# *Variant: NM_001754.5(RUNX1):c.485G>A (p.Arg162Lys)*

Version: 3.0

*CA16602490*

*376021 (ClinVar)*

**Gene**: RUNX1 (HGNC:861)
**Condition**: hereditary thrombocytopenia and hematologic cancer predisposition syndrome (MONDO:0011071)
**Inheritance Mode**: Autosomal dominant inheritance
**UUID:** c20346bb-711e-4d5f-bf45-8f14822fa448
**Approved on**: 2026-04-29
**Published on**: 2026-04-29

## *HGVS expressions*

**NM_001754.5:c.485G>A**
NM_001754.5(RUNX1):c.485G>A (p.Arg162Lys)
NC_000021.9:g.34880580C>T
CM000683.2:g.34880580C>T
NC_000021.8:g.36252877C>T
CM000683.1:g.36252877C>T
NC_000021.7:g.35174747C>T
NG_011402.2:g.1109132G>A
ENST00000675419.1:c.485G>A
ENST00000300305.7:c.485G>A
ENST00000344691.8:c.404G>A
ENST00000358356.9:c.404G>A
ENST00000399237.6:c.449G>A
ENST00000399240.5:c.404G>A
ENST00000437180.5:c.485G>A
ENST00000482318.5:c.*75G>A
NM_001001890.2:c.404G>A
NM_001122607.1:c.404G>A
NM_001754.4:c.485G>A
NM_001001890.3:c.404G>A
NM_001122607.2:c.404G>A

**Likely Pathogenic**

**Met criteria codes** 3

PM1_Strong PM2_Supporting PP3

**Not Met criteria codes** 23

PM6 PVS1 PM3 PM5 PM4 BA1 BS1 BS4 BS3 BS2 BP5 BP7 BP4 BP3 BP1 BP2 PS1 PS2 PS3 PS4 PP1 PP2 PP4

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 for RUNX1 Version 3.1.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

***Myeloid Malignancy VCEP***

**NM_001754.5(RUNX1):c.485G>A (p.Arg162Lys) is a missense variant which affects one of the hotspot residues (R162) in the RHD (PM1_strong). This variant has a REVEL score ≥ 0.88 (0.949) (PP3) and a MAF ≤ 0.00005 in gnomAD v4 across all subpopulations with at least 20x coverage for RUNX1 (PM2_supporting). In summary, this variant meets criteria to be classified as likely pathogenic. ACMG/AMP criteria applied, as specified by the Myeloid Malignancy Variant Curation Expert Panel for RUNX1: PM1_strong, PM2_supporting, PP3.**

**Met criteria codes**

| | | |
|---|---|---|
| **PM1_Strong** | ✔ | This variant affects the following hotspot residue within the RHD: R162 (PM1_strong). |
| **PM2_Supporting** | ✔ | This variant has a MAF ≤ 0.00005 in gnomAD v4.0 in all subpopulations with at least 20X coverage for RUNX1 (PM2_supporting). |
| **PP3** | ✔ | This missense variant has a REVEL score ≥ 0.88 (0.949) (PP3). |

**Not Met criteria codes**

| | | |
|---|---|---|
| **PM6** | ✖ | De novo data for this variant has not been reported in literature. |
| **PVS1** | ✖ | This variant is not a null variant. |
| **PM3** | ✖ | Not applicable |
| **PM5** | ✖ | PM1 applied |
| **PM4** | ✖ | This variant is not an in-frame deletion/insertion. |
| **BA1** | ✖ | This variant does not have a MAF ≥ 0.0015 (0.15%) in any general continental population dataset. |
| **BS1** | ✖ | This variant does not have a MAF between 0.00015 (0.015%) and 0.0015 (0.15%) in any general continental dataset. |
| **BS4** | ✖ | Segregation data for this variant has not been reported in literature. |
| **BS3** | ✖ | This variant has not been featured in in vitro or in vivo functional studies that show no damaging effect on protein function or splicing. |
| **BS2** | ✖ | Not applicable |

| | | | |
|---|---|---|---|
| **BP5** | | ✖ | Not applicable |
| **BP7** | ℹ | ✖ | This variant is not a synonymous or intronic variant. |
| **BP4** | ℹ | ✖ | This missense variant does not have a REVEL score < 0.50. |
| **BP3** | | ✖ | This rule is not applicable for MM-VCEP. |
| **BP1** | | ✖ | This rule is not applicable for MM-VCEP. |
| **BP2** | ℹ | ✖ | This variant has not been observed in trans with a pathogenic variant for a fully penetrant dominant gene/disorder or observed in cis with a pathogenic variant in any inheritance pattern. |
| **PS1** | ℹ | ✖ | There has not yet been a missense change resulting in the same change in protein which has been determined to be pathogenic at this amino acid residue. |
| **PS2** | | ✖ | De novo data for this variant has not been reported in literature. |
| **PS3** | ℹ | ✖ | While there is functional data for this variant (PMID: 25840971; 9533875), it does not meet the thresholds set for even PS3_moderate, which requires reduced transactivation to at least 20% of WT or impact in 2 secondary assays. |
| **PS4** | ℹ | ✖ | Invitae tested a proband (70s) with thrombocytopenia and anemia, who didn't have a suggestive family history; however, the variant was not confirmed in the germline. There are published reports of this variant in patients with hematological neoplasm, but either somatic status has been confirmed or germline origin is again unknown (PMID: 19808697, 22689681, 24523240, 24659740, 25592059, 26273060, 27220669, 27534895, 28659335, 28933735, 30373888, 31649132, 32045476, 32208489, COSMIC). Furthermore, R162K has been considered one of the most recurrent somatic missense variants in sporadic AML based on not being observed in a cohort with 103 germline SNV (p<0.05) (PMID: 32208489). |
| **PP1** | ℹ | ✖ | Segregation data for this variant has not been reported in literature. |
| **PP2** | | ✖ | This rule is not applicable for MM-VCEP. |
| **PP4** | | ✖ | Not applicable |

Curation History

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