The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_001754.5(RUNX1):c.1277C>G (p.Pro426Arg)

Version: 1.0

CA410147531

2678496 (ClinVar)

Gene: RUNX1 (HGNC:861)
Condition: hereditary thrombocytopenia and hematologic cancer predisposition syndrome (MONDO:0011071)
Inheritance Mode: Autosomal dominant inheritance
UUID: 2882b4be-ff36-41b5-b26a-75e1cbb0be25
Approved on: 2024/9/30
Published on: 2024/9/30

HGVS expressions

NM_001754.5:c.1277C>G
NM_001754.5(RUNX1):c.1277C>G (p.Pro426Arg)
NC_000021.9:g.34792301G>C
CM000683.2:g.34792301G>C
NC_000021.8:g.36164598G>C
CM000683.1:g.36164598G>C
NC_000021.7:g.35086468G>C
NG_011402.2:g.1197411C>G
ENST00000675419.1:c.1277C>G
ENST00000300305.7:c.1277C>G
ENST00000344691.8:c.1196C>G
ENST00000399240.5:c.1004C>G
ENST00000437180.5:c.1277C>G
ENST00000482318.5:c.*867C>G
NM_001001890.2:c.1196C>G
NM_001754.4:c.1277C>G
NM_001001890.3:c.1196C>G

Uncertain Significance

Met criteria codes 2

PM2_Supporting BP4

Not Met criteria codes 23

PS1 PS2 PS3 BA1 PP1 PP2 PP3 PP4 PM6 PVS1 PM1 PM3 PM5 PM4 BS1 BS4 BS3 BS2 BP5 BP7 BP3 BP1 BP2

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.1277C>G (p.Pro426Arg) is a missense variant which has a REVEL score < 0.50 (0.254), and a SpliceAI score ≤ 0.20 (0.0) (BP4). This variant is completely absent from all population databases with at least 20x coverage for RUNX1 (PM2_Supporting). In summary, the clinical significance of this variant is uncertain. ACMG/AMP criteria applied, as specified by the Myeloid Malignancy Variant Curation Expert Panel for RUNX1: BP4, PM2_supporting.

Met criteria codes

PM2_Supporting	✔	This variant is completely absent from all population databases with at least 20x coverage for RUNX1 (PM2_Supporting).
BP4	✔	This missense variant has a REVEL score < 0.50 (0.254), and a SpliceAI score ≤ 0.20 (0.0) (BP4).

Not Met criteria codes

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.
BA1	✖	This variant does not have a MAF ≥ 0.0015 (0.15%) in any general continental population dataset.
PP1	✖	Segregation data for this variant has not been reported in literature.
PP2	✖	This rule is not applicable for MM-VCEP.
PP3	✖	This missense variant does not have a REVEL score of ≥ 0.88.
PP4	✖	This rule is not applicable for MM-VCEP.
PM6	✖	De novo data for this variant has not been reported in literature.
PVS1	✖	This variant is not a null variant.
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.
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.

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.
BS2		✖	This rule is not applicable for MM-VCEP.
BP5		✖	This rule is not applicable for MM-VCEP.
BP7		✖	This variant is not a synonymous or intronic variant.
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.

Curation History

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See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_001754.5(RUNX1):c.1277C>G (p.P...	Uncertain Significance	Hereditary Thrombocytopenia And Hematologic Cancer Predisposition Syndrome	2024-09-30	1.0	ClinGen Myeloid Malignancy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 2	RUNX1

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