

Variant: *NM_001005361.3(DNM2):c.1564C>T (p.Arg522Cys)*

Version: 1.0

CA404039368 [↗](#)

986927 (ClinVar) [↗](#)

Gene: DNM2 ([HGNC:1785](#))

Condition: centronuclear myopathy ([MONDO:0018947](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: 2422e9c5-0079-408f-87b1-69444c139744

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HGVS expressions

NM_001005361.3:c.1564C>T

NM_001005361.3(DNM2):c.1564C>T (p.Arg522Cys)

NC_000019.10:g.10812270C>T

CM000681.2:g.10812270C>T

NC_000019.9:g.10922946C>T

CM000681.1:g.10922946C>T

NC_000019.8:g.10783946C>T

NG_008792.1:g.99192C>T

ENST00000681972.1:n.995C>T

ENST00000355667.11:c.1564C>T

ENST00000389253.9:c.1564C>T

ENST00000355667.10:c.1564C>T

ENST00000359692.10:c.1552C>T

ENST00000389253.8:c.1564C>T

ENST00000408974.8:c.1552C>T

ENST00000585892.5:c.1564C>T

ENST00000587830.2:c.838C>T

ENST00000590787.1:n.3063C>T

ENST00000590806.5:n.3752C>T

NM_001005360.2:c.1564C>T

NM_001005361.2:c.1564C>T

NM_001005362.2:c.1552C>T

NM_001190716.1:c.1564C>T

NM_004945.3:c.1552C>T

NM_001190716.2:c.1564C>T

NM_001005360.3:c.1564C>T

NM_001005362.3:c.1552C>T

NM_004945.4:c.1552C>T

Likely Pathogenic

Met criteria codes 5

PP2

PP3

PM5

PM2_Supporting

PS4_Supporting

Not Met criteria codes 3

BP4

BA1

BS1

Expert Panel

Congenital Myopathies VCEP [↗](#)

Criteria Specification Information

Evidence submitted by expert panel

Congenital Myopathies VCEP

The variant NM_001005361.3:c.1564C>T in DNM2 is a missense variant predicted to cause substitution of arginine by cysteine at amino acid 522 (p.Arg522Cys). The highest population minor allele frequency in gnomAD v4.1.0 is 8.526e-7 (1/1172834 alleles) in non-Finnish European which meets PM2_Supporting. DNM2, in which the variant was identified, is defined by the ClinGen Congenital Myopathies VCEP as a gene that has a low rate of benign missense variation and where pathogenic missense variants are a common mechanism of disease (PP2). The REVEL computational prediction analysis tool produced a score of 0.746, which is above the threshold of 0.7, evidence that correlates with impact to DNM2 function (PP3). Two different missense variants, p.Arg522His and p.Arg522Leu (ClinVar IDs: 158514 and 373110), in the same codon have been classified as (likely) pathogenic on ClinVar, of which p.Arg522His has been classified as pathogenic for centronuclear myopathy by the ClinGen Congenital Myopathies VCEP (PM5). This variant has been reported in one proband with centronuclear myopathy who presented with predominantly distal muscle weakness, ptosis, ophthalmoplegia/ paresis, facial weakness, weak deep tendon reflexes, stepping gait, central nuclei, fiber hypotrophy, and Type 1 fiber predominance (0.25pts, PS4_Supporting; PMID: 22396310). In summary, the variant meets criteria to be classified as likely pathogenic for centronuclear myopathy. ACMG/AMP criteria met, as specified by the ClinGen Congenital Myopathies VCEP: PM5, PS4_Supporting, PM2_Supporting, PP2, PP3 (ClinGen Congenital Myopathies VCEP specifications version 1.0.0; September 8th, 2025).

Met criteria codes

PP2			DNM2, in which the variant was identified, is defined by the ClinGen Congenital Myopathies VCEP as a gene that has a low rate of benign missense variation and where pathogenic missense variants are a common mechanism of disease
PP3			The REVEL computational prediction analysis tool produced a score of 0.746, which is above the threshold of 0.7
PM5			Two different missense variants, p.Arg522His and p.Arg522Leu (ClinVar IDs: 158514 and 373110), in the same codon have been classified as (likely) pathogenic on ClinVar, of which p.Arg522His has been classified as pathogenic for centronuclear myopathy by the ClinGen Congenital Myopathies VCEP
PM2_Supporting			The MAF in gnomAD v.4.1.0 is 8.526e-7 (1/1172834) in non-Finnish European which meets PM2_Supporting
PS4_Supporting			One proband with centronuclear myopathy presented with predominantly distal muscle weakness, ptosis, ophthalmoplegia/paresis, facial weakness, weak deep tendon reflexes, stepping gait, central nuclei, fiber hypotrophy, and Type 1 fiber predominance (0.25pts; PMID: 22396310).

Not Met criteria codes

BP4			The REVEL computational prediction analysis tool produced a score of 0.746, which meets PP3
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BA1			The MAF in gnomAD v.4.1.0 is 8.526e-7 (1/1172834) in non-Finnish European which meets PM2_Supporting
BS1			The MAF in gnomAD v.4.1.0 is 8.526e-7 (1/1172834) in non-Finnish European which meets PM2_Supporting

Curation History 

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