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.688T>C (p.Trp230Arg)

Version: 1.3

CA220541

92677 (ClinVar)

Gene: MTM1 (HGNC:4534)
Condition: centronuclear myopathy (MONDO:0018947)
Inheritance Mode: X-linked inheritance
UUID: 7276602c-cd60-4ace-9d02-4c1b1cf9ab59
Approved on: 2025/5/12
Published on: 2025/12/9

HGVS expressions

NM_000252.3:c.688T>C
NM_000252.3(MTM1):c.688T>C (p.Trp230Arg)
NC_000023.11:g.150645692T>C
CM000685.2:g.150645692T>C
NC_000023.10:g.149814165T>C
CM000685.1:g.149814165T>C
NC_000023.9:g.149564823T>C
NG_008199.1:g.82119T>C
ENST00000684910.1:c.*221T>C
ENST00000685439.1:c.343T>C
ENST00000685944.1:c.688T>C
ENST00000686212.1:n.290T>C
ENST00000687215.1:c.*443T>C
ENST00000688152.1:c.*132T>C
ENST00000688403.1:c.-57T>C
ENST00000689314.1:c.733T>C
ENST00000689694.1:c.688T>C
ENST00000689810.1:c.*337T>C
ENST00000690282.1:c.-57T>C
ENST00000690351.1:c.*340T>C
ENST00000691232.1:c.343T>C
ENST00000691482.1:n.1703T>C
ENST00000691686.1:c.688T>C
ENST00000691851.1:c.688T>C
ENST00000692015.1:c.475T>C
ENST00000692638.1:c.*493T>C
ENST00000692852.1:c.679-4024T>C
ENST00000692915.1:c.*895T>C
ENST00000370396.7:c.688T>C
ENST00000306167.11:n.555T>C
ENST00000370396.6:c.688T>C
ENST00000490530.1:n.627T>C
NM_000252.2:c.688T>C
NM_001376906.1:c.688T>C
NM_001376907.1:c.577T>C
NM_001376908.1:c.688T>C

Likely Pathogenic

Met criteria codes 4

PP4_Moderate | PM2_Supporting | PS4_Moderate | PP3

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.688T>C variant in MTM1 is a missense variant predicted to cause substitution of tryptophan by arginine at amino acid 230 (p.Trp230Arg). This variant is absent from gnomAD v4.1.0 (PM2_supporting). The computational predictor REVEL gives a score of 0.932, which is above the threshold of 0.7, evidence that correlates with impact to MTM1 function (PP3). This variant has been reported in 3 probands with X-linked myotubular myopathy (PS4_moderate; PMIDs: 15725586, 30884204, Invitae Internal Data). At least one patient with this variant displayed round muscle fibers that were both peripheral halo and centrally located (PP4_moderate; PMID: 30884204). In summary, this variant meets the criteria to be classified as likely pathogenic for X-linked centronuclear myopathy based on the ACMG/AMP criteria applied, as specified by the ClinGen Congenital Myopathies VCEP: PS4_moderate, PP4_moderate, PM2_supporting, PP3 (ClinGen Congenital Myopathies VCEP Specifications Version 1.0.0; 5/12/2025).

Met criteria codes

PP4_Moderate	✔	At least one patient with this variant displayed round muscle fibers that were both peripheral halo and centrally located (PP4_moderate; PMID: 30884204).
PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0 (PM2_supporting). Coverage of the gene in this region is adequate.
PS4_Moderate	✔	This variant has been reported in 3 probands with X-linked myotubular myopathy (PS4_moderate; PMIDs: 15725586, 30884204, Invitae Internal Data).
PP3	✔	The computational predictor REVEL gives a score of 0.932, which is above the threshold of 0.7, evidence that correlates with impact to MTM1 function (PP3).

Curation History

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