

Variant: NM_000252.3(MTM1):c.141_144del

Version: 1.0

CA255668 [↗](#)

11057 (ClinVar) [↗](#)

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

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

Inheritance Mode: X-linked inheritance

UUID: fa05e62c-7632-4ef7-856e-5304d55f8d85

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HGVS expressions

NM_000252.3:c.141_144del

NM_000252.3(MTM1):c.141_144del

NC_000023.11:g.150598596_150598599del

CM000685.2:g.150598596_150598599del

NC_000023.10:g.149767060_149767063del

CM000685.1:g.149767060_149767063del

NC_000023.9:g.149517718_149517721del

NG_008199.1:g.35014_35017del

ENST00000684910.1:c.136+2026_136+2029del

ENST00000685439.1:c.-3-20442_-3-20439del

ENST00000685944.1:c.141_144del

ENST00000687215.1:c.-145_-142del

ENST00000687365.1:n.196_199del

ENST00000688152.1:c.141_144del

ENST00000688403.1:c.-301+29734_-301+29737del

ENST00000689314.1:c.141_144del

ENST00000689694.1:c.141_144del

ENST00000689810.1:c.141_144del

ENST00000690282.1:c.-301+29878_-301+29881del

ENST00000690351.1:c.136+2026_136+2029del

ENST00000691232.1:c.-3-20442_-3-20439del

ENST00000691686.1:c.141_144del

ENST00000691851.1:c.141_144del

ENST00000692015.1:c.141_144del

ENST00000692638.1:c.136+2026_136+2029del

ENST00000692852.1:c.141_144del

ENST00000692915.1:c.141_144del

ENST00000693422.1:n.202_205del

ENST00000370396.7:c.141_144del

ENST00000306167.11:n.180_183del

ENST00000370396.6:c.141_144del

ENST00000424519.1:c.141_144del

ENST00000490530.1:n.170+2026_170+2029del

NM_000252.2:c.141_144del

NM_001376906.1:c.141_144del

NM_001376907.1:c.141_144del

NM_001376908.1:c.141_144del

Pathogenic

Met criteria codes 6

- PM2_Supporting
- PVS1
- PS4
- PP1
- PP4
- PM6

Not Met criteria codes 2

- BS1
- BA1

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 c.141_144del (p.Glu48LeufsTer24) variant in MTM1 is a deletion variant predicted to cause a premature stop codon in biologically-relevant-exon 4/15 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). This variant is absent from gnomAD v4.1.0 (PM2_Supporting). The c.141_144del variant has been identified in at least 6 male probands with severe centronuclear myopathy, one of which was de novo with unconfirmed parental relationships, and one severely affected female (PMIDs: 9285787, 30241883, 33062893, 33164942, 10063835) (PS4, PM6). Additionally, the variant segregated with disease in an uncle and a male sibling from two separate families (PMID: 9285787) (PP1). At least one patient with this variant displayed a muscle biopsy consistent with centronuclear myopathy (PMID:33164942) (PP4). In summary, this variant meets the criteria to be classified as pathogenic for X-linked centronuclear myopathy based on the ACMG/AMP criteria applied, as specified by the ClinGen Congenital Myopathies VCEP: PVS1, PS4, PM6, PM2_Supporting, PP1, PP4. (ClinGen Congenital Myopathies VCEP specifications version 1; 8/7/2024)

Met criteria codes

PM2_Supporting			This variant is absent from gnomAD v4.1.0.
PVS1			The variant is an out of frame deletion that results in a frameshift and termination 24 AA downstream (in exon 4/15)
PS4			The c.141_144del variant has been identified in at least 6 male probands with severe centronuclear myopathy, one of which was de novo with unconfirmed parental relationships, and one severely affected female (PMIDs 9285787, 30241883, 33062893, 33164942, 10063835).
PP1			The c.141_144del variant was Identified in 4 individuals with severe centronuclear myopathy and segregated with disease in an uncle and a male sibling from two separate families (PMID: 9285787)
PP4			The c.141_144del variant has been identified in at least 6 male probands with severe centronuclear myopathy, and at least one of these probands had a muscle biopsy that is specific for centronuclear myopathy and MTM1 variants (PMID: 33164942).
PM6			The c.141_144del variant has been identified in at least 6 male probands with severe centronuclear myopathy, one of which was de novo with unconfirmed parental relationships, and one severely affected female (PMIDs 9285787, 30241883, 33062893, 33164942, 10063835).

Not Met criteria codes

BS1

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This variant is absent from gnomAD v4.1.0.

BA1

i

×

This variant is absent from gnomAD v4.1.0.

Curation History [↗](#)

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