

Variant: NM_001754.5(RUNX1):c.787C>T (p.Pro263Ser)

Version: 1.1

CA10014358 [↗](#)

464008 (ClinVar) [↗](#)

Gene: RUNX1 ([HGNC:861](#))

Condition: hereditary thrombocytopenia and hematologic cancer predisposition syndrome ([MONDO:0011071](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: 6008d288-a114-40c0-b768-5f36eaaecb6c

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HGVS expressions

NM_001754.5(RUNX1):c.787C>T (p.Pro263Ser)

NM_001754.5:c.787C>T

NC_000021.9:g.34834428G>A

CM000683.2:g.34834428G>A

NC_000021.8:g.36206725G>A

CM000683.1:g.36206725G>A

NC_000021.7:g.35128595G>A

NG_011402.2:g.1155284C>T

ENST00000675419.1:c.787C>T

ENST00000300305.7:c.787C>T

ENST00000344691.8:c.706C>T

ENST00000358356.9:c.706C>T

ENST00000399237.6:c.751C>T

ENST00000399240.5:c.532+25046C>T

ENST00000437180.5:c.787C>T

ENST00000469087.1:n.323C>T

ENST00000482318.5:c.*377C>T

NM_001001890.2:c.706C>T

NM_001122607.1:c.706C>T

NM_001754.4:c.787C>T

NM_001001890.3:c.706C>T

NM_001122607.2:c.706C>T

Uncertain Significance

Met criteria codes **1**

BP4

Not Met criteria codes **25**

BS2 PVS1 BS1 BS4 BS3
BP5 BP7 BP3 BP1 BP2 PS1
PS2 PS3 PS4 BA1 PP1 PP2
PP3 PP4 PM6 PM2 PM1
PM3 PM5 PM4

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 Version 2

[↗](#) PDF

[↗](#) Criteria Specification Approval History

[↗](#) Criteria Specifications for this VCEP

Myeloid Malignancy VCEP

NM_001754.5(RUNX1):c.787C>T (p.Pro263Ser) is a missense variant which has a REVEL score of 0.286 and a SpliceAI score ≤ 0.20 , meeting the threshold for BP4. It is reported at a frequency of 0.0002620 (4/15268 alleles) in the Admixed American population in gnomAD v2.1.1, which does not meet population-based criteria. Although reported in a patient with chronic myelomonocytic leukemia (PMID: 24764152), germline status is not confirmed and other reports concern acquired variants. 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: BP4.

Met criteria codes

BP4			This missense variant has a REVEL score < 0.50 (0.286) and a SpliceAI score ≤ 0.20 (0.03 donor loss) (BP4).
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Not Met criteria codes

BS2			MM-VCEP deemed N/A for RUNX1
PVS1			Not a null variant.
BS1			This variant has MAF between 0.00015 (0.015%) and 0.0015 (0.15%) in any general continental dataset but is not present in 5 or more alleles (MAF 0.0002620, Admixed American, 4/15268 alleles).
BS4			No data currently available
BS3			In vitro or in vivo functional data has not been reported for this variant in the literature.
BP5			MM-VCEP deemed N/A for RUNX1
BP7			This variant is not a synonymous or intronic variant.
BP3			MM-VCEP deemed N/A for RUNX1
BP1			MM-VCEP deemed N/A for RUNX1
BP2			No evidence available.
PS1			There has not yet been a different missense change determined to be pathogenic at this amino acid residue.
PS2			No data currently available
PS3			In vitro or in vivo functional data has not been reported for this variant in the literature.

PS4		✖	1 patient from PMID: 24764152 with chronic myelomonocytic leukemia is reported with the Pro263Ser variant at a VAF of 49%. Patient also had variants in SETBP1 and U2AF1. However, information on germ line confirmation is not available. Proband does not meet criteria for PS4.
BA1		✖	This variant does not have a MAF $\geq$ 0.0015 (0.15%) in any general continental population dataset.
PP1		✖	No data currently available
PP2		✖	MM-VCEP deemed N/A for RUNX1
PP3		✖	This missense variant DOES NOT have a REVEL score >0.88 (0.286)
PP4		✖	MM-VCEP deemed N/A for RUNX1
PM6		✖	No data currently available
PM2		✖	Variant reported in gnomAD
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		✖	MM-VCEP deemed N/A for RUNX1
PM5		✖	There has not yet been a different missense change determined to be pathogenic at this amino acid residue.
PM4		✖	This variant is not an in-frame deletion/insertion.

Curation History 		
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