

Variant: NM_001130987.2(DYSF):c.3166C>T (p.Arg1056Ter)

Version: 1.0

CA277609 [↗](#)

217225 (ClinVar) [↗](#)

Gene: DYSF ([HGNC:8291](#))
Condition: autosomal recessive limb-girdle muscular dystrophy ([MONDO:0015152](#))
Inheritance Mode: Autosomal recessive inheritance
UUID: ba4dd811-09bc-44ef-bea5-0cf88387c2f8
Approved on: 2025/7/29
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HGVS expressions

NM_001130987.2(DYSF):c.3166C>T (p.Arg1056Ter)
NM_001130987.2:c.3166C>T
NC_000002.12:g.71570679C>T
CM000664.2:g.71570679C>T
NC_000002.11:g.71797809C>T
CM000664.1:g.71797809C>T
NC_000002.10:g.71651317C>T
NG_008694.1:g.122057C>T
ENST00000698057.1:c.538C>T
ENST00000258104.8:c.3112C>T
ENST00000410020.8:c.3166C>T
ENST00000258104.7:c.3112C>T
ENST00000394120.6:c.3115C>T
ENST00000409366.5:c.3115C>T
ENST00000409582.7:c.3163C>T
ENST00000409651.5:c.3208C>T
ENST00000409744.5:c.3073C>T
ENST00000409762.5:c.3163C>T
ENST00000410020.7:c.3166C>T
ENST00000410041.1:c.3166C>T
ENST00000413539.6:c.3205C>T
ENST00000429174.6:c.3112C>T
ENST00000461565.1:n.278C>T
NM_001130455.1:c.3115C>T
NM_001130976.1:c.3070C>T
NM_001130977.1:c.3070C>T
NM_001130978.1:c.3112C>T
NM_001130979.1:c.3205C>T
NM_001130980.1:c.3163C>T
NM_001130981.1:c.3163C>T
NM_001130982.1:c.3208C>T
NM_001130983.1:c.3115C>T
NM_001130984.1:c.3073C>T
NM_001130985.1:c.3166C>T
NM_001130986.1:c.3073C>T
NM_001130987.1:c.3166C>T
NM_003494.3:c.3112C>T

NM_001130455.2:c.3115C>T
NM_001130976.2:c.3070C>T
NM_001130977.2:c.3070C>T
NM_001130978.2:c.3112C>T
NM_001130979.2:c.3205C>T
NM_001130980.2:c.3163C>T
NM_001130981.2:c.3163C>T
NM_001130982.2:c.3208C>T
NM_001130983.2:c.3115C>T
NM_001130984.2:c.3073C>T
NM_001130985.2:c.3166C>T
NM_001130986.2:c.3073C>T
NM_003494.4:c.3112C>T

Pathogenic

Met criteria codes 4

- PP4_Strong
- PM2_Supporting
- PVS1
- PM3_Strong

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.3112C>T p.(Arg1038Ter) variant in DYSF, which is also known as NM_001130987.2: c.3166C>T p.(Arg1056Ter), is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 29/55, leading to nonsense mediated decay in a gene in which loss of function is an established disease mechanism (PVS1). This variant has been reported in at least five individuals with signs of dysferlinopathy (PMID: 36983702, 23243261, 17698709, 16010686), including confirmed in trans with a likely pathogenic or pathogenic DYSF variant in three patients (NM_003494.4: c.2643+1G>A, 1.0 pt, PMID: 36983702; NM_003494.4: c.4497del p.(Phe1499LeufsTer4), 1.0 pt, PMID: 23243261; NM_003494.4: c.3832C>T p.(Gln1278Ter), 1.0 pt, PMID: 16010686, 7698709). At least one of the patients with this variant and a second presumed diagnostic DYSF allele displayed progressive limb girdle muscle weakness and disease range dysferlin expression in blood monocytes, which is highly specific for DYSF-related LGMD (PP4_Strong; PMID: 36983702). The filtering allele frequency for this variant is 0.00005974 in gnomAD v4.1.0 exomes (the upper bound of the 95% confidence interval for 57/1111956 European (non-Finnish) chromosomes, which is less than the VCEP threshold of 0.0001 (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; 07/29/2025): PVS1, PM3_Strong, PP4_Strong, PM2_Supporting.

Met criteria codes

PP4_Strong



At least one of the patients with this variant and a second presumed diagnostic DYSF allele displayed progressive limb girdle muscle weakness and disease range dysferlin expression in blood monocytes, which is highly specific for DYSF-related LGMD (PP4_Strong; PMID: 36983702).

PM2_Supporting			The filtering allele frequency for this variant is 0.00005974 in gnomAD v4.1.0 exomes (the upper bound of the 95% confidence interval for 57/1111956 European (non-Finnish) chromosomes, which is less than the VCEP threshold of 0.0001 (PM2_Supporting). Note that the filtering allele frequency for this variant using the combined allele count in the African/African American population is 0.0001755 (7/74916 combined alleles), which does not meet the criterion. But in the exome data, there are only 2 alleles in the African/African American population, and the MAF of 0.00005974 meets the criterion.
PVS1			The NM_003494.4: c.3112C>T p.(Arg1038Ter) variant in DYSF, which is also known as NM_001130987.2: c.3166C>T p.(Arg1056Ter), is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 29/55, leading to nonsense mediated decay in a gene in which loss of function is an established disease mechanism (PVS1).
PM3_Strong			This variant has been reported in at least five individuals with signs of dysferlinopathy (PMID: 36983702, 23243261, 17698709, 16010686), including confirmed in trans with a likely pathogenic or pathogenic DYSF variant in three patients (NM_003494.4: c.2643+1G>A, 1.0 pt, PMID: 36983702; NM_003494.4: c.4497del p.(Phe1499LeufsTer4), 1.0 pt, PMID: 23243261; NM_003494.4: c.3832C>T p.(Gln1278Ter), 1.0 pt, PMID: 16010686, 7698709).

Curation History 			
			
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