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_001100.4(ACTA1):c.39C>A (p.Asp13Glu)

Version: 1.0

CA345151708

951155 (ClinVar)

Gene: ACTA1 (HGNC:58)
Condition: alpha-actinopathy (MONDO:0100084)
Inheritance Mode: Autosomal dominant inheritance
UUID: d0fccf15-f47a-4ff4-bd85-deba07e00f3f
Approved on: Mon, 10 Mar 2025 00:00:00 +0000
Published on: Mon, 28 Sep 2026 00:00:00 +0000

HGVS expressions

NM_001100.4(ACTA1):c.39C>A (p.Asp13Glu)
NM_001100.4:c.39C>A
NC_000001.11:g.229433077G>T
CM000663.2:g.229433077G>T
NC_000001.10:g.229568824G>T
CM000663.1:g.229568824G>T
NC_000001.9:g.227635447G>T
NG_006672.1:g.6020C>A
ENST00000366683.4:c.39C>A
ENST00000684723.1:c.-6-197C>A
ENST00000366683.3:c.39C>A
ENST00000366684.7:c.39C>A
NM_001100.3:c.39C>A

Likely Pathogenic

Met criteria codes 5

PS2 PP2 PP3 PP1_Moderate PM2_Supporting

Not Met criteria codes 2

BA1 BS1

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 ACTA1 Version 2.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Congenital Myopathies VCEP

The NM_001100.4(ACTA1):c.39C>A variant in ACTA1 is a missense variant predicted to cause a substitution of aspartate by glutamate at amino acid 13 (p.Asp13Glu). This variant is absent from gnomAD v4.1.1 (PM2_Supporting). ACTA1, in which the variant was identified, is defined by the ClinGen Congenital Myopathies VCEP as a gene that has a low rate of benign missense variation and where pathogenic missense variants are a common mechanism of dominant disease (PP2). The computational predictor REVEL gives a score of 0.903, which is above the threshold of 0.7, so evidence does correlate with impact on ACTA1 function (PP3). This variant has been observed in the

heterozygous state in two individuals with progressive cardiomyopathy (requiring transplantation in one) and milder muscle weakness, one of which was confirmed de novo (PS2, PS4_Supporting; Labcorp Genetics SCV001395135.7, GeneDx SCV001823123.1). Additionally, the variant segregated with disease in two individuals from one family (PP1_Moderate). In summary, this variant meets the criteria to be classified as likely pathogenic for autosomal dominant alpha-actinopathy based on the ACMG/AMP criteria applied, as specified by the ClinGen Congenital Myopathies VCEP: PS2, PP1_Moderate, PS4_Supporting, PM2_Supporting, PP2, PP3 (ClinGen Congenital Myopathies VCEP specifications version 2.0).

Met criteria codes

PS2	✔	This variant has been observed as de novo in one individual with confirmed parentage (PS2; Labcorp Genetics SCV001395135.7).
PP2	✔	ACTA1, in which the variant was identified, is defined by the ClinGen Congenital Myopathies VCEP as a gene that has a low rate of benign missense variation and where pathogenic missense variants are a common mechanism of dominant disease
PP3	✔	The REVEL score is 0.903, which is above the threshold of 0.7
PP1_Moderate	✔	This variant segregated with disease in two individuals from one family (PP1_Moderate, GeneDx SCV001823123.1).
PM2_Supporting	✔	This variant is absent from gnomAD v4.1.1 meeting PM2_Supporting.

Not Met criteria codes

BA1	✖	This variant is absent from gnomAD v4.1.1 meeting PM2_Supporting.
BS1	✖	This variant is absent from gnomAD v4.1.1 meeting PM2_Supporting.

Curation History

Showing 1 to 1 of 1 rows

See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_001100.4(ACTA1):c.39C>A (p.Asp1...	Likely Pathogenic	Alpha-Actinopathy	2026-09-28	1.0	ClinGen Congenital Myopathies Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for ACTA1 Version 2.0	ACTA1

Showing 1 to 1 of 1 rows

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