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Variant: NM_001754.5(RUNX1):c.328A>C (p.Lys110Gln)

Version: 2.0

CA410203432

3367215 (ClinVar)

Gene: RUNX1 (HGNC:861)
Condition: hereditary thrombocytopenia and hematologic cancer predisposition syndrome (MONDO:0011071)
Inheritance Mode: Autosomal dominant inheritance
UUID: 330a8e63-9235-4c9a-afc2-d05f0bf9cc33
Approved on: 2026/4/29
Published on: 2026/4/29

HGVS expressions

NM_001754.5(RUNX1):c.328A>C (p.Lys110Gln)
NM_001754.5:c.328A>C
NC_000021.9:g.34886866T>G
CM000683.2:g.34886866T>G
NC_000021.8:g.36259163T>G
CM000683.1:g.36259163T>G
NC_000021.7:g.35181033T>G
NG_011402.2:g.1102846A>C
ENST00000675419.1:c.328A>C
ENST00000300305.7:c.328A>C
ENST00000344691.8:c.247A>C
ENST00000358356.9:c.247A>C
ENST00000399237.6:c.292A>C
ENST00000399240.5:c.247A>C
ENST00000437180.5:c.328A>C
ENST00000455571.5:c.289A>C
ENST00000482318.5:c.59-6153A>C
NM_001001890.2:c.247A>C
NM_001122607.1:c.247A>C
NM_001754.4:c.328A>C
NM_001001890.3:c.247A>C
NM_001122607.2:c.247A>C

Likely Pathogenic

Met criteria codes 5

PS4_Supporting BP2 PM1_Strong PM2_Supporting PP3

Not Met criteria codes 20

PM3 PM5 PM4 PM6 BA1 BS2 BS1 BS4 BS3 BP4 BP3 BP5 BP7 PS1 PS2 PS3 PVS1 PP1 PP2 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 for RUNX1 Version 3.1.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Myeloid Malignancy VCEP

NM_001754.5(RUNX1):c.328A>C (p.Lys110Gln) is a missense variant which affects one of the hotspot residues (K110) in the RHD (PM1_strong). This variant has a REVEL score ≥ 0.88 (0.957) (PP3) and is completely absent from all population databases with at least 20x coverage for RUNX1 (PM2_supporting). It has been observed in a homozygous state (BP2) in a proband meeting at least one of the RUNX1 phenotypic criteria (AML) (PS4_supporting; PMID: 28855357). 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, BP2, and PS4_supporting.

Met criteria codes

PS4_Supporting	✔	This variant has been reported in one proband meeting at least one of the RUNX1-phenotypic criteria (PS4_ Supporting; PMID: 28855357).
BP2	✔	This variant is detected in a homozygous state in an individual (BP2; PMID: 28855357).
PM1_Strong	✔	This variant affects one of the hotspot residues established by the MM-VCEP in the RHD: K110 (PM1_strong).
PM2_Supporting	✔	This variant is completely absent from all population databases (gnomAD v2.1.1, v3.1.2, and v4.0.0) with at least 20x coverage for RUNX1 (PM2_supporting).
PP3	✔	This missense variant has a REVEL score >0.88 (0.957) (PP3).

Not Met criteria codes

PM3	✖	The MMVCEP does not evaluate this rule.
PM5	✖	This variant is a missense change at the same residue (p.Lys110Gln), where two or more (3) different missense changes have been previously established as likely pathogenic (ClinVar ID: 1518631 and ClinGen: CA410203418, and ClinVar ID: 561234 and ClinGen: CA410203419) and pathogenic variants (ClinVar ID: 14465 and ClinGen: CA248613) based on MM-VCEP rules for RUNX1 and RNA data. Additionally, agreement in splicing predictors (SSF and MES) shows no splicing effects (PM5_Strong). However, this rule is not applicable in combination with PM1.
PM4	✖	This rule cannot be applied since this is a missense variant.
PM6	✖	This rule cannot be applied since, to our knowledge, we have no information about segregation reported in any study.
BA1	✖	This rule cannot be applied since the variant is completely absent from all population databases.
BS2	✖	The MMVCEP does not evaluate this rule.

BS1		✖	This rule cannot be applied since the variant is completely absent from all population databases.
BS4		✖	This rule cannot be applied since, to our knowledge, we have no information about segregation in the reported study.
BS3		✖	To our knowledge, no in vitro or in vivo functional studies are available for this variant.
BP4		✖	This rule cannot be applied since this missense variant does not have a REVEL score <0.50 (0.957).
BP3		✖	The MMVCEP does not evaluate this rule.
BP5		✖	The MMVCEP does not evaluate this rule.
BP7		✖	This rule cannot be applied since this is a missense variant.
PS1		✖	This rule cannot be applied because, to our knowledge, this missense variant does not result in the same amino acid change as a previously identified pathogenic variant, regardless of nucleotide change.
PS2		✖	This rule cannot be applied since, to our knowledge, we have no information about segregation reported in any study.
PS3		✖	To our knowledge, no in vitro or in vivo functional studies are available for this variant.
PVS1		✖	This rule cannot be applied since this is a missense variant.
PP1		✖	This rule cannot be applied since, to our knowledge, we have no information about cosegregation in the reported study.
PP2		✖	The MMVCEP does not evaluate this rule.
PP4		✖	The MMVCEP does not evaluate this rule.

Curation History

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