The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_001754.5(RUNX1):c.988T>G (p.Phe330Val)

Version: 1.1

CA410148771

1716418 (ClinVar)

Gene: RUNX1 (HGNC:861)
Condition: hereditary thrombocytopenia and hematologic cancer predisposition syndrome (MONDO:0011071)
Inheritance Mode: Autosomal dominant inheritance
UUID: 2b2ba19e-5dc8-415c-990c-f18727a398ba
Approved on: 2025/1/15
Published on: 2025/1/15

HGVS expressions

NM_001754.5:c.988T>G
NM_001754.5(RUNX1):c.988T>G (p.Phe330Val)
NC_000021.9:g.34792590A>C
CM000683.2:g.34792590A>C
NC_000021.8:g.36164887A>C
CM000683.1:g.36164887A>C
NC_000021.7:g.35086757A>C
NG_011402.2:g.1197122T>G
ENST00000675419.1:c.988T>G
ENST00000300305.7:c.988T>G
ENST00000344691.8:c.907T>G
ENST00000399240.5:c.715T>G
ENST00000437180.5:c.988T>G
ENST00000482318.5:c.*578T>G
NM_001001890.2:c.907T>G
NM_001754.4:c.988T>G
NM_001001890.3:c.907T>G

Uncertain Significance

Met criteria codes 2

PM2_Supporting BP4

Not Met criteria codes 19

PS1 PS2 PS3 PS4 BA1 PP1 PP2 PP3 PM6 PM1 PM3 PM5 BS1 BS4 BS3 BP5 BP1 BP2 PVS1

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.988T>G (p.Phe330Val) is a missense variant which is absent from gnomAD v2 and v3 (PM2_supporting). This variant has not been reported in the literature. The computational predictor REVEL gives a score of 0.474, which is below the threshold of 0.50, and the splice site predictor SpliceAI indicated that the variant has no impact on splicing, evidence that does not predict a damaging effect on RUNX1 function (BP4). In summary, this variant meets the criteria to be classified as a variant of uncertain significance (VUS) for autosomal dominant hereditary thrombocytopenia and hematologic cancer predisposition syndrome based on the ACMG/AMP criteria applied, as specified by the ClinGen Myeloid Malignancy VCEP: PM2_supporting and BP4.

Met criteria codes

PM2_Supporting	✔	Completely absent from gnomAD with a mean coverage of at least 20X (v2 and v3).
BP4	✔	REVEL score = 0.474, which is less than the v2 threshold of 0.50. SpliceAI doesn't predict any significant splicing impact (Δ scores ≤ 0.20).

Not Met criteria codes

PS1	✖	No relevant cases found in literature search, including LOVD, HGMD, ClinVar, COSMIC, and Mastermind.
PS2	✖	No relevant cases found in literature search, including LOVD, HGMD, ClinVar, COSMIC, and Mastermind.
PS3	✖	No literature was found in LOVD, HGMD, ClinVar, COSMIC, and Mastermind.
PS4	✖	No cases found in literature search, including LOVD, HGMD, ClinVar, COSMIC, and Mastermind.
BA1	✖	Completely absent from gnomAD with a mean coverage of at least 20X (v2 and v3).
PP1	✖	No relevant cases found in literature search, including LOVD, HGMD, ClinVar, COSMIC, and Mastermind.
PP2	✖	Not applicable
PP3	✖	REVEL score = 0.474, which is not higher than the v2 threshold of 0.88. SpliceAI doesn't predict any significant splicing impact (Δ scores ≤ 0.20).
PM6	✖	No relevant cases found in literature search, including LOVD, HGMD, ClinVar, COSMIC, and Mastermind.
PM1	✖	Not located at a hotspot (R107, K110, A134, R162, R166, S167, R169, G170, K194, T196, D198, R210, R204) or within residues 89-204.
PM3	✖	Not applicable
PM5	✖	F330/F303 variants have not been reported in COSMIC or Mastermind.
BS1	✖	Completely absent from gnomAD with a mean coverage of at least 20X (v2 and v3).

BS4	✖	No relevant cases found in literature search, including LOVD, HGMD, ClinVar, COSMIC, and Mastermind.
BS3	✖	No literature was found in LOVD, HGMD, ClinVar, COSMIC, and Mastermind.
BP5	✖	Not applicable
BP1	✖	Not applicable
BP2	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PVS1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_001754.5(RUNX1):c.988T>G (p.Ph...	Uncertain Significance	Hereditary Thrombocytopenia And Hematologic Cancer Predisposition Syndrome	2025-01-15	1.1	ClinGen Myeloid Malignancy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 2	RUNX1
View	NM_001754.5(RUNX1):c.988T>G (p.Ph...	Uncertain Significance	Hereditary Thrombocytopenia And Hematologic Cancer Predisposition Syndrome	2024-07-25	1.0	ClinGen Myeloid Malignancy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 2	RUNX1

Showing 1 to 2 of 2 rows

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