The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_001754.5(RUNX1):c.114C>T (p.Arg38=)

Version: 1.0

CA512318994

1114762 (ClinVar)

Gene: RUNX1 (HGNC:861)
Condition: hereditary thrombocytopenia and hematologic cancer predisposition syndrome (MONDO:0011071)
Inheritance Mode: Autosomal dominant inheritance
UUID: 37856af3-6a77-4bd8-b814-ed2a47f9f926
Approved on: 2022/8/23
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HGVS expressions

NM_001754.5(RUNX1):c.114C>T (p.Arg38=)
NM_001754.5:c.114C>T
NC_000021.9:g.34887080G>A
CM000683.2:g.34887080G>A
NC_000021.8:g.36259377G>A
CM000683.1:g.36259377G>A
NC_000021.7:g.35181247G>A
NG_011402.2:g.1102632C>T
ENST00000675419.1:c.114C>T
ENST00000300305.7:c.114C>T
ENST00000344691.8:c.33C>T
ENST00000358356.9:c.33C>T
ENST00000399237.6:c.78C>T
ENST00000399240.5:c.33C>T
ENST00000437180.5:c.114C>T
ENST00000455571.5:c.75C>T
ENST00000475045.6:c.114C>T
ENST00000482318.5:c.59-6367C>T
NM_001001890.2:c.33C>T
NM_001122607.1:c.33C>T
NM_001754.4:c.114C>T
NM_001001890.3:c.33C>T
NM_001122607.2:c.33C>T

Likely Benign

Met criteria codes 3

BP4 BP7 PM2_Supporting

Not Met criteria codes 23

PM1 PM3 PM5 PM4 PM6 BA1 BS2 BS1 BS4 BS3 BP3 BP1 BP2 BP5 PS1 PS2 PS3 PS4 PVS1 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.114C>T (p.Arg38=) is a synonymous variant. Evolutionary conservation prediction algorithms predict the site as not being conserved (PhyloP score 1.53< 2.0 or the variant is the reference nucleotide in one primate and three mammal species) (BP7). This synonymous variant has a SpliceAI score ≤ 0.20 (0.02). The variant is absent from gnomAD with mean of 20X coverage (gnomAD v2.1 or v3.1.2) (PM2_supporting). In summary, this variant meets the criteria to be classified as likely benign. ACMG/AMP criteria applied, as specified by the Myeloid Malignancy Variant Curation Expert Panel for RUNX1: PM2_supporting, BP7, BP4

Met criteria codes

BP4	✔	This synonymous/intronic/UTR/frameshift variant has a SpliceAI score ≤ 0.20 (0.02).
BP7	✔	: Evolutionary conservation prediction algorithms predict the site as not being conserved (PhyloP score 1.53< 2.0 or the variant is the reference nucleotide in one primate and/or three mammal species)
PM2_Supporting	✔	Variant is not present in population databases (gnomAD v2.1 or v3.1.2)

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 NOR is it within residues 89-204
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, as this is variant is located in a non-coding region.
PM4	✖	This in-frame deletion/insertion DOES NOT affect at least one of the other residues (AA 89-204) within the RHD, as it is at location AA 38
PM6	✖	This variant has not been reported in probands in the literature.
BA1	✖	Variant is not present in population databases (gnomAD v2.1 or v3.1.2)
BS2	✖	This rule is not applicable for MM-VCEP
BS1	✖	Variant is not present in population databases (gnomAD v2.1 or v3.1.2)
BS4	✖	This variant has not been reported in affected family members.

BS3	ℹ	✖	This variant has not been featured in in vitro or in vivo functional studies that show no damaging effect on protein function or splicing
BP3		✖	This rule is not applicable for MM-VCEP
BP1		✖	This rule is not applicable for MM-VCEP
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.
BP5		✖	This rule is not applicable for MM-VCEP
PS1	ℹ	✖	This is a synonymous variant.
PS2		✖	This variant has not been reported in probands in the literature.
PS3	ℹ	✖	This variant has not been featured in in vitro or in vivo functional studies showing a damaging effect on the gene or gene product.
PS4	ℹ	✖	This variant has not been reported in probands.
PVS1	ℹ	✖	This is a synonymous variant, not a null variant.
PP1	ℹ	✖	This variant was not found to co-segregate with disease in multiple affected family members.
PP2		✖	This rule is not applicable for MM-VCEP
PP3	ℹ	✖	This synonymous/intronic variant does not have a SpliceAI score of ≥ 0.38 (0.02).
PP4		✖	This rule is not applicable for MM-VCEP

Curation History

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