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# *Variant: NM_001754.5(RUNX1):c.1268G>C (p.Arg423Pro)*

Version: 2.0

*CA410147569*

*579565 (ClinVar)*

**Gene**: RUNX1 (HGNC:861)
**Condition**: hereditary thrombocytopenia and hematologic cancer predisposition syndrome (MONDO:0011071)
**Inheritance Mode**: Autosomal dominant inheritance
**UUID:** 6ca7de45-ad81-4ca4-9f9e-8b128ed07c9f
**Approved on**: 2025/2/24
**Published on**: 2025/2/24

## *HGVS expressions*

**NM_001754.5(RUNX1):c.1268G>C (p.Arg423Pro)**
**NM_001754.5:c.1268G>C**
NC_000021.9:g.34792310C>G
CM000683.2:g.34792310C>G
NC_000021.8:g.36164607C>G
CM000683.1:g.36164607C>G
NC_000021.7:g.35086477C>G
NG_011402.2:g.1197402G>C
ENST00000675419.1:c.1268G>C
ENST00000300305.7:c.1268G>C
ENST00000344691.8:c.1187G>C
ENST00000399240.5:c.995G>C
ENST00000437180.5:c.1268G>C
ENST00000482318.5:c.*858G>C
NM_001001890.2:c.1187G>C
NM_001754.4:c.1268G>C
NM_001001890.3:c.1187G>C

**Likely Benign**

**Met criteria codes** 2

BS1 BP4

**Not Met criteria codes** 19

PM1 PM3 PM4 PM6 BS2 BS4 BS3 PVS1 BP5 BP7 BP3 BP1 BP2 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 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.1268G>C (p.Arg423Pro) is a missense variant. MAF of 0.0001793 (0.01793%, 5/27882 alleles) in the Ashkenazi Jewish subpopulation of the gnomAD v4.1.0 cohort is between 0.00015 (0.015%) and 0.0015 (0.15%) (BS1). This missense variant has a REVEL score < 0.50 (0.486) and a SpliceAI score ≤ 0.20 (0.0) (BP4). In summary, this variant meets criteria to be classified as likely benign. ACMG/AMP criteria applied, as specified by the Myeloid Malignancy Variant Curation Expert Panel for RUNX1: BS1, BP4.**

**Met criteria codes**

| | | |
|---|---|---|
| **BS1** | ✔ | gnomAD v.4.1.0: 5/27882 alleles in Ashkenazi Jewish, MAF: 0.01793%; 1/5850 alleles in Middle Eastern, MAF 0.017%. Total 102 alleles/1531096, MAF 0.006662%. MAF of 0.0001793 (0.01793%, 5/27882 alleles) in the Ashkenazi Jewish subpopulation of the gnomAD v4.1.0 cohort is between 0.00015 (0.015%) and 0.0015 (0.15%) (BS1). |
| **BP4** | ✔ | -REVEL: 0.486 - SplicAI: 0 This missense variant has a REVEL score < 0.50 (0.486) and a SpliceAI score ≤ 0.20 (0) (BP4). |

**Not Met criteria codes**

| | | |
|---|---|---|
| **PM1** | ✖ | This variant does not affect any of the following amino acid residues, nor is it located within the RHD: R107, K110, A134, R162, R166, S167, R169, G170, K194, T196, D198, R201, R204 OR within residues 89-204. |
| **PM3** | ✖ | This rule is not applicable for MM-VCEP |
| **PM4** | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **PM6** | ✖ | De novo data for this variant has not been reported in literature. |
| **BS2** | ✖ | This rule is not applicable for MM-VCEP |
| **BS4** | ✖ | No relevant literature was found in LOVD, HGMD, ClinVar, COSMIC, Mastermind, and Google/Google Scholar searches. |
| **BS3** | ✖ | No relevant literature was found in LOVD, HGMD, ClinVar, COSMIC, Mastermind, and Google/Google Scholar searches. |
| **PVS1** | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **BP5** | ✖ | This rule is not applicable for MM-VCEP |
| **BP7** | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **BP3** | ✖ | This rule is not applicable for MM-VCEP |

| | | | |
|---|---|---|---|
| **BP1** | | ✖ | This rule is not applicable for MM-VCEP |
| **BP2** | ⓘ | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **PS2** | | ✖ | De novo data for this variant has not been reported in literature. |
| **PS3** | ⓘ | ✖ | In vitro or in vivo functional data has not been reported for this variant in the literature. |
| **PS4** | ⓘ | ✖ | The germline variant has not been reported, but the variant has been detected in a gastric cancer at a VAF<5% (PMID: 30239046). |
| **PP1** | ⓘ | ✖ | No relevant literature was found in LOVD, HGMD, ClinVar, COSMIC, Mastermind, and Google/Google Scholar searches. |
| **PP2** | | ✖ | This rule is not applicable for MM-VCEP |
| **PP4** | | ✖ | This rule is not applicable for MM-VCEP |

Curation History

Showing 1 to 2 of 2 rows

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