

Variant: NM_001130987.2(DYSF):c.757C>T (p.Gln253Ter)

Version: 1.0

CA10606688 [↗](#)

290209 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 963bc9b6-9fb1-45c8-b949-286d31b48168

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HGVS expressions

NM_001130987.2:c.757C>T
NM_001130987.2(DYSF):c.757C>T (p.Gln253Ter)
NC_000002.12:g.71513919C>T
CM000664.2:g.71513919C>T
NC_000002.11:g.71741049C>T
CM000664.1:g.71741049C>T
NC_000002.10:g.71594557C>T
NG_008694.1:g.65297C>T
ENST00000258104.8:c.661C>T
ENST00000410020.8:c.757C>T
ENST00000258104.7:c.661C>T
ENST00000394120.6:c.664C>T
ENST00000409366.5:c.664C>T
ENST00000409582.7:c.754C>T
ENST00000409651.5:c.757C>T
ENST00000409744.5:c.664C>T
ENST00000409762.5:c.754C>T
ENST00000410020.7:c.757C>T
ENST00000410041.1:c.757C>T
ENST00000413539.6:c.754C>T
ENST00000429174.6:c.661C>T
NM_001130455.1:c.664C>T
NM_001130976.1:c.661C>T
NM_001130977.1:c.661C>T
NM_001130978.1:c.661C>T
NM_001130979.1:c.754C>T
NM_001130980.1:c.754C>T
NM_001130981.1:c.754C>T
NM_001130982.1:c.757C>T
NM_001130983.1:c.664C>T
NM_001130984.1:c.664C>T
NM_001130985.1:c.757C>T
NM_001130986.1:c.664C>T
NM_001130987.1:c.757C>T
NM_003494.3:c.661C>T
NM_001130455.2:c.664C>T
NM_001130976.2:c.661C>T

NM_001130977.2:c.661C>T
NM_001130978.2:c.661C>T
NM_001130979.2:c.754C>T
NM_001130980.2:c.754C>T
NM_001130981.2:c.754C>T
NM_001130982.2:c.757C>T
NM_001130983.2:c.664C>T
NM_001130984.2:c.664C>T
NM_001130985.2:c.757C>T
NM_001130986.2:c.664C>T
NM_003494.4:c.661C>T

Pathogenic

Met criteria codes 4

PM2_Supporting PVS1 PP4 PM3

Not Met criteria codes 22

BS1 BS4 BS3 BS2 BP5 BP7
BP4 BP3 BP1 BP2 PS1 PS2
PS3 PS4 BA1 PP1 PP2 PP3
PM6 PM1 PM5 PM4

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.661C>T p.(Gln221Ter) variant in DYSF, which is also known as NM_001130987.2: c.757C>T p.(Gln253Ter), is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 6/55, leading to nonsense mediated decay in a gene in which loss of function is an established disease mechanism (PVS1). This variant has been detected in a homozygous state in two patients with LGMD (1.0 pt, ClinVar SCV003309109.1 internal data communication, PMID: 30564623, Jain Foundation Dysferlin Registry internal data communication) (PM3, PP4). This variant is absent from gnomAD v2.1.1 and v3.1.2 (PM2_Supporting). 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 1.0.0; 01/08/2025): PVS1, PM2_Supporting, PM3, PP4.

Met criteria codes

PM2_Supporting		✓	This variant is absent from gnomAD v2.1.1 and v.3.1.2 (PM2_Supporting).
PVS1		✓	The NM_003494.4: 661C>T (p.Gln221Ter) variant in DYSF is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 6/55 leading to nonsense mediated decay in a gene in which loss of function is an established disease mechanism (PVS1).
PP4		✓	At least one patient with this variant displayed a progressive limb girdle pattern of muscle weakness (PP4; ClinVar SCV003309109.1).
PM3		✓	

This variant has been detected in a homozygous state in two individuals (1.0 pt; ClinVar SCV003309109.1, PMID: 30564623; Jain Foundation Dysferlin Registry) (PM3).

Not Met criteria codes

BS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP5			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP7			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

PS4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM6			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM5			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History 		
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