

Variant: *NM_001754.5(RUNX1):c.1275G>A (p.Pro425=)*

Version: 1.0

CA10587358 [↗](#)

258183 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 23ae6c1f-ffcd-4b6e-b6be-45a90e5f9506

Approved on: 2022/7/5

Published on: 2022/7/5

HGVS expressions

NM_001754.5:c.1275G>A

NM_001754.5(RUNX1):c.1275G>A (p.Pro425=)

NC_000021.9:g.34792303C>T

CM000683.2:g.34792303C>T

NC_000021.8:g.36164600C>T

CM000683.1:g.36164600C>T

NC_000021.7:g.35086470C>T

NG_011402.2:g.1197409G>A

ENST00000675419.1:c.1275G>A

ENST00000300305.7:c.1275G>A

ENST00000344691.8:c.1194G>A

ENST00000399240.5:c.1002G>A

ENST00000437180.5:c.1275G>A

ENST00000482318.5:c.*865G>A

NM_001001890.2:c.1194G>A

NM_001754.4:c.1275G>A

NM_001001890.3:c.1194G>A

Likely Benign

Met criteria codes **2**

BP7 BP4

Not Met criteria codes **24**

BS2 PVS1 BS1 BS4 BS3
BP5 BP3 BP1 BP2 PS1 PS2
PS3 PS4 BA1 PP1 PP2 PP3
PP4 PM6 PM2 PM1 PM3
PM5 PM4

Evidence Links **0**

Expert Panel

Myeloid Malignancy VCEP [↗](#)

Criteria Specification Information **!**

[↗](#) Criteria Specifications for this VCEP

Evidence submitted by expert panel

Myeloid Malignancy VCEP

The c.1275G>A (p.Pro425=) variant is a synonymous (silent) variant that is not predicted by SpliceAI to impact splicing (BP4); in addition, an evolutionary conservation algorithm predicts the site as being non-conserved (PhyloP score = -1.62676 in GRCh38), and the variant allele is the reference nucleotide in one primate and/or three mammal species (BP7). The variant also has not been reported in cases or the literature. In summary, this variant meets the criteria to be classified as likely benign for hereditary thrombocytopenia and hematologic cancer predisposition syndrome based on the ACMG/AMP criteria applied, as specified by the ClinGen Myeloid Malignancy VCEP: BP4 and BP7.

Met criteria codes

BP7			The c.1275G>A (p.Pro425=) variant is a synonymous (silent) variant that is not predicted by SpliceAI to impact splicing. In addition, an evolutionary conservation algorithm predicts the site as being non-conserved (PhyloP score = -1.62676 in GRCh38), and the variant allele is the reference nucleotide in one primate and/or three mammal species.
BP4			SpliceAI doesn't predict any significant splicing impact (Δ scores $\leq$ 0.20).

Not Met criteria codes

BS2			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
BS1			gnomAD (v2): ALL: 0.0006959% (1/143694) - NFE: 0.001824% (1/54828) gnomAD (v3): ALL: 0.002008% (3/149438) - NFE: 0.004460% (3/67262)
BS4			No literature was found in LOVD, HGMD, ClinVar, COSMIC, Mastermind, and Google/Google Scholar searches.
BS3			No literature was found in LOVD, HGMD, ClinVar, COSMIC, Mastermind, and Google/Google Scholar searches.
BP5			Not applicable
BP3			Not applicable
BP1			Not applicable
BP2			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 literature was found in LOVD, HGMD, ClinVar, COSMIC, Mastermind, and Google/Google Scholar searches.

PS3			No literature was found in LOVD, HGMD, ClinVar, COSMIC, Mastermind, and Google/Google Scholar searches.
PS4			The germline variant has not been reported in cases (LOVD, HGMD, ClinVar, Mastermind, and Google/Google Scholar), but the somatic variant has been detected in a breast and endometrial tumor (COSMIC Genomic Mutation ID: COSV55867658).
BA1			gnomAD (v2): ALL: 0.0006959% (1/143694) - NFE: 0.001824% (1/54828) gnomAD (v3): ALL: 0.002008% (3/149438) - NFE: 0.004460% (3/67262)
PP1			No literature was found in LOVD, HGMD, ClinVar, COSMIC, Mastermind, and Google/Google Scholar searches.
PP2			Not applicable
PP3			SpliceAI doesn't predict any significant splicing impact (Δ scores $\leq$ 0.20).
PP4			Not applicable
PM6			No literature was found in LOVD, HGMD, ClinVar, COSMIC, Mastermind, and Google/Google Scholar searches.
PM2			gnomAD (v2): ALL: 0.0006959% (1/143694) - NFE: 0.001824% (1/54828) gnomAD (v3): ALL: 0.002008% (3/149438) - NFE: 0.004460% (3/67262)
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

Curation History [↗](#)

Showing 1 to 1 of 1 rows

--

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.