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Variant: NM_001754.5(RUNX1):c.829C>T (p.Pro277Ser)

Version: 1.0

CA410150264

1362194 (ClinVar)

Gene: RUNX1 (HGNC:861)
Condition: hereditary thrombocytopenia and hematologic cancer predisposition syndrome (MONDO:0011071)
Inheritance Mode: Autosomal dominant inheritance
UUID: 8da1986b-f2f3-43f0-9c4c-1189a0963738
Approved on: 2024/9/16
Published on: 2024/9/16

HGVS expressions

NM_001754.5(RUNX1):c.829C>T (p.Pro277Ser)
NM_001754.5:c.829C>T
NC_000021.9:g.34799439G>A
CM000683.2:g.34799439G>A
NC_000021.8:g.36171736G>A
CM000683.1:g.36171736G>A
NC_000021.7:g.35093606G>A
NG_011402.2:g.1190273C>T
ENST00000675419.1:c.829C>T
ENST00000300305.7:c.829C>T
ENST00000344691.8:c.748C>T
ENST00000399240.5:c.556C>T
ENST00000437180.5:c.829C>T
ENST00000482318.5:c.*419C>T
NM_001001890.2:c.748C>T
NM_001754.4:c.829C>T
NM_001001890.3:c.748C>T

Uncertain Significance

Met criteria codes 2

PM2_Supporting BP4

Not Met criteria codes 17

PS1 PS2 PS3 PS4 BA1 PP1 PP3 PM6 PVS1 PM1 PM5 PM4 BS1 BS4 BS3 BP7 BP2

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.829C>T (p.Pro277Ser) s a missense variant which is absent from all population databases, including gnomAD v2.1.1 and gnomAD v3.1.2, which provide coverage of at least 20x for the RUNX1 gene at this genomic position (PM2_supporting). Additionally, this missense variant has a REVEL score <0.50 (0.447) (BP4) and affects a residue located outside of the RHD or amino acids 89-204. To our knowledge, this variant has not been reported before in patients with RUNX1-related disorders, and functional studies are not available. In summary, the clinical significance of this variant is uncertain. ACMG/AMP criteria have been applied, as specified by the Myeloid Malignancy Variant Curation Expert Panel for RUNX1: PM2_supporting, BP4.

Met criteria codes

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).
BP4	✔	This missense variant has a REVEL score <0.50 (0.447) (BP4).

Not Met criteria codes

PS1	✖	This rule cannot be applied because, to our knowledge, this missense variant does not generate 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, this variant has not been reported in any study.
PS3	✖	To our knowledge, no in vitro or in vivo functional studies are available for this variant.
PS4	✖	This rule cannot be applied since, to our knowledge, this variant has not been reported in any study.
BA1	✖	This rule cannot be applied since the variant is completely absent from all population databases.
PP1	✖	This rule cannot be applied since, to our knowledge, this variant has not been reported in any study and we have no information about its cosegregation with the disease.
PP3	✖	This rule cannot be applied since this missense variant does not have a REVEL score >0.88 (0.447).
PM6	✖	This rule cannot be applied since, to our knowledge, this variant has not been reported in any study.
PVS1	✖	This rule cannot be applied since this is a missense variant.
PM1	✖	This rule cannot be applied since this missense variant affects amino acid residue 277, which is out of RHD or residues 89-204.
PM5	✖	This rule cannot be applied because, to our knowledge, this missense variant does not impact an amino acid residue where a different pathogenic missense change has previously been observed.
PM4	✖	This rule cannot be applied since this is a missense variant.

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, this variant has not been reported in any study and we have no information about its cosegregation with the disease.
BS3		✖	To our knowledge, no in vitro or in vivo functional studies are available for this variant.
BP7		✖	This rule cannot be applied since this is a missense variant.
BP2		✖	This rule cannot be applied since, to our knowledge, this variant has not been reported in any study.

Curation History

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