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Variant: NM_001754.5(RUNX1):c.1307C>T (p.Ser436Phe)

Version: 1.0

CA410147430

3666186 (ClinVar)

Gene: RUNX1 (HGNC:861)
Condition: hereditary thrombocytopenia and hematologic cancer predisposition syndrome (MONDO:0011071)
Inheritance Mode: Autosomal dominant inheritance
UUID: 7011c167-79f1-46f0-8ac0-0022217229b7
Approved on: 2025/5/2
Published on: 2025/5/2

HGVS expressions

NM_001754.5:c.1307C>T
NM_001754.5(RUNX1):c.1307C>T (p.Ser436Phe)
NC_000021.9:g.34792271G>A
CM000683.2:g.34792271G>A
NC_000021.8:g.36164568G>A
CM000683.1:g.36164568G>A
NC_000021.7:g.35086438G>A
NG_011402.2:g.1197441C>T
ENST00000675419.1:c.1307C>T
ENST00000300305.7:c.1307C>T
ENST00000344691.8:c.1226C>T
ENST00000399240.5:c.1034C>T
ENST00000437180.5:c.1307C>T
ENST00000482318.5:c.*897C>T
NM_001001890.2:c.1226C>T
NM_001754.4:c.1307C>T
NM_001001890.3:c.1226C>T

Uncertain Significance

Met criteria codes 2

PM2_Supporting BP4

Not Met criteria codes 23

PVS1 PM6 PM1 PM3 PM5
BA1 BS1 BS4 BS3 BS2 BP5
BP7 BP3 BP1 BP2 PS1 PS2
PS3 PS4 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

Evidence submitted by expert panel

Myeloid Malignancy VCEP

NM_001754.5(RUNX1):c.947A>G (p.Glu316Gly) is a missense variant which has not been reported in any populations featured in any version of gnomAD, allowing for application of PM2_Supporting. This variant has a SpliceAI score of 0 and a REVEL score of 0.325, allowing for application of BP4. In summary, this variant meets criteria to be classified as a variant of uncertain significance. ACMG/AMP criteria applied, as specified by the Myeloid Malignancy Variant Curation Expert Panel for RUNX1: PM2_Supporting, BP4.

Met criteria codes

PM2_Supporting	✔	This variant is completely absent from all population databases with at least 20x coverage for RUNX1 (PM2_Supporting).
BP4	✔	This missense variant has a REVEL score < 0.50 (0.325) and a SpliceAI score ≤ 0.20 (0) (BP4).

Not Met criteria codes

PVS1	✖	This variant is not a null variant.
PM6	✖	De novo data for this variant has not been reported in literature.
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 RUNX1.
PM5	✖	There has not yet been a different missense change determined to be pathogenic at this amino acid residue.
BA1	✖	This variant does not have a MAF ≥ 0.0015 (0.15%) in any general continental population dataset.
BS1	✖	This variant does not have a MAF between 0.00015 (0.015%) and 0.0015 (0.15%) in any general continental dataset.
BS4	✖	Segregation data for this variant has not been reported in literature.
BS3	✖	In vitro or in vivo functional data has not been reported for this variant in the literature.
BS2	✖	This rule is not applicable for RUNX1.
BP5	✖	This rule is not applicable for RUNX1.
BP7	✖	This variant is not a synonymous or intronic variant.
BP3	✖	This rule is not applicable for RUNX1.

BP1		✖	This rule is not applicable for RUNX1.
BP2	ℹ	✖	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.
PS1	ℹ	✖	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	ℹ	✖	This variant has not been featured in in vitro or in vivo functional studies showing a damaging effect on the gene or gene product.
PS4	ℹ	✖	The prevalence of the variant in affected individuals has not been reported to be significantly increased compared with the prevalence in controls.
PP1	ℹ	✖	Segregation data for this variant has not been reported in literature.
PP2		✖	This rule is not applicable for RUNX1.
PP3	ℹ	✖	This missense variant does not have a REVEL score of ≥ 0.88 or a SpliceAI score ≥ 0.38.
PP4		✖	This rule is not applicable for RUNX1.

Curation History

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See Report	Preferred Variant Title	Classification ℹ	Condition	Published Date	Version ℹ	Criteria Specification	Gene
View	NM_001754.5(RUNX1):c.1307C>T (p.S...	Uncertain Significance	Hereditary Thrombocytopenia And Hematologic Cancer Predisposition Syndrome	2025-05-02	1.0	ClinGen Myeloid Malignancy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 2	RUNX1

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