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.401C>T (p.Ala134Val)

Version: 1.1

CA410202690

1484777 (ClinVar)

Gene: RUNX1 (HGNC:861)
Condition: hereditary thrombocytopenia and hematologic cancer predisposition syndrome (MONDO:0011071)
Inheritance Mode: Autosomal dominant inheritance
UUID: 5c7a8e1e-ee26-4a2d-b939-711c5c6df9d6
Approved on: Fri, 02 Oct 2026 00:00:00 +0000
Published on: Fri, 02 Oct 2026 00:00:00 +0000

HGVS expressions

NM_001754.5:c.401C>T
NM_001754.5(RUNX1):c.401C>T (p.Ala134Val)
NC_000021.9:g.34880664G>A
CM000683.2:g.34880664G>A
NC_000021.8:g.36252961G>A
CM000683.1:g.36252961G>A
NC_000021.7:g.35174831G>A
NG_011402.2:g.1109048C>T
ENST00000675419.1:c.401C>T
ENST00000300305.7:c.401C>T
ENST00000344691.8:c.320C>T
ENST00000358356.9:c.320C>T
ENST00000399237.6:c.365C>T
ENST00000399240.5:c.320C>T
ENST00000437180.5:c.401C>T
ENST00000455571.5:c.362C>T
ENST00000482318.5:c.108C>T
NM_001001890.2:c.320C>T
NM_001122607.1:c.320C>T
NM_001754.4:c.401C>T
NM_001001890.3:c.320C>T
NM_001122607.2:c.320C>T

Likely Pathogenic

Met criteria codes 3

PP3 PM1_Strong PM2_Supporting

Not Met criteria codes 23

PP1 PP2 PP4 PM3 PM5 BA1 PM4 PM6 BS2 BS1 BS4 BS3 PS1 PS2 PS3 PS4 BP4 BP3 BP1 BP2 PVS1 BP5 BP7

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.401C>T (p.Ala134Val) is a missense variant which affects one of the hotspot residues (Ala134) within the RHD (amino acids 89-204; PM1_Strong). This variant 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). 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: PM1_Strong, PP3, PM2_Supporting.

Met criteria codes

PP3	✔	This missense variant has a REVEL score ≥ 0.88 (0.949) (PP3).
PM1_Strong	✔	This variant affects the following hotspot residue within the RHD: A134 (PM1_strong).
PM2_Supporting	✔	This variant is completely absent from all population databases with at least 20x coverage for RUNX1 (PM2_Supporting).

Not Met criteria codes

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.
PM3	✖	This rule is not applicable for MM-VCEP.
PM5	✖	This variant is a missense change at the same residue (p.Ala134) where a different missense change has been previously established as a pathogenic variant (ClinVar ID 14468) based on MM-VCEP rules for RUNX1 and RNA data or agreement in splicing predictors (SSF and MES) show no splicing effects. PM5 cannot be applied since PM1_strong is met.
BA1	✖	This variant does not have a MAF ≥ 0.0015 (0.15%) in any general continental population dataset.
PM4	✖	This variant is not an in-frame deletion/insertion.
PM6	✖	De novo data for this variant has not been reported in literature.
BS2	✖	This rule is not applicable for MM-VCEP.
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.
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.
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.
PVS1	✖	This variant is not a null variant.
BP5	✖	This rule is not applicable for MM-VCEP.
BP7	✖	This variant is not a synonymous or intronic variant.

Curation History

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