

Variant: *NM\_001754.5(RUNX1):c.1281C>A (p.Arg427=)*

Version: 1.0

CA512341128 [↗](#)

2132477 (ClinVar) [↗](#)

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

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

**Inheritance Mode:** Autosomal dominant inheritance

**UUID:** 74532b13-8ccd-43cd-8ddf-fff963641bc5

**Approved on:** 2024/9/10

**Published on:** 2024/9/10

## HGVS expressions

**NM\_001754.5:c.1281C>A**

**NM\_001754.5(RUNX1):c.1281C>A (p.Arg427=)**

NC\_000021.9:g.34792297G>T

CM000683.2:g.34792297G>T

NC\_000021.8:g.36164594G>T

CM000683.1:g.36164594G>T

NC\_000021.7:g.35086464G>T

NG\_011402.2:g.1197415C>A

ENST00000675419.1:c.1281C>A

ENST00000300305.7:c.1281C>A

ENST00000344691.8:c.1200C>A

ENST00000399240.5:c.1008C>A

ENST00000437180.5:c.1281C>A

ENST00000482318.5:c.\*871C>A

NM\_001001890.2:c.1200C>A

NM\_001754.4:c.1281C>A

NM\_001001890.3:c.1200C>A

Likely Benign

Met criteria codes **3**

BP4

PM2\_Supporting

BP7

Not Met criteria codes **22**

BA1

BP3

BP1

BP2

BP5

BS1

BS4

BS3

PP1

PP2

PP3

PP4

PM6

PM1

PM3

PM5

PM4

PS1

PS2

PS3

PS4

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.1281C>A (p.Arg427=) is a synonymous variant which has a SpliceAI score  $\leq 0.20$  (0.0) (BP4). This variant has a SpliceAI score  $\leq 0.20$  (0.0) and evolutionary conservation algorithms predict the site as not being conserved (PhyloP score  $\leq 2.0$  (0.25)) (BP7). This variant is completely absent from all population databases with at least 20x coverage for RUNX1 (PM2\_Supporting). 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: BP4, BP7, PM2\_supporting.

Met criteria codes

|                |                                                                                   |                                                                                   |                                                                                                                                                                                         |
|----------------|-----------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| BP4            |  |  | This synonymous variant has a SpliceAI score $\leq 0.20$ (0.0) (BP4).                                                                                                                   |
| PM2_Supporting |  |  | This variant is completely absent from all population databases with at least 20x coverage for RUNX1 (PM2_Supporting).                                                                  |
| BP7            |  |  | This variant has a SpliceAI score $\leq 0.20$ (0.0) and evolutionary conservation prediction algorithms predict the site as not being conserved (PhyloP score $\leq 2.0$ (0.25)) (BP7). |

Not Met criteria codes

|     |                                                                                     |                                                                                     |                                                                                                                                                                                             |
|-----|-------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| BA1 |    |    | This variant does not have a MAF $\geq 0.0015$ (0.15%) in any general continental population dataset.                                                                                       |
| BP3 |                                                                                     |    | This rule is not applicable for MM-VCEP.                                                                                                                                                    |
| BP1 |                                                                                     |  | This rule is not applicable for MM-VCEP.                                                                                                                                                    |
| BP2 |  |  | 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. |
| BP5 |                                                                                     |  | This rule is not applicable for MM-VCEP.                                                                                                                                                    |
| 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 |  |  | In vitro or in vivo functional data has not been reported for this variant in the literature.                                                                                               |
| PP1 |  |  | Segregation data for this variant has not been reported in literature.                                                                                                                      |
| PP2 |                                                                                     |  | This rule is not applicable for MM-VCEP.                                                                                                                                                    |
| PP3 |  |  | This synonymous or intronic variant does not have a REVEL score $\geq 0.88$ or a SpliceAI score $\geq 0.38$ .                                                                               |
| PP4 |                                                                                     |  | This rule is not applicable for MM-VCEP.                                                                                                                                                    |

|      |                                                                                    |                                                                                    |                                                                                                            |
|------|------------------------------------------------------------------------------------|------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------|
| PM6  |     |     | De novo data for this variant has not been reported in literature.                                         |
| PM1  |                                                                                    |   | This variant is not a missense variant.                                                                    |
| PM3  |                                                                                    |   | This rule is not applicable for MM-VCEP.                                                                   |
| PM5  |   |   | There has not yet been a different missense change determined to be pathogenic at this amino acid residue. |
| PM4  |   |   | This variant is not an in-frame deletion/insertion.                                                        |
| PS1  |   |   | There has not yet been a missense change determined to be pathogenic at this amino acid residue.           |
| 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  |   |   | Proband data for this variant has not been reported in literature.                                         |
| PVS1 |  |  | This variant is not a null variant.                                                                        |

| Curation History                                                                                                                                                                                                                                 |  |  |
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