

Variant: NM_001754.5(RUNX1):c.319C>T (p.Arg107Cys)

Version: 1.0

CA410203489 [↗](#)

1338536 (ClinVar) [↗](#)

Gene: RUNX1 (HGNC:861)

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 21a8e654-df9e-4889-bfdc-9ea5e5c0fde6

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HGVS expressions

NM_001754.5:c.319C>T

NM_001754.5(RUNX1):c.319C>T (p.Arg107Cys)

NC_000021.9:g.34886875G>A

CM000683.2:g.34886875G>A

NC_000021.8:g.36259172G>A

CM000683.1:g.36259172G>A

NC_000021.7:g.35181042G>A

NG_011402.2:g.1102837C>T

ENST00000675419.1:c.319C>T

ENST00000300305.7:c.319C>T

ENST00000344691.8:c.238C>T

ENST00000358356.9:c.238C>T

ENST00000399237.6:c.283C>T

ENST00000399240.5:c.238C>T

ENST00000437180.5:c.319C>T

ENST00000455571.5:c.280C>T

ENST00000482318.5:c.59-6162C>T

NM_001001890.2:c.238C>T

NM_001122607.1:c.238C>T

NM_001754.4:c.319C>T

NM_001001890.3:c.238C>T

NM_001122607.2:c.238C>T

Likely Pathogenic

Met criteria codes **4**

PP3 PS3_Moderate PM1

PM2_Supporting

Not Met criteria codes **22**

PS1 PS2 PS4 PP1 PP2 PP4

PM3 PM5 PM4 PM6 PVS1

BA1 BS1 BS4 BS3 BS2 BP5

BP7 BP4 BP3 BP1 BP2

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

























This variant affects one of the hotspot residues (residue 107) established by the MM-VCEP for RUNX1 (PM1). The variant exhibits altered function in 2 secondary assays. <https://www.embopress.org/doi/epdf/10.1038/sj.emboj.7601568?src=getftr> NM001001890.3 c.238C>T p.R80C - Moderate to severe loss of DNA binding and >5 fold decrease in CFBF binding (PS3_moderate). REVEL score is ≥ 0.88 (0.923) and SpliceAI is ≤ 0.20 (0.00) (PP3). This variant is completely absent from population databases (gnomad v4.0) 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, PS3_moderate, PP3, PM2_supporting.

Met criteria codes

PP3			REVEL score is ≥ 0.88 (0.923) and SpliceAI is ≤ 0.20 (0.00) (PP3)
PS3_Moderate			The variant exhibits altered function in 2 secondary assays. https://www.embopress.org/doi/epdf/10.1038/sj.emboj.7601568?src=getftr NM001001890.3 c.238C>T p.R80C - Moderate to severe loss of DNA binding and >5 fold decrease in CFBF binding
PM1			This variant affects one of the hotspot residues (residue 107) established by the MM-VCEP for RUNX1 (PM1).
PM2_Supporting			This variant is completely absent from population databases (gnomad v4.0) with at least 20x coverage for RUNX1 (PM2_supporting).

Not Met criteria codes

PS1			Not same Amino Acid change
PS2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS4			Somatic hotspot - reviewed 41 pubs - none confirmed germline.
PP1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
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			Cannot be applied due to the application of PM1

PM4			Not a frameshift variant
PM6			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PVS1			Not a null variant
BA1			This variant is completely absent from all population databases with at least 20x coverage for RUNX1 (PM2_supporting).
BS1			This variant is completely absent from all population databases with at least 20x coverage for RUNX1 (PM2_supporting).
BS4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS2			This rule is not applicable for MM-VCEP
BP5			This rule is not applicable for MM-VCEP
BP7			Not a synonymous or intronic variant
BP4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP3			This rule is not applicable for MM-VCEP
BP1			This rule is not applicable for MM-VCEP
BP2			No homozygotes present in gnomAD v2.1.1. or v3.1.2

Curation History [↗](#)

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