

Variant: NM_001754.5(RUNX1):c.227G>C (p.Arg76Pro)

Version: 1.1

CA410203853 [↗](#)

2422003 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 83eb9d71-5be9-482f-b0c4-d1096b085a3c

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HGVS expressions

NM_001754.5(RUNX1):c.227G>C (p.Arg76Pro)

NM_001754.5:c.227G>C

NC_000021.9:g.34886967C>G

CM000683.2:g.34886967C>G

NC_000021.8:g.36259264C>G

CM000683.1:g.36259264C>G

NC_000021.7:g.35181134C>G

NG_011402.2:g.1102745G>C

ENST00000675419.1:c.227G>C

ENST00000300305.7:c.227G>C

ENST00000344691.8:c.146G>C

ENST00000358356.9:c.146G>C

ENST00000399237.6:c.191G>C

ENST00000399240.5:c.146G>C

ENST00000437180.5:c.227G>C

ENST00000455571.5:c.188G>C

ENST00000482318.5:c.59-6254G>C

NM_001001890.2:c.146G>C

NM_001122607.1:c.146G>C

NM_001754.4:c.227G>C

NM_001001890.3:c.146G>C

NM_001122607.2:c.146G>C

Uncertain Significance

Met criteria codes **2**

PP3

PM2_Supporting

Not Met criteria codes **24**

PS1

PS2

PS3

PS4

BA1

PP1

PP2

PP4

PM1

PM3

PM5

PM4

PM6

BS2

BS1

BS4

BS3

BP4

BP3

BP1

BP2

PVS1

BP5

BP7

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.227G>C (p.Arg76Pro) is a missense variant. This variant is completely absent from all population databases with 30x coverage for RUNX1 in gnomAD v2.1.1 and v3.1.2 (PM2_supporting). The REVEL score is ≥ 0.88 (0.906) (PP3). 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

PP3			This missense variant has a REVEL score ≥ 0.88 (0.906) (PP3). SpliceAI score is < 0.38 (0).
PM2_Supporting			This variant is completely absent from all population databases with 30x coverage for RUNX1 in gnomAD v2.1.1 and v3.1.2 (PM2_supporting).

Not Met criteria codes

PS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2			To our knowledge, no publication has reported this variant to date.
PS3			To our knowledge, functional assays have not been reported for this variant.
PS4			Clinvar has one entry for this variant but the affected status is unknown. To our knowledge, no publication has reported this variant to date.
BA1			This variant is completely absent from all population databases with 30x coverage for RUNX1 in gnomAD v2.1.1 and v3.1.2 (PM2_supporting).
PP1			To our knowledge, no publication has reported this variant to date.
PP2			This rule is not applicable to the MMVCEP.
PP4			This rule is not applicable to the MMVCEP.
PM1			This variant does not reside within a region of RUNX1 that is defined as a mutational hotspot or critical functional domain by the ClinGen MMVCEP.
PM3			This rule is not applicable to the MMVCEP.”
PM5			

Another missense variant [c.226C>T, p.Arg76Cys] in the same codon but the affected status is unknown (ClinVar Variation ID 576717). However, this other variant has not (yet) met the criteria to be classified as pathogenic or likely pathogenic by the ClinGen MMVCEP.

PM4			This is a missense variant.
PM6			To our knowledge, no publication has reported this variant to date.
BS2			To our knowledge, no publication has reported this variant to date.
BS1			This variant is completely absent from all population databases with 30x coverage for RUNX1 in gnomAD v2.1.1 and v3.1.2 (PM2_supporting).
BS4			To our knowledge, no publication has reported this variant to date.
BS3			To our knowledge, this variant was not evaluated in transactivation assays.
BP4			This missense variant has a REVEL score ≥ 0.88 (0.906) (PP3). SpliceAI score is < 0.38 (0).
BP3			This rule is not applicable to the MMVCEP.
BP1			This rule is not applicable to the MMVCEP.
BP2			To our knowledge, no publication has reported this variant to date.
PVS1			This is a missense variant.
BP5			This rule is not applicable to the MMVCEP.
BP7			This is a missense variant.

Curation History 

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