Variant: NM_001754.5(RUNX1):c.421T>C (p.Ser141Pro)

Version: 1.0

CA410202645

2628467 (ClinVar)

Gene: RUNX1 (HGNC:861)
Condition: hereditary thrombocytopenia and hematologic cancer predisposition syndrome (MONDO:0011071)
Inheritance Mode: Autosomal dominant inheritance
UUID: db5984d2-5d52-4fda-b6d9-208e32f327c1
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HGVS expressions

NM_001754.5:c.421T>C
NM_001754.5(RUNX1):c.421T>C (p.Ser141Pro)
NC_000021.9:g.34880644A>G
CM000683.2:g.34880644A>G
NC_000021.8:g.36252941A>G
CM000683.1:g.36252941A>G
NC_000021.7:g.35174811A>G
NG_011402.2:g.1109068T>C
ENST00000675419.1:c.421T>C
ENST00000300305.7:c.421T>C
ENST00000344691.8:c.340T>C
ENST00000358356.9:c.340T>C
ENST00000399237.6:c.385T>C
ENST00000399240.5:c.340T>C
ENST00000437180.5:c.421T>C
ENST00000455571.5:c.382T>C
ENST00000482318.5:c.*11T>C
NM_001001890.2:c.340T>C
NM_001122607.1:c.340T>C
NM_001754.4:c.421T>C
NM_001001890.3:c.340T>C
NM_001122607.2:c.340T>C

Uncertain Significance

Met criteria codes 3

PP3 PM2_Supporting
PM1_Supporting

Not Met criteria codes 23

PP1 PP2 PP4 PM3 PM5
PM4 PM6 PVS1 BA1 BS1
BS4 BS3 BS2 BP5 BP7 BP4
BP3 BP1 BP2 PS1 PS2 PS3
PS4

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.421T>C (p.Ser141Pro) is a missense variant which has a REVEL score ≥ 0.88 (0.97) (PP3). This variant affects a residue within the Runt Homology domain (AA 89-204) but does not affect an established hotspot residue (PM1_Supporting). 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: PP3, PM1_supporting, PM2_supporting.

Met criteria codes

PP3	ℹ	✓	This missense variant has a REVEL score ≥ 0.88 (0.97) (PP3).
PM2_Supporting	ℹ	✓	This variant is completely absent from all population databases with at least 20x coverage for RUNX1 (PM2_Supporting).
PM1_Supporting	ℹ	✓	This variant affects one of the other residues (AA 89-204) within the RHD (PM1_Supporting).

Not Met criteria codes

PP1	ℹ	✖	Segregation data for this variant has not been reported in literature.
PP2		✖	This rule is not applicable for MM-VCEP.
PP4		✖	This rule is not applicable for MM-VCEP.
PM3		✖	This rule is not applicable for MM-VCEP.
PM5	ℹ	✖	There has not yet been a different missense change determined to be pathogenic at this amino acid residue.
PM4	ℹ	✖	This variant is not an in-frame deletion/insertion.
PM6	ℹ	✖	De novo data for this variant has not been reported in literature.
PVS1	ℹ	✖	This variant is not a null variant.
BA1	ℹ	✖	This variant does not have a MAF ≥ 0.0015 (0.15%) in any general continental population dataset.
BS1	ℹ	✖	This variant does not have a MAF between 0.00015 (0.015%) and 0.0015 (0.15%) in any general continental dataset.
BS4	ℹ	✖	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.
BP4	✖	This missense variant does not have a REVEL score < 0.50.
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.
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.

Curation History

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