

Variant: NM_001276345.2(TNNT2):c.508GAG[3]
(p.Glu173del)

Version: 1.0

CA004651 [↗](#)

43648 (ClinVar) [↗](#)

Gene: TNNT2 ([HGNC:7139](#))
Condition: hypertrophic cardiomyopathy ([MONDO:0005045](#))
Inheritance Mode: Autosomal dominant inheritance
UUID: d3f3f93b-d3df-4db4-a82f-ef5711de2db4
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HGVS expressions

NM_001276345.2:c.508GAG[3]
NM_001276345.2:c.517_519del
NM_001276345.2(TNNT2):c.508GAG[3] (p.Glu173del)
NC_000001.11:g.201363386_201363388del
CM000663.2:g.201363386_201363388del
NC_000001.10:g.201332514_201332516del
CM000663.1:g.201332514_201332516del
NC_000001.9:g.199599137_199599139del
NG_007556.1:g.19299_19301del
ENST00000455702.7:c.502_504del
ENST00000367318.10:c.487_489del
ENST00000367322.6:c.484_486del
ENST00000412633.3:c.487_489del
ENST00000422165.6:c.517_519del
ENST00000438742.6:c.469_471del
ENST00000455702.6:c.502_504del
ENST00000651504.1:n.981_983del
ENST00000656932.1:c.517_519del
ENST00000658476.1:c.487_489del
ENST00000660295.1:c.487_489del
ENST00000662159.1:c.163-1380_163-1378del
ENST00000663843.1:c.*417_*419del
ENST00000666449.1:c.487_489del
ENST00000236918.11:c.517_519del
ENST00000360372.8:c.397_399del
ENST00000367315.6:c.493_495del
ENST00000367317.8:c.472_474del
ENST00000367318.9:c.487_489del
ENST00000367320.6:c.397_399del
ENST00000367322.5:c.487_489del
ENST00000421663.6:c.310_312del
ENST00000438742.5:c.472_474del
ENST00000455702.5:c.517_519del
ENST00000458432.6:c.310_312del
ENST00000460780.5:n.810_812del

	ENST00000466570.5:n.743_745del
	ENST00000491504.5:n.1726_1728del
	ENST00000509001.5:c.487_489del
	ENST00000515042.5:n.413_415del
	NM_000364.3:c.517_519del
	NM_001001430.2:c.487_489del
	NM_001001431.2:c.487_489del
	NM_001001432.2:c.472_474del
	NM_001276345.1:c.517_519del
	NM_001276346.1:c.397_399del
	NM_001276347.1:c.487_489del
	NM_000364.4:c.517_519del
	NM_001001430.3:c.487_489del
	NM_001001431.3:c.487_489del
	NM_001001432.3:c.472_474del
	NM_001276346.2:c.397_399del
	NM_001276347.2:c.487_489del

Pathogenic

Met criteria codes 6

PM2_SupportingPS4_ModeratePP1_StrongPS3_SupportingPM4PM6_Supporting

Not Met criteria codes 4

BS1BS3PS2BA1

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.517_519del (p.Glu173del) - This variant has been reported in individuals with HCM and other cardiomyopathies (LMM data, PMIDs: 7898523, 11606294, 12707239, 20624503, 22144547, 22260945, 24792744, 27532257, 27662471, 28771489) and is statistically increased in individuals with cardiomyopathy compared to controls [OR lower 95% CI >10]. Therefore, the PS4_Moderate criterion has been applied. This variant is absent from gnomAD v2.1.1 (PM2_Supporting; http://gnomad.broadinstitute.org). This variant segregated with disease in multiple affected individuals across multiple families (PP1_Strong; OMGL Data, LMM Data, PMID: 7898523). This variant has been confirmed as de novo (PM6_Supporting; OMGL Data). Functional studies have been reported and are sufficient to apply PS3_Supporting (PMID: 10497196, 10731693, 14636924, 22579624, 24480310, 27036851). This variant is a deletion 1 amino acid and is not predicted to alter the protein reading-frame (PM4). In summary, this variant has been classified as Pathogenic for HCM in an autosomal dominant manner based on PS4_Moderate, PM2_Supporting, PP1_Strong, PM6_Supporting, PS3_Supporting, and PM4.

Met criteria codes

PM2_Supporting

This variant is absent from gnomAD v2.1.1 (PM2_Supporting; http://gnomad.broadinstitute.org).

PS4_Moderate

This variant has been reported in individuals with HCM (LMM data, PMIDs: 7898523, 11606294, 12707239, 20624503, 22144547, 22260945, 24792744, 27532257, 27662471, 28771489) and is statistically increased in individuals with cardiomyopathy compared to controls [OR lower 95% CI >10]. Therefore, PS4_Moderate criteria has been applied.

PP1_Strong			This variant segregated with disease in multiple affected individuals across multiple families (PP1_Strong; OMGL Data, LMM Data, PMID: 7898523).
PS3_Supporting			Functional studies have been reported and are sufficient to apply PS3_Supporting (PMID: 10497196, 10731693, 14636924, 22579624, 24480310, 27036851).
PM4			This variant is a deletion 1 amino acid and is not predicted to alter the protein reading-frame (PM4).
PM6_Supporting			This variant has been confirmed as a de novo occurrences (PM6_Supporting; OMGL Data).

Not Met criteria codes

BS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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