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Variant: NM_001754.5(RUNX1):c.740C>T (p.Pro247Leu)

Version: 1.0

CA410206786

3948880 (ClinVar)

Gene: RUNX1 (HGNC:861)
Condition: hereditary thrombocytopenia and hematologic cancer predisposition syndrome (MONDO:0011071)
Inheritance Mode: Autosomal dominant inheritance
UUID: e5d90690-2d2f-46e8-9200-76e4fb75d9d6
Approved on: 2026/5/27
Published on: 2026/5/27

HGVS expressions

NM_001754.5(RUNX1):c.740C>T (p.Pro247Leu)
NM_001754.5:c.740C>T
NC_000021.9:g.34834475G>A
CM000683.2:g.34834475G>A
NC_000021.8:g.36206772G>A
CM000683.1:g.36206772G>A
NC_000021.7:g.35128642G>A
NG_011402.2:g.1155237C>T
ENST00000675419.1:c.740C>T
ENST00000300305.7:c.740C>T
ENST00000344691.8:c.659C>T
ENST00000358356.9:c.659C>T
ENST00000399237.6:c.704C>T
ENST00000399240.5:c.532+24999C>T
ENST00000437180.5:c.740C>T
ENST00000469087.1:n.276C>T
ENST00000482318.5:c.*330C>T
NM_001001890.2:c.659C>T
NM_001122607.1:c.659C>T
NM_001754.4:c.740C>T
NM_001001890.3:c.659C>T
NM_001122607.2:c.659C>T

Uncertain Significance

Met criteria codes 2

BP4 PM2_Supporting

Not Met criteria codes 24

BP5 BP7 BP3 BP1 BP2
PVS1 PS1 PS2 PS3 PS4
BA1 PP1 PP2 PP3 PP4
PM1 PM3 PM5 PM4 PM6
BS1 BS4 BS3 BS2

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 3.1.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Myeloid Malignancy VCEP

NM_001754.5(RUNX1):c.740C>T (p.Pro247Leu) is a missense variant which which is completely absent from all population databases with at least 20x coverage for RUNX1 (PM2_Supporting). This missense variant has a REVEL score < 0.50 (0.465), and a SpliceAI score ≤ 0.20 (0.02) (BP4). In summary, the clinical significance of this variant is uncertain. ACMG/AMP criteria applied, as specified by the Myeloid Malignancy Variant Curation Expert Panel for RUNX1: PM2_Supporting, BP4.

Met criteria codes

BP4	✔	This missense variant has a REVEL score < 0.50 (0.465), and a SpliceAI score ≤ 0.20 (0.02) (BP4).
PM2_Supporting	✔	This variant is completely absent from all population databases with at least 20x coverage for RUNX1 (PM2_Supporting).

Not Met criteria codes

BP5	✖	This rule is not applicable for MM-VCEP.
BP7	✖	This variant is not a synonymous or intronic variant.
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.
PS1	✖	There has not yet been a missense change 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.
BA1	✖	This variant does not have a MAF ≥ 0.0015 (0.15%) in any general continental population dataset.
PP1	✖	Segregation data for this variant has not been reported in literature.

PP2		✖	This rule is not applicable for MM-VCEP.
PP3	ℹ	✖	This missense variant does not have a REVEL score of ≥ 0.88.
PP4		✖	This rule is not applicable for MM-VCEP.
PM1		✖	This variant does not affect any of the following amino acid residues, nor is it located within the RHD: R107, K110, A134, R162, R166, S167, R169, G170, K194, T196, D198, R201, R204 OR within residues 89-204.
PM3		✖	This rule is not applicable for MM-VCEP.
PM5	ℹ	✖	There has not yet been a different missense change determined to be pathogenic at this amino acid residue.
PM4	ℹ	✖	This variant is not an in-frame deletion/insertion.
PM6	ℹ	✖	De novo data for this variant has not been reported in literature.
BS1	ℹ	✖	This variant does not have a MAF between 0.00015 (0.015%) and 0.0015 (0.15%) in any general continental dataset.
BS4	ℹ	✖	Segregation data for this variant has not been reported in literature.
BS3	ℹ	✖	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.

Curation History

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See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_001754.5(RUNX1):c.740C>T (p.Pro…	Uncertain Significance	Hereditary Thrombocytopenia And Hematologic Cancer Predisposition Syndrome	2026-05-27	1.0	ClinGen Myeloid Malignancy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for RUNX1 Version 3.1.0	RUNX1

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