

Variant: *NM\_001754.5(RUNX1):c.993C>A (p.Ser331Arg)*

Version: 1.0

[CA410148731](#)

[2717108 \(ClinVar\)](#)

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

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

**Inheritance Mode:** Autosomal dominant inheritance

**UUID:** fe330da8-73fc-41f0-a915-98a93774b7c0

**Approved on:** 2025-01-15

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### HGVS expressions

**NM\_001754.5:c.993C>A**

NM\_001754.5(RUNX1):c.993C>A (p.Ser331Arg)

NC\_000021.9:g.34792585G>T

CM000683.2:g.34792585G>T

NC\_000021.8:g.36164882G>T

CM000683.1:g.36164882G>T

NC\_000021.7:g.35086752G>T

NG\_011402.2:g.1197127C>A

ENST00000675419.1:c.993C>A

ENST00000300305.7:c.993C>A

ENST00000344691.8:c.912C>A

ENST00000399240.5:c.720C>A

ENST00000437180.5:c.993C>A

ENST00000482318.5:c.\*583C>A

NM\_001001890.2:c.912C>A

NM\_001754.4:c.993C>A

NM\_001001890.3:c.912C>A

Uncertain Significance

Met criteria codes **2**

BP4 PM2\_Supporting

Not Met criteria codes **24**

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

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](#)





Evidence submitted by expert panel

**Myeloid Malignancy VCEP**

**NM\_001754.5(RUNX1):c.993C>A (p.Ser331Arg) is a missense variant which has a REVEL score < 0.50 (0.144), and a SpliceAI score ≤ 0.20 (0.0) (BP4). This variant is completely absent from all population databases with at least 20x coverage for RUNX1 (PM2\_Supporting). 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, PM2\_supporting.**






















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#### Met criteria codes

<b>BP4</b>			This missense variant has a REVEL score < 0.50 (0.144), and a SpliceAI score ≤ 0.20 (0.0) (BP4).
<b>PM2_Supporting</b>			This variant is completely absent from all population databases with at least 20x coverage for RUNX1 (PM2_Supporting).

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#### Not Met criteria codes

<b>PVS1</b>			This variant is not a null variant.
<b>BA1</b>			This variant does not have a MAF ≥ 0.0015 (0.15%) in any general continental population dataset.
<b>BS4</b>			Segregation data for this variant has not been reported in literature.
<b>BS3</b>			In vitro or in vivo functional data has not been reported for this variant in the literature.
<b>BS1</b>			This variant does not have a MAF between 0.00015 (0.015%) and 0.0015 (0.15%) in any general continental dataset.
<b>BS2</b>			This rule is not applicable for MM-VCEP.
<b>BP7</b>			This variant is not a synonymous or intronic variant.
<b>BP5</b>			This rule is not applicable for MM-VCEP.
<b>BP2</b>			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.
<b>BP3</b>			This rule is not applicable for MM-VCEP.
<b>BP1</b>			This rule is not applicable for MM-VCEP.
<b>PS2</b>			De novo data for this variant has not been reported in literature.
<b>PS4</b>			Proband data for this variant has not been reported in literature.

<b>PS3</b>			In vitro or in vivo functional data has not been reported for this variant in the literature.
<b>PS1</b>			There has not yet been a missense change determined to be pathogenic at this amino acid residue.
<b>PP1</b>			Segregation data for this variant has not been reported in literature.
<b>PP4</b>			This rule is not applicable for MM-VCEP.
<b>PP3</b>			This missense variant does not have a REVEL score of $\geq 0.88$ .
<b>PP2</b>			This rule is not applicable for MM-VCEP.
<b>PM1</b>			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.
<b>PM5</b>			There has not yet been a different missense change determined to be pathogenic at this amino acid residue.
<b>PM3</b>			This rule is not applicable for MM-VCEP.
<b>PM4</b>			This variant is not an in-frame deletion/insertion.
<b>PM6</b>			De novo data for this variant has not been reported in literature.

Curation History [↗](#)




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