

Variant: NM_001130987.2(DYSF):c.3756T>C (p.Tyr1252=)

Version: 1.0

CA233935 [↗](#)

167024 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 55338086-d5ae-4c37-afa4-92f9f453f6a6

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HGVS expressions

NM_001130987.2:c.3756T>C

NM_001130987.2(DYSF):c.3756T>C (p.Tyr1252=)

NC_000002.12:g.71598745T>C

CM000664.2:g.71598745T>C

NC_000002.11:g.71825875T>C

CM000664.1:g.71825875T>C

NC_000002.10:g.71679383T>C

NG_008694.1:g.150123T>C

ENST00000698057.1:c.1128T>C

ENST00000698058.1:c.345T>C

ENST00000698059.1:c.345T>C

ENST00000258104.8:c.3702T>C

ENST00000410020.8:c.3756T>C

ENST00000258104.7:c.3702T>C

ENST00000394120.6:c.3705T>C

ENST00000409366.5:c.3705T>C

ENST00000409582.7:c.3753T>C

ENST00000409651.5:c.3798T>C

ENST00000409744.5:c.3663T>C

ENST00000409762.5:c.3753T>C

ENST00000410020.7:c.3756T>C

ENST00000410041.1:c.3756T>C

ENST00000413539.6:c.3795T>C

ENST00000429174.6:c.3702T>C

ENST00000475076.5:n.530T>C

ENST00000479049.6:n.587T>C

ENST00000493767.1:n.423T>C

NM_001130455.1:c.3705T>C

NM_001130976.1:c.3660T>C

NM_001130977.1:c.3660T>C

NM_001130978.1:c.3702T>C

NM_001130979.1:c.3795T>C

NM_001130980.1:c.3753T>C

NM_001130981.1:c.3753T>C

NM_001130982.1:c.3798T>C

NM_001130983.1:c.3705T>C

NM_001130984.1:c.3663T>C

NM_001130985.1:c.3756T>C
NM_001130986.1:c.3663T>C
NM_001130987.1:c.3756T>C
NM_003494.3:c.3702T>C
NM_001130455.2:c.3705T>C
NM_001130976.2:c.3660T>C
NM_001130977.2:c.3660T>C
NM_001130978.2:c.3702T>C
NM_001130979.2:c.3795T>C
NM_001130980.2:c.3753T>C
NM_001130981.2:c.3753T>C
NM_001130982.2:c.3798T>C
NM_001130983.2:c.3705T>C
NM_001130984.2:c.3663T>C
NM_001130985.2:c.3756T>C
NM_001130986.2:c.3663T>C
NM_003494.4:c.3702T>C

Likely Benign

Met criteria codes 2

BP7_Strong BP4

Not Met criteria codes 3

BP2 PM3 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.3702T>C p.(Tyr1234=) variant in DYSF, which is also known as NM_001130987.2: c.3756T>C (p.Tyr1252=), is a synonymous (silent) variant that affects the last nucleotide of exon 33. The SpliceAI prediction score for this variant is 0.00 (BP4), and RNASeq data showed this variant does not affect splicing (PMID: 36983702; BP7_Strong_RNA). This variant has been identified in three individuals with suspected LGMD, all with at least two additional DYSF variants including those classified as pathogenic. However, phase was not known in any of these individuals (PMID: 18853459, 36983702; PM3 and BP2 not met). The Grpmax variant allele frequency for this variant in gnomAD v4.1.0 is 0.0005834 (35/59994 Admixed American chromosomes), which is greater than the LGMD VCEP threshold (<0.0001) for PM2_Supporting (criterion not met). This population also includes one homozygous individual. In summary, this variant meets the criteria to be classified as Likely Benign 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; 10/29/2025): BP4, BP7_Strong_RNA.

Met criteria codes

BP7_Strong



The variant is in the last nucleotide of exon 33 but RNASeq data showed this variant does not affect splicing (PMID: 36983702; BP7_Strong_RNA).

BP4			The SpliceAI prediction score for this variant is 0.00 (BP4).
Not Met criteria codes			
BP2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM3			This variant has been identified in three individuals with suspected LGMD, all with at least two additional variants present including those classified as pathogenic. However, phase was not known in any of these individuals (PMID: 18853459, 36983702; PM3 and BP2 not met).
PM2			The Grpmax variant allele frequency for this variant in gnomAD v4.1.0 is 0.0005834 (35/59994 Admixed American chromosomes), which is greater than the LGMD VCEP threshold (<0.0001) for PM2_Supporting (criterion not met). This population also includes one homozygous individual.

Curation History 			
    			
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