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Variant: NM_001276345.2(TNNT2):c.890G>A (p.Trp297Ter)

Version: 1.0

CA005312

177636 (ClinVar)

Gene: TNNT2 (HGNC:7139)
Condition: hypertrophic cardiomyopathy (MONDO:0005045)
Inheritance Mode: Autosomal dominant inheritance
UUID: 76f96ea3-4750-4169-9a00-f6e11ea64943
Approved on: 2025-11-14
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HGVS expressions

NM_001276345.2:c.890G>A
NM_001276345.2(TNNT2):c.890G>A (p.Trp297Ter)
NC_000001.11:g.201359217C>T
CM000663.2:g.201359217C>T
NC_000001.10:g.201328345C>T
CM000663.1:g.201328345C>T
NC_000001.9:g.199594968C>T
NG_007556.1:g.23461G>A
ENST00000455702.7:c.875G>A
ENST00000367318.10:c.860G>A
ENST00000367322.6:c.848G>A
ENST00000412633.3:c.851G>A
ENST00000422165.6:c.881G>A
ENST00000438742.6:c.839G>A
ENST00000651504.1:n.1351G>A
ENST00000656932.1:c.890G>A
ENST00000658476.1:c.925G>A
ENST00000660295.1:c.860G>A
ENST00000662159.1:c.*249G>A
ENST00000663843.1:c.*790G>A
ENST00000666449.1:c.*135G>A
ENST00000236918.11:c.890G>A
ENST00000360372.8:c.761G>A
ENST00000367315.6:c.869G>A
ENST00000367317.8:c.842G>A
ENST00000367318.9:c.860G>A
ENST00000367320.6:c.761G>A
ENST00000367322.5:c.851G>A
ENST00000421663.6:c.674G>A
ENST00000458432.6:c.674G>A
ENST00000460780.5:n.2009G>A
ENST00000476888.5:n.307G>A
ENST00000491504.5:n.2099G>A
ENST00000509001.5:c.860G>A
NM_000364.3:c.881G>A
NM_001001430.2:c.860G>A
NM_001001431.2:c.851G>A

NM_001001432.2:c.842G>A
NM_001276345.1:c.890G>A
NM_001276346.1:c.761G>A
NM_001276347.1:c.860G>A
NM_000364.4:c.881G>A
NM_001001430.3:c.860G>A
NM_001001431.3:c.851G>A
NM_001001432.3:c.842G>A
NM_001276346.2:c.761G>A
NM_001276347.2:c.860G>A

Likely Pathogenic

Met criteria codes 4

PM4 PP1_Strong PM2_Supporting PS4_Moderate

Not Met criteria codes 3

BS3 PVS1 PS3

Evidence Links 0

Expert Panel

Cardiomyopathy VCEP

Criteria Specification Information

- **Criteria Specification:** *ClinGen Cardiomyopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for TNNT2 Version 1.0.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Cardiomyopathy VCEP

NM_001276345.2(TNNT2):c.890G>A (p.Trp297Ter). This variant has been reported in individuals with HCM (LMM data, Richard 2003 PMID: 12707239, Gandjbakhch 2010 PMID: 25575096, Brito 2012 PMID: 22857948, Lopes 2013 PMID: 23396983, Bales 2016 PMID: 26936621, Walsh 2017 PMID: 27532257, Mademont-Soler 2017 PMID: 28771489, Ho 2018 PMID: 30297972) and has been identified in been identified in 1 out of 242296 (0.002% FAF 95% CI) of global pan-ethnic chromosomes in gnomAD (PM2_Supporting; https://gnomad.broadinstitute.org/; v.2.1). This variant is statistically increased in individuals with HCM compared to controls [OR lower 95% CI >10]. Therefore, PS4_Moderate criterion has been applied. This variant segregated with disease in 7 affected relatives from 6 families (PP1_Strong; Richard 2003 PMID: 12707239, Gandjbakhch 2010 PMID: 20439259, Brito 2012 PMID: 22857948, D. Brito pers comm, GeneDx pers comm; LMM data). This nonsense variant leads to a premature termination codon at position 297. This alteration occurs within the terminal 50 bases of the last exon and is therefore likely to escape nonsense mediated decay (NMD) and result in a truncated protein that is missing 2 amino acids (PM4). In summary, this variant meets criteria to be classified as likely pathogenic for hypertrophic cardiomyopathy in an autosomal dominant manner based on PS4_Moderate, PM2_Supporting, PP1_Strong and PM4.

Met criteria codes

PM4	✔	2 aa deleted
PP1_Strong	✔	This variant segregated with disease in 7 affected relatives from 6 families (Richard 2003 PMID: 12707239, Gandjbakhch 2010 PMID: 20439259, Brito 2012 PMID: 22857948, D. Brito pers comm, GeneDx pers comm; LMM data)
PM2_Supporting	✔	

gnomad 2.1 Latino 1 33806 Upper 95% CI: 0.01% PM2 not met gnomad 2.1 total 1/242296 Upper 95% CI 0.002% Pm2 Met gnomad 4.1 : Admixed American 1 59510 Upper 95% CI: 0.008% PM2 not met Non-Finnish European 5 1178844 Upper 95% CI: 0.009% PM2 not met Non-Finnish European 5 1178844

PS4_Moderate		✔	This variant has been reported in individuals with HCM (LMM data, Richard 2003 PMID: 12707239, Gandjbakhch 2010 PMID: 25575096, Brito 2012 PMID: 22857948, Lopes 2013 PMID: 23396983, Bales 2016 PMID: 26936621, Walsh 2017 PMID: 27532257, Mademont-Soler 2017 PMID: 28771489, Ho 2018 PMID: 30297972) and has been identified in been identified in 1 out of 242296 (0.002% FAF 95% CI) of global pan-ethnic chromosomes in gnomAD (https://gnomad.broadinstitute.org/; v.2.1). This variant is statistically increased in individuals with HCM compared to controls [OR lower 95% CI >10]. Therefore, PS4_Moderate criteria has been applied and the PM2_Supporting criterion has been applied (PM2_Supporting).

Not Met criteria codes

BS3		✖	none
PVS1		✖	End codon in 299, this PTC is occuring 2 aa before, so no NMD expected and LOF not dx mechanism
PS3		✖	none

Curation History

Showing 1 to 1 of 1 rows