

Variant: *NM_005159.5(ACTC1):c.850A>T (p.Ile284Phe)*

Version: 1.0

CA019962 [↗](#)

45191 (ClinVar) [↗](#)

Gene: ACTC1 ([HGNC:70](#))

Condition: hypertrophic cardiomyopathy ([MONDO:0005045](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: 92989cc9-1b37-431b-88dc-403615912054

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HGVS expressions

NM_005159.5(ACTC1):c.850A>T (p.Ile284Phe)

NM_005159.5:c.850A>T

NC_000015.10:g.34791254T>A

CM000677.2:g.34791254T>A

NC_000015.9:g.35083455T>A

CM000677.1:g.35083455T>A

NC_000015.8:g.32870747T>A

NG_007553.1:g.9473A>T

ENST00000560563.2:n.1750A>T

ENST00000290378.6:c.850A>T

ENST00000647798.1:n.944A>T

ENST00000650163.1:n.930A>T

ENST00000290378.4:c.850A>T

ENST00000557860.1:n.540A>T

NM_005159.4:c.850A>T

NR_120329.1:n.299+13823T>A

Likely Pathogenic

Met criteria codes **4**

PP1_Moderate

PS4_Moderate

PM2_Supporting

PP3

Not Met criteria codes **7**

PM1

BS1

BS4

BP4

BP1

BA1

PP2

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 ACTC1 Version 1.0.0*

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Cardiomyopathy VCEP

NM_005159.5(ACTC1):c.850A>T (p.Ile284Phe) - This variant has been identified in individuals with HCM as well as other cardiomyopathies ([deciphergenomics.org](#), OMGL data, PMID 27532257) and is statistically increased in individuals with HCM compared to controls [OR lower

95% CI >10]. Therefore, the PS4_Moderate criteria has been applied. This variant segregated with disease in 3 affected relatives with HCM in 3 families and 3 affected relatives with DCM/LVNC in one family (UK Laboratories; PP1_Moderate). This variant is absent from gnomAD v2.1.1 (PM2_Supporting; <http://gnomad.broadinstitute.org>). Computational prediction tools suggest that this variant may impact the protein (REVEL score >0.7; PP3). Therefore, this variant is classified as Likely Pathogenic for HCM in an autosomal dominant manner based on PS4_Moderate, PP1_Moderate, PM2_Supporting, PP3.

Met criteria codes

PP1_Moderate			This variant segregated with disease in 3 affected relatives with HCM in 3 families and 3 affected relatives with DCM/LVNC in one family (UK Laboratories; PP1_Moderate).
PS4_Moderate			This variant has been reported in individuals with HCM (deciphergenomics.org, OMGL data, PMID 27532257) and is statistically increased in individuals with HCM compared to controls [OR lower 95% CI >10]. Therefore, the PS4_Moderate criteria has been applied.
PM2_Supporting			This variant is absent from gnomAD v2.1.1 (PM2_Supporting; http://gnomad.broadinstitute.org).
PP3			Computational prediction tools suggest that this variant may impact the protein (REVEL score >0.7; PP3).

Not Met criteria codes

PM1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP1			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
PP2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

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