Variant: NM_001754.5(RUNX1):c.599C>A (p.Pro200His)

Version: 1.0

CA410207960

1004688 (ClinVar)

Gene: RUNX1 (HGNC:861)
Condition: hereditary thrombocytopenia and hematologic cancer predisposition syndrome (MONDO:0011071)
Inheritance Mode: Autosomal dominant inheritance
UUID: 149407af-db7c-48f3-a958-05ee667b179e
Approved on: 2024-08-12
Published on: 2024-08-12

HGVS expressions

NM_001754.5:c.599C>A
NM_001754.5(RUNX1):c.599C>A (p.Pro200His)
NC_000021.9:g.34859488G>T
CM000683.2:g.34859488G>T
NC_000021.8:g.36231785G>T
CM000683.1:g.36231785G>T
NC_000021.7:g.35153655G>T
NG_011402.2:g.1130224C>A
ENST00000675419.1:c.599C>A
ENST00000300305.7:c.599C>A
ENST00000344691.8:c.518C>A
ENST00000358356.9:c.518C>A
ENST00000399237.6:c.563C>A
ENST00000399240.5:c.518C>A
ENST00000437180.5:c.599C>A
ENST00000467577.1:n.91C>A
ENST00000482318.5:c.*189C>A
NM_001001890.2:c.518C>A
NM_001122607.1:c.518C>A
NM_001754.4:c.599C>A
NM_001001890.3:c.518C>A
NM_001122607.2:c.518C>A

Uncertain Significance

Met criteria codes 3

PM2_Supporting PP3
PM1_Supporting

Not Met criteria codes 23

BA1 PP1 PP2 PP4 PM6
PM3 PM5 PM4 BS1 BS4
BS3 PVS1 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.599C>A (p.Pro200His) is a missense variant which is completely absent from all population databases with at least 20x coverage for RUNX1 (PM2_supporting). It has a REVEL score of 0.947 (REVEL score ≥ 0.88), meeting PP3. This missense variant is located within the Runt Homology Domain (AA 89-204), but does not occur in an established hotspot residue (PM1_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: PM1_supporting, PM2_supporting, and PP3.

Met criteria codes

PM2_Supporting	ⓘ	✓	Variant is absent from control population databases. PM2_supporting
PP3	ⓘ	✓	REVEL score= 0.947 (REVELscore ≥ 0.88)
PM1_Supporting	ⓘ	✓	Meets PM1_supporting. Variant affecting one of the other amino acid residues 89-204 within the RHD.

Not Met criteria codes

BA1	ⓘ	✖	Variant is absent from control population databases. PM2_supporting met
PP1	ⓘ	✖	No case study found
PP2		✖	This rule is not applicable for MM-VCEP
PP4		✖	This rule is not applicable for MM-VCEP
PM6	ⓘ	✖	No case study found
PM3		✖	This rule is not applicable for MM-VCEP
PM5	ⓘ	✖	A Missense change at amino acid residue 200 has not been determined to be pathogenic before
PM4	ⓘ	✖	This is a missense variant
BS1	ⓘ	✖	Variant is absent from control population databases. PM2_supporting met
BS4	ⓘ	✖	No case study found

BS3	ℹ	✖	No study found
PVS1	ℹ	✖	This is a missense variant
BS2		✖	This rule is not applicable for MM-VCEP
BP5		✖	This rule is not applicable for MM-VCEP
BP7	ℹ	✖	This is a missense variant
BP4	ℹ	✖	This rule is not applicable for MM-VCEP
BP3		✖	This is a missense variant
BP1		✖	This rule is not applicable for MM-VCEP
BP2	ℹ	✖	No case study found
PS1	ℹ	✖	This amino acid change at residue 200 has not been determined to be pathogenic before
PS2		✖	No case study found
PS3	ℹ	✖	No study found
PS4	ℹ	✖	No case study found

Curation History

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