

Variant: NM_001754.5(RUNX1):c.1145C>G (p.Pro382Arg)

Version: 1.0

CA410147964 [↗](#)

1397177 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: fbdb105-5b65-4444-be1c-7f86b8c491a1

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HGVS expressions

NM_001754.5(RUNX1):c.1145C>G (p.Pro382Arg)

NM_001754.5:c.1145C>G

NC_000021.9:g.34792433G>C

CM000683.2:g.34792433G>C

NC_000021.8:g.36164730G>C

CM000683.1:g.36164730G>C

NC_000021.7:g.35086600G>C

NG_011402.2:g.1197279C>G

ENST00000675419.1:c.1145C>G

ENST00000300305.7:c.1145C>G

ENST00000344691.8:c.1064C>G

ENST00000399240.5:c.872C>G

ENST00000437180.5:c.1145C>G

ENST00000482318.5:c.*735C>G

NM_001001890.2:c.1064C>G

NM_001754.4:c.1145C>G

NM_001001890.3:c.1064C>G

Uncertain Significance

Met criteria codes **2**

PM2_Supporting

PP3

Not Met criteria codes **16**

BA1

BP4

BP2

BP7

BS1

BS4

BS3

PP1

PM6

PM1

PM5

PM4

PS1

PS2

PS3

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.1145C>G (p.Pro382Arg) is a missense variant which is absent from all population databases, including gnomAD v2.1.1 and gnomAD v3.1.2, both of which provide coverage of at least 20x for the RUNX1 gene at this genomic position (PM2_supporting). This missense variant has a REVEL score >0.88 (0.942) (PP3). To our knowledge, this variant has not been reported before, and there are no other pathogenic or likely pathogenic amino acid changes affecting the same residue. In summary, the clinical significance of this variant is uncertain. ACMG/AMP criteria applied, as specified by the Myeloid Malignancy Variant Curation Expert Panel for RUNX1: PM2_supporting, PP3.

Met criteria codes

PM2_Supporting			This variant is completely absent from all population databases (gnomAD v2.1.1, v3.1.2, and v4.0.0) with at least 20x coverage for RUNX1 (PM2_supporting).
PP3			This missense variant has a REVEL score >0.88 (0.942) (PP3).

Not Met criteria codes

BA1			This rule cannot be applied since the variant is completely absent from all population databases.
BP4			This rule cannot be applied since this missense variant does not have a REVEL score <0.50 (0.942).
BP2			This rule cannot be applied since, to our knowledge, this variant has not been reported in any study.
BP7			This rule cannot be applied since this is a missense variant.
BS1			This rule cannot be applied since the variant is completely absent from all population databases.
BS4			This rule cannot be applied since, to our knowledge, this variant has not been reported in any study and we have no information about segregation.
BS3			To our knowledge, no in vitro or in vivo functional studies are available for this variant.
PP1			This rule cannot be applied since, to our knowledge, this variant has not been reported in any study and we have no information about its cosegregation with the disease.
PM6			This rule cannot be applied since, to our knowledge, this variant has not been reported in any study.
PM1			This rule cannot be applied since this missense variant affects amino acid residue 382, which is out of RHD or residues 89-204
PM5			This rule cannot be applied because, to our knowledge, this missense variant does not impact an amino acid residue where a different pathogenic missense change has previously been observed.
PM4			This rule cannot be applied since this is a missense variant.

