, evidence that correlates with impact to DYSF function. In addition, SpliceAI gives a score of 0.31 for donor gain. (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 1.0.0; 06/10/2025): PM3_Supporting, PP4_Strong, PM2_Supporting, PP3.

Met criteria codes

PM3_Supporting ✔

This variant has been reported in unknown phase with a pathogenic variant in at least one individual with features consistent with LGMD (NM_003494.4: c.3137G>A p.(Arg1064His), 0.5 pts, PMID: 36983702, 30564623, LOVD Individual #00221252) (PM3_Supporting). c.3137G>A p.(Arg1064His) is independently P, cannot check co-occurrence Eurofins Ntd Llc (ga) is only submitter in ClinVar (assume Nallamilli case), no other cases in LOVD

PP4_Strong		✔	This variant has been reported with a second presumed diagnostic DYSF variant in an individual with progressive limb girdle muscle weakness and disease range dysferlin expression by blood monocyte assay, which is highly specific for DYSF-related LGMD (PMID: 3698370; PP4_Strong).
PM2_Supporting		✔	This variant is absent from gnomAD v4.1.0 (PM2_Supporting).
PP3		✔	The computational predictor REVEL gives a score of 0.83, which is above the LGMD VCEP threshold of 0.70, evidence that correlates with impact to DYSF function (PP3).

Not Met criteria codes

PM5		✖	SpliceAI score 0.31 for donor gain - PM5 not applicable

Curation History

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