

Variant: NM_001754.5(RUNX1):c.231C>T (p.Ser77=)

Version: 1.0

CA512318903 [↗](#)

861921 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 7ccaed33-76a7-4e66-86e3-4822111fde5f

Approved on: 2024/6/24

Published on: 2024/6/24

HGVS expressions

NM_001754.5:c.231C>T

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NC_000021.9:g.34886963G>A

CM000683.2:g.34886963G>A

NC_000021.8:g.36259260G>A

CM000683.1:g.36259260G>A

NC_000021.7:g.35181130G>A

NG_011402.2:g.1102749C>T

ENST00000675419.1:c.231C>T

ENST00000300305.7:c.231C>T

ENST00000344691.8:c.150C>T

ENST00000358356.9:c.150C>T

ENST00000399237.6:c.195C>T

ENST00000399240.5:c.150C>T

ENST00000437180.5:c.231C>T

ENST00000455571.5:c.192C>T

ENST00000482318.5:c.59-6250C>T

NM_001001890.2:c.150C>T

NM_001122607.1:c.150C>T

NM_001754.4:c.231C>T

NM_001001890.3:c.150C>T

NM_001122607.2:c.150C>T

Likely Benign

Met criteria codes 2

BS1 BP4

Not Met criteria codes 24

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

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.231C>T (p.Ser77=) is a synonymous variant which has a MAF of 0.00001 (0.001%, 108718/243164, 1 allele) in the European (Non-Finnish) subpopulations of the gnomAD cohort, which is between 0.00015 (0.015%) and 0.0015 (0.15%) (BS1). No splicing impact or creation of cryptic splice sites is predicted by SSF and MES. SpliceAI predicts no impact to splicing (score: 0.00) (BP4). This variant was reported in ClinVar in 2022 by Invitae, but the affected status of the proband is unknown (Variation ID 861921). In summary, this variant meets criteria to be classified as likely benign. ACMG/AMP criteria applied, as specified by the Myeloid Malignancy Variant Curation Expert Panel for RUNX1: BS1, BP4.

Met criteria codes			
BS1			MAF of 0.00001 (0.001%, 108718/243164, 1 allele) in the European (Non-Finnish) subpopulations of the gnomAD cohort is between 0.00015 (0.015%) and 0.0015 (0.15%) (BS1).
BP4			No splicing impact or creation of cryptic splice sites predicted by SSF and MES. Splice AI predicts no impact to splicing (score: 0.00).
Not Met criteria codes			
PM1			This variant does not affect one of the hotspot residues established by the MM-VCEP for RUNX1.
PM3			This rule is not applicable for MM-VCEP.
PM5			This rule is not applicable because the variant is not missense.
PM4			This rule is not applicable because the variant is not an inframe indel.
PM6			This rule is not applicable because there are no reports of this variant with assumed de novo occurrences.
PM2			This rule is not applicable because BS1 is met.
BS2			This rule is not applicable for MM-VCEP.
BS4			This rule is not applicable because there are no reports of this variant in other family members.
BS3			This rule is not applicable because there are no functional studies showing the damaging effect on protein function or splicing.
PVS1			This rule is not applicable because the variant is not loss of function.
PS1			This rule is not applicable because the variant is not missense.
PS2			This rule is not applicable because there are no reports of this variant in affected family members.

PS3			This rule is not applicable because there are no functional studies supporting a damaging effect on the gene or gene product.
PS4			This rule is not applicable because there are no reports of this variant in any probands meeting at least one of the RUNX1-phenotypic criteria. This variant was reported in ClinVar in 2022 by Invitae but the affected status of the proband is unknown (Variation ID 861921).
BP3			This rule is not applicable for MM-VCEP.
BP1			This rule is not applicable for MM-VCEP.
BP2			This rule is not applicable because variant is only seen once in gnomAD cohort.
BP5			This rule is not applicable for MM-VCEP.
BP7			This rule is not applicable because UCSC gives this synonymous variant a phyloP score of 3.70931.
BA1			This rule is not applicable because BS1 is met.
PP1			This rule is not applicable because there are no reports of this variant in other family members.
PP2			This rule is not applicable for MM-VCEP.
PP3			This rule is not applicable because the variant is not missense.
PP4			This rule is not applicable for MM-VCEP.

Curation History 		
    		
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