

Variant: NM_000252.3(MTM1):c.1353G>A (p.Gln451=)

Version: 1.0

CA271787 [↗](#)

158923 (ClinVar) [↗](#)

Gene: MTM1 ([HGNC:4534](#))

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

Inheritance Mode: X-linked inheritance

UUID: e8bd73b1-cdb8-4575-bd65-f890ba644dd5

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HGVS expressions

NM_000252.3:c.1353G>A

NM_000252.3(MTM1):c.1353G>A (p.Gln451=)

NC_000023.11:g.150659756G>A

CM000685.2:g.150659756G>A

NC_000023.10:g.149828229G>A

CM000685.1:g.149828229G>A

NC_000023.9:g.149578887G>A

NG_008199.1:g.96183G>A

ENST00000684910.1:c.*886G>A

ENST00000685439.1:c.1008G>A

ENST00000685944.1:c.1353G>A

ENST00000686212.1:n.955G>A

ENST00000687215.1:c.*1108G>A

ENST00000688152.1:c.*797G>A

ENST00000688403.1:c.609G>A

ENST00000689314.1:c.1398G>A

ENST00000689694.1:c.1353G>A

ENST00000689810.1:c.*1002G>A

ENST00000690282.1:c.609G>A

ENST00000690351.1:c.*1005G>A

ENST00000691232.1:c.1008G>A

ENST00000691482.1:n.2368G>A

ENST00000691686.1:c.1261-615G>A

ENST00000691851.1:c.1053+9855G>A

ENST00000692015.1:c.1140G>A

ENST00000692638.1:c.*1151G>A

ENST00000692852.1:c.1164G>A

ENST00000692915.1:c.*1499G>A

ENST00000370396.7:c.1353G>A

ENST00000306167.11:n.1220G>A

ENST00000370396.6:c.1353G>A

NM_000252.2:c.1353G>A

NM_001376906.1:c.1353G>A

NM_001376907.1:c.1242G>A

NM_001376908.1:c.1353G>A

Likely Pathogenic

Met criteria codes 4

PM2_SupportingPS4_ModeratePP3PM6

Not Met criteria codes 5

BA1BP4BP1BS1PP2

Evidence Links 0

Expert Panel

Congenital Myopathies VCEP

Criteria Specification Information

Criteria Specification: ClinGen Congenital Myopathies Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for MTM1 Version 1.0.0

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Congenital Myopathies VCEP

The NM_000252.3:c.1353G>A variant in MTM1 is a synonymous variant (p.Gln451=) located near the canonical donor site of intron 12. The variant is absent from gnomAD v4.1.0 meeting PM2_Supporting. The silent variant is predicted to impact splicing by SpliceAI (PP3). This variant has been reported in at least three probands, one with myotubular myopathy, one with congenital myopathy and abnormal muscle biopsy, and another with neonatal hypotonia. One of the three was a de novo occurrence with unconfirmed parental relationships (PS4_Moderate, PM6; PMID: 10790201; LabCorp, ClinVar: SCV001391223.5). In summary, the variant meets the criteria to be classified as likely pathogenic for X-linked centronuclear myopathy. ACMG/AMP criteria met, as specified by the ClinGen Congenital Myopathies VCEP: PS4_Moderate, PM6, PM2_Supporting, PP3 (ClinGen Congenital Myopathies VCEP specifications version 1.0.0; 1/13/2025).

Met criteria codes

PM2_Supporting

This variant was absent from gnomAD v4 meeting PM2_Supporting

PS4_Moderate

This variant has been reported in at least three probands, one with myotubular myopathy, one with congenital myopathy and abnormal muscle biopsy, and another with neonatal hypotonia (PMID: 10790201; LabCorp, ClinVar: SCV001391223.5)

PP3

This variant is located near the the canonical donor site of intron 12 and is predicted to lead to abnormal splicing. The SpliceAI score was 0.87.

PM6

The variant was reported to be de novo in a proband (LabCorp, ClinVar: SCV001391223.5)

Not Met criteria codes

BA1

This variant was absent from gnomAD v4 meeting PM2_Supporting

BP4

The variant is predicted to impact splicing.

BP1

Both missense and truncating variants in MTM1 are disease-causing.

BS1	 	This variant was absent from gnomAD v4 meeting PM2_Supporting
PP2		MTM1 is not a gene that is constrained for missense variation. Hence PP2 is not applicable.

Curation History 		
 Showing 1 to 1 of 1 rows		

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