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Variant: NM_001754.5(RUNX1):c.193G>C (p.Ala65Pro)

Version: 1.0

CA410203954

2807004 (ClinVar)

Gene: RUNX1 (HGNC:861)
Condition: hereditary thrombocytopenia and hematologic cancer predisposition syndrome (MONDO:0011071)
Inheritance Mode: Autosomal dominant inheritance
UUID: e1fcab36-5b5f-4b75-80b9-329f389de224
Approved on: 2024/9/12
Published on: 2024/9/12

HGVS expressions

NM_001754.5:c.193G>C
NM_001754.5(RUNX1):c.193G>C (p.Ala65Pro)
NC_000021.9:g.34887001C>G
CM000683.2:g.34887001C>G
NC_000021.8:g.36259298C>G
CM000683.1:g.36259298C>G
NC_000021.7:g.35181168C>G
NG_011402.2:g.1102711G>C
ENST00000675419.1:c.193G>C
ENST00000300305.7:c.193G>C
ENST00000344691.8:c.112G>C
ENST00000358356.9:c.112G>C
ENST00000399237.6:c.157G>C
ENST00000399240.5:c.112G>C
ENST00000437180.5:c.193G>C
ENST00000455571.5:c.154G>C
ENST00000482318.5:c.59-6288G>C
NM_001001890.2:c.112G>C
NM_001122607.1:c.112G>C
NM_001754.4:c.193G>C
NM_001001890.3:c.112G>C
NM_001122607.2:c.112G>C

Uncertain Significance

Met criteria codes 1

PM2_Supporting

Not Met criteria codes 25

PM1 PM3 PM5 PM4 PM6 BS2 BS1 BS4 BS3 PVS1 BP5 BP7 BP4 BP3 BP1 BP2 BA1 PS1 PS2 PS3 PS4 PP1 PP2 PP3 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.193G>C (p.Ala65Pro) is a missense variant in exon 4. This variant has not been observed in any population according to gnomAD (PM2_Supporting). The nucleotide substitution is not predicted to disrupt splicing (SpliceAI score = 0.01). The effect of the amino acid change is uncertain, as the REVEL score of 0.545 falls between 0.5 and 0.88, and functional evidence is not available in the literature for this variant. There are no reported cases. Overall, the clinical significance of this variant is uncertain. ACMG/AMP criteria applied, as specified by the Myeloid Malignancy Variant Curation Expert Panel for RUNX1: 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).

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	✖	not applicable
PM5	✖	There are 2 other missense variants at this residue, but none have been determined to be pathogenic.
PM4	✖	This is not an in/del variant.
PM6	✖	De novo data for this variant has not been reported in literature
BS2	✖	not applicable
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.
PVS1	✖	This is not a null variant;
BP5	✖	not applicable
BP7	✖	This is not a silent variant.

BP4	ℹ	✖	This missense variant does not have a REVEL score < 0.50 (0.545).
BP3		✖	not applicable
BP1		✖	not applicable
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.
BA1	ℹ	✖	This variant does not have a MAF ≥ 0.0015 (0.15%) in any general continental population dataset.
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	✖	In vitro or in vivo functional data has not been reported for this variant in the literature.
PS4	ℹ	✖	Proband data for this variant has not been reported in literature.
PP1	ℹ	✖	Segregation data for this variant has not been reported in literature.
PP2		✖	not applicable
PP3	ℹ	✖	This missense variant does not have a REVEL score of ≥ 0.88 (0.545).
PP4		✖	not applicable

Curation History

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