The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000252.3(MTM1):c.670C>T (p.Arg224Ter)

Version: 1.0

CA255672

11060 (ClinVar)

Gene: MTM1 (HGNC:4534)
Condition: centronuclear myopathy (MONDO:0018947)
Inheritance Mode: X-linked inheritance
UUID: c0426f8d-dddf-447f-8b10-e0b31d0a6e1d
Approved on: 2024/8/7
Published on: 2024/10/1

HGVS expressions

NM_000252.3:c.670C>T
NM_000252.3(MTM1):c.670C>T (p.Arg224Ter)
NC_000023.11:g.150641410C>T
CM000685.2:g.150641410C>T
NC_000023.10:g.149809883C>T
CM000685.1:g.149809883C>T
NC_000023.9:g.149560541C>T
NG_008199.1:g.77837C>T
ENST00000684910.1:c.*203C>T
ENST00000685439.1:c.325C>T
ENST00000685944.1:c.670C>T
ENST00000686212.1:n.272C>T
ENST00000687215.1:c.*425C>T
ENST00000688152.1:c.*114C>T
ENST00000688403.1:c.-75C>T
ENST00000689314.1:c.715C>T
ENST00000689694.1:c.670C>T
ENST00000689810.1:c.*319C>T
ENST00000690282.1:c.-75C>T
ENST00000690351.1:c.*322C>T
ENST00000691232.1:c.325C>T
ENST00000691482.1:n.1685C>T
ENST00000691686.1:c.670C>T
ENST00000691851.1:c.670C>T
ENST00000692015.1:c.457C>T
ENST00000692638.1:c.*475C>T
ENST00000692852.1:c.670C>T
ENST00000692915.1:c.*877C>T
ENST00000370396.7:c.670C>T
ENST00000306167.11:n.537C>T
ENST00000370396.6:c.670C>T
ENST00000490530.1:n.609C>T
NM_000252.2:c.670C>T
NM_001376906.1:c.670C>T
NM_001376907.1:c.559C>T
NM_001376908.1:c.670C>T

Pathogenic

Met criteria codes 3

PS4 PVS1 PM2_Supporting

Not Met criteria codes 2

BA1 BS1

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.670C>T (p.Arg224Ter) variant in MTM1 is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 8/15 and to lead 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). This variant has been reported in 5 probands with X-linked myotubular myopathy (PS4; PMID: 9305655, 10063835, 11552027). 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, PM2_Supporting. (ClinGen Congenital Myopathies VCEP specifications version 1; 8/7/2024)

Met criteria codes

PS4	✔	Identified in 5 probands with X-Linked Myotubular Myopathy (PMID: 9305655, 10063835, 11552027)
PVS1	✔	This nonsense variant is predicted to cause a premature stop codon in biologically-relevant-exon 8/15 is predicted to lead to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism
PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0

Not Met criteria codes

BA1	✖	This variant is absent from gnomAD v4.1.0
BS1	✖	This variant is absent from gnomAD v4.1.0

Curation History

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