

Variant: *NM_001754.5(RUNX1):c.1389C>G (p.Pro463=)*

Version: 1.1

CA10014178 [↗](#)

258184 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 9ae68387-9090-4f9d-933e-8799521dac42

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HGVS expressions

NM_001754.5:c.1389C>G

NM_001754.5(RUNX1):c.1389C>G (p.Pro463=)

NC_000021.9:g.34792189G>C

CM000683.2:g.34792189G>C

NC_000021.8:g.36164486G>C

CM000683.1:g.36164486G>C

NC_000021.7:g.35086356G>C

NG_011402.2:g.1197523C>G

ENST00000675419.1:c.1389C>G

ENST00000300305.7:c.1389C>G

ENST00000344691.8:c.1308C>G

ENST00000399240.5:c.1116C>G

ENST00000437180.5:c.1389C>G

ENST00000482318.5:c.*979C>G

NM_001001890.2:c.1308C>G

NM_001754.4:c.1389C>G

NM_001001890.3:c.1308C>G

Benign

Met criteria codes 4

BA1 BP4 BP2 BP7

Not Met criteria codes 22

BS2 BS1 BS4 BS3 BP3 BP1
PVS1 BP5 PS1 PS2 PS3
PS4 PP1 PP2 PP3 PP4
PM1 PM3 PM5 PM4 PM6
PM2

Evidence Links 1

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_001754.4(RUNX1):c.1389C>G (p.Pro463=) is a synonymous variant which has a minor allele frequency of 0.1206 (1976/16382 alleles) in the African subpopulation of the gnomAD cohort, meeting the threshold for BA1. It is detected in a homozygous state in 202 individuals in gnomAD (BP2). Splicing predictors SSF and MES indicate no significant impact on the canonical splice site, and no cryptic splice sites are created (BP4). Evolutionary conservation algorithms predict the site as not being conserved (BP7). In summary, this variant meets criteria to be classified as benign. ACMG/AMP criteria applied, as specified by the Myeloid Malignancy Variant Curation Expert Panel for RUNX1: **BA1, BP2, BP4, BP7**.

Met criteria codes

BA1			gnomAD Allele Frequency of 0.1206 (12%, 1976/16382 alleles) in the African subpopulation >0.0015
BP4			This synonymous variant is predicted by SSF and MES to lead to either an increase in the canonical splice site score or a decrease of the canonical splice site score by no more than 10% and no putative cryptic splice sites are created.
BP2			This variant is detected in homozygous state (202) in gnomAD population database (BP2).
BP7			A synonymous variant for which splicing prediction algorithms predict no impact to the splice consensus sequence nor the creation of a new splice site AND the nucleotide is not highly conserved (phyloP100way: -0.503315 <0.1).

Not Met criteria codes

BS2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS4			No data
BS3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP1			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
BP5			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

PS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2			No evidence
PS3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS4			Reported in multiple individuals but only one patient had MDS. The phenotype reported in other patients did not meet the RUNX1 phenotype criteria
			This variant was identified in 2 unrelated patients. The first one was diagnosed with myeloma at the age of 35 and the second one was diagnosed with myelodysplastic syndrome at the age of 50. PubMed:27106701 
PP1			No evidence
PP2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM3			Not applicable
PM5			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM6			No evidence
PM2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline



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