

Variant: NM_001754.5(RUNX1):c.580A>G (p.Lys194Glu)

Version: 2.0

CA410208003 [↗](#)

3668347 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: e0820c5d-288d-4431-9179-0486d5120fa4

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HGVS expressions

NM_001754.5(RUNX1):c.580A>G (p.Lys194Glu)

NM_001754.5:c.580A>G

NC_000021.9:g.34859507T>C

CM000683.2:g.34859507T>C

NC_000021.8:g.36231804T>C

CM000683.1:g.36231804T>C

NC_000021.7:g.35153674T>C

NG_011402.2:g.1130205A>G

ENST00000675419.1:c.580A>G

ENST00000300305.7:c.580A>G

ENST00000344691.8:c.499A>G

ENST00000358356.9:c.499A>G

ENST00000399237.6:c.544A>G

ENST00000399240.5:c.499A>G

ENST00000437180.5:c.580A>G

ENST00000467577.1:n.72A>G

ENST00000482318.5:c.*170A>G

NM_001001890.2:c.499A>G

NM_001122607.1:c.499A>G

NM_001754.4:c.580A>G

NM_001001890.3:c.499A>G

NM_001122607.2:c.499A>G

Likely Pathogenic

Met criteria codes 3

PP3

PM2_Supporting

PM1_Strong

Not Met criteria codes 23

PVS1

BA1

BP5

BP7

BP4

BP3

BP1

BP2

BS1

BS4

BS3

BS2

PP1

PP2

PP4

PS1

PS2

PS3

PS4

PM3

PM5

PM4

PM6

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 for RUNX1 Version 3.1.0

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

Myeloid Malignancy VCEP

NM_001754.5(RUNX1):c.580A>G (p.Lys194Glu) is a missense variant which affects one of the hotspot residues (K194) in the RHD (PM1_strong). This variant has a REVEL score ≥ 0.88 (0.956) (PP3) and is completely absent from all population databases with at least 20x coverage for RUNX1 (PM2_supporting). In summary, this variant meets criteria to be classified as likely pathogenic. ACMG/AMP criteria applied, as specified by the Myeloid Malignancy Variant Curation Expert Panel for RUNX1: PM1_strong, PP3, PM2_supporting.

Met criteria codes

PP3			This missense variant has a REVEL score ≥ 0.88 (0.956) (PP3).
PM2_Supporting			This variant is completely absent from all population databases with at least 20x coverage for RUNX1 (PM2_Supporting).
PM1_Strong			This variant affects at least one of the following hotspot residues within the RHD: K194 (PM1_strong).

Not Met criteria codes

PVS1			This variant is not a null variant.
BA1			This variant does not have a MAF ≥ 0.0015 (0.15%) in any general continental population dataset.
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.
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
PP1			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
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.
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.
PM6			De novo data for this variant has not been reported in literature.

Curation History 		
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