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_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
Approved on: 2025/11/13
Published on: 2025/11/13

HGVS expressions

NM_005159.5:c.850A>T
NM_005159.5(ACTC1):c.850A>T (p.Ile284Phe)
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 BA1 BS1 BS4 BP4 BP1 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
BA1	✖	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
PP2	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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