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_001754.5(RUNX1):c.318G>T (p.Trp106Cys)

Version: 1.1

CA410203495

2844927 (ClinVar)

Gene: RUNX1 (HGNC:861)
Condition: hereditary thrombocytopenia and hematologic cancer predisposition syndrome (MONDO:0011071)
Inheritance Mode: Autosomal dominant inheritance
UUID: 4d68bf03-afbc-4fd9-8590-a86ea062a479
Approved on: Mon, 05 Oct 2026 00:00:00 +0000
Published on: Mon, 05 Oct 2026 00:00:00 +0000

HGVS expressions

NM_001754.5(RUNX1):c.318G>T (p.Trp106Cys)
NM_001754.5:c.318G>T
NC_000021.9:g.34886876C>A
CM000683.2:g.34886876C>A
NC_000021.8:g.36259173C>A
CM000683.1:g.36259173C>A
NC_000021.7:g.35181043C>A
NG_011402.2:g.1102836G>T
ENST00000675419.1:c.318G>T
ENST00000300305.7:c.318G>T
ENST00000344691.8:c.237G>T
ENST00000358356.9:c.237G>T
ENST00000399237.6:c.282G>T
ENST00000399240.5:c.237G>T
ENST00000437180.5:c.318G>T
ENST00000455571.5:c.279G>T
ENST00000482318.5:c.59-6163G>T
NM_001001890.2:c.237G>T
NM_001122607.1:c.237G>T
NM_001754.4:c.318G>T
NM_001001890.3:c.237G>T
NM_001122607.2:c.237G>T

Likely Pathogenic

Met criteria codes 3

PM5_Strong PP3 PM2_Supporting

Not Met criteria codes 23

PVS1 PM6 PM1 PM3 PM4
BA1 BS1 BS4 BS3 BS2 BP5
BP7 BP4 BP3 BP1 BP2 PS1
PS2 PS3 PS4 PP1 PP2 PP4

Evidence Links 0

Expert Panel

Myeloid Malignancy VCEP

Criteria Specification Information

- **Criteria Specification:** *ClinGen Myeloid Malignancy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for RUNX1 Version 3.1*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Myeloid Malignancy VCEP

NM_001754.5(RUNX1):c.318G>T (p.Trp106Cys) is a missense variant which has a REVEL score ≥ 0.88 (0.95) (PP3) and is completely absent from all population databases with at least 20x coverage for RUNX1 (PM2_Supporting). This variant is a missense change at the same residue (p.Trp106) where two different missense changes have been previously established as pathogenic variants (PM5_Strong; ClinVar ID: 436617, 1045299). In summary, this variant meets criteria to be classified as likely pathogenic. ACMG/AMP criteria applied, as specified by the Myeloid Malignancy Variant Curation Expert Panel for RUNX1: PP3, PM2_Supporting, PM5_Strong

Met criteria codes

PM5_Strong	✔	This variant is a missense change at the same residue (p.Trp106) where two or more (2) different missense changes have been previously established as pathogenic variants (ClinVar ID 436617 and ClinVar ID 1045299) based on MM-VCEP rules for RUNX1 and RNA data or agreement in splicing predictors (SSF and MES) show no splicing effects (PM5_Strong).
PP3	✔	This missense variant has a REVEL score ≥ 0.88 (0.949) (PP3).
PM2_Supporting	✔	This variant is completely absent from all population databases with at least 20x coverage for RUNX1 (PM2_Supporting).

Not Met criteria codes

PVS1	✖	This variant is not a null variant.
PM6	✖	De novo data for this variant has not been reported in literature.
PM1	✖	This code was not applied due to the application of PM5_Strong.
PM3	✖	This rule is not applicable for MM-VCEP.
PM4	✖	This variant is not an in-frame deletion/insertion.
BA1	✖	This variant does not have a MAF ≥ 0.0015 (0.15%) in any general continental population dataset.
BS1	✖	This variant does not have a MAF between 0.00015 (0.015%) and 0.0015 (0.15%) in any general continental dataset.
BS4	✖	Segregation data for this variant has not been reported in literature.
BS3	✖	In vitro or in vivo functional data has not been reported for this variant in the literature.

BS2		✖	This rule is not applicable for MM-VCEP.
BP5		✖	This rule is not applicable for MM-VCEP.
BP7		✖	This variant is not a synonymous or intronic variant.
BP4		✖	This missense variant does not have a REVEL score < 0.50.
BP3		✖	This rule is not applicable for MM-VCEP.
BP1		✖	This rule is not applicable for MM-VCEP.
BP2		✖	This variant has not been observed in trans with a pathogenic variant for a fully penetrant dominant gene/disorder or observed in cis with a pathogenic variant in any inheritance pattern.
PS1		✖	There has not yet been a missense change resulting in the same change in protein which has been determined to be pathogenic at this amino acid residue.
PS2		✖	De novo data for this variant has not been reported in literature.
PS3		✖	In vitro or in vivo functional data has not been reported for this variant in the literature.
PS4		✖	Proband data for this variant has not been reported in literature.
PP1		✖	Segregation data for this variant has not been reported in literature.
PP2		✖	This rule is not applicable for MM-VCEP.
PP4		✖	This rule is not applicable for MM-VCEP.

Curation History

Showing 1 to 2 of 2 rows

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