

Variant: *NM_001754.5(RUNX1):c.1037G>C (p.Arg346Pro)*

Version: 1.0

CA410148448 [↗](#)

1999266 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: fc31d363-ab8a-409b-8047-5e26fb0194c6

Approved on: 2024/8/1

Published on: 2024/8/1

HGVS expressions

NM_001754.5(RUNX1):c.1037G>C (p.Arg346Pro)

NM_001754.5:c.1037G>C

NC_000021.9:g.34792541C>G

CM000683.2:g.34792541C>G

NC_000021.8:g.36164838C>G

CM000683.1:g.36164838C>G

NC_000021.7:g.35086708C>G

NG_011402.2:g.1197171G>C

ENST00000675419.1:c.1037G>C

ENST00000300305.7:c.1037G>C

ENST00000344691.8:c.956G>C

ENST00000399240.5:c.764G>C

ENST00000437180.5:c.1037G>C

ENST00000482318.5:c.*627G>C

NM_001001890.2:c.956G>C

NM_001754.4:c.1037G>C

NM_001001890.3:c.956G>C

Uncertain Significance

Met criteria codes **1**

PM2_Supporting

Not Met criteria codes **14**

PM1 PM5 PM6 BS1 PS1
PS2 PS4 BP4 BP1 BP5 BP7
BA1 PP2 PP3

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.1037G>C (p.Arg346Pro) is a missense variant which is absent from gnomAD v2 and v3 (PM2_Supporting). The computational predictor REVEL gives a score of 0.666, which is neither above nor below the thresholds predicting a damaging or benign impact on RUNX1 function, but the splice site predictor SpliceAI indicated that the variant has no impact on splicing. In summary, this variant meets the criteria to be classified as a 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.

Met criteria codes

PM2_Supporting			Completely absent from gnomAD with a mean coverage of at least 20X (v2 and v3).
----------------	---	---	---

Not Met criteria codes

PM1			Not located at a hotspot (R107, K110, A134, R162, R166, S167, R169, G170, K194, T196, D198, R210, R204) or within residues 89-204.
PM5			Q346/Q319 variants are reported in COSMIC and/or Mastermind, but not at a high enough frequency that they would be likely classified as LP/P.
PM6			No literature was found in LOVD, HGMD, ClinVar, COSMIC, Mastermind, and Google/Google Scholar searches.
BS1			Completely absent from gnomAD with a mean coverage of at least 20X (v2 and v3).
PS1			No relevant cases found in literature search, including LOVD, HGMD, ClinVar, COSMIC, Mastermind, and Google/Google Scholar searches.
PS2			No literature was found in LOVD, HGMD, ClinVar, COSMIC, Mastermind, and Google/Google Scholar searches.
PS4			No literature was found in LOVD, HGMD, ClinVar, COSMIC, Mastermind, and Google/Google Scholar searches.
BP4			REVEL score = 0.666, which is not less than the v2 threshold of 0.50. SpliceAI doesn't predict any significant splicing impact (Δ scores $\leq$ 0.20).
BP1			Not applicable
BP5			Not applicable
BP7			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1			Completely absent from gnomAD with a mean coverage of at least 20X (v2 and v3).
PP2			Not applicable

PP3

REVEL score = 0.666, which is not higher than the v2 threshold of 0.88. SpliceAI doesn't predict any significant splicing impact (Δ scores $\leq$ 0.20).

Curation History [↗](#)

Showing 1 to 1 of 1 rows

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.