

Variant: *NM_001754.5(RUNX1):c.741C>T (p.Pro247=)*

Version: 1.0

CA16616523 [↗](#)

415835 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 2f04ea68-4598-4d14-a8ac-578110f008a4

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HGVS expressions

NM_001754.5(RUNX1):c.741C>T (p.Pro247=)

NM_001754.5:c.741C>T

NC_000021.9:g.34834474G>A

CM000683.2:g.34834474G>A

NC_000021.8:g.36206771G>A

CM000683.1:g.36206771G>A

NC_000021.7:g.35128641G>A

NG_011402.2:g.1155238C>T

ENST00000675419.1:c.741C>T

ENST00000300305.7:c.741C>T

ENST00000344691.8:c.660C>T

ENST00000358356.9:c.660C>T

ENST00000399237.6:c.705C>T

ENST00000399240.5:c.532+25000C>T

ENST00000437180.5:c.741C>T

ENST00000469087.1:n.277C>T

ENST00000482318.5:c.*331C>T

NM_001001890.2:c.660C>T

NM_001122607.1:c.660C>T

NM_001754.4:c.741C>T

NM_001001890.3:c.660C>T

NM_001122607.2:c.660C>T

Likely Benign

Met criteria codes **3**

BP4 BP7 PM2_Supporting

Not Met criteria codes **23**

PS1 PS2 PS3 PS4 BP3 BP1
BP2 BP5 PP1 PP2 PP3 PP4
BA1 PM6 PM1 PM3 PM5
PM4 BS2 BS1 BS4 BS3
PVS1

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

Myeloid Malignancy VCEP

NM_001754.5(RUNX1):c.741C>T (p.Pro247=) is a synonymous variant. As such, a REVEL score is not calculable, and there is no predicted effect on protein function. SpliceAI predicted the following: Acceptor loss 0, Donor loss 0, Acceptor gain 0, Donor gain 0. As such, there is no in silico evidence of an effect on splicing(BP4). Evolutionary conservation prediction algorithms predict the site as not being conserved (PhyloP score 1.06724 < 2.0)(BP7). This variant 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 benign. ACMG/AMP criteria applied, as specified by the Myeloid Malignancy Variant Curation Expert Panel for RUNX1: BP4, BP7, PM2_supporting.

Met criteria codes

BP4			This variant is a SYNONYMOUS variant, which does not result in a protein codon change. As such, a REVEL score is not calculable, and there is no predicted effect on protein function. SpliceAI predicted the following: Acceptor loss 0, Donor loss 0, Acceptor gain 0, Donor gain 0. As such, there is no in silico evidence of an effect on splicing. Therefore, BP4 IS MET.
BP7			This variant is a SYNONYMOUS variant, which does not result in a protein codon change. As such, a REVEL score is not calculable, and there is no predicted effect on protein function. SpliceAI predicted the following: Acceptor loss 0, Donor loss 0, Acceptor gain 0, Donor gain 0. As such, there is no in silico evidence of an effect on splicing. Evolutionary conservation prediction algorithms predict the site as not being conserved (PhyloP score 1.06724 < 2.0) Therefore, BP7 IS MET.
PM2_Supporting			This variant is completely absent from all population databases with at least 20x coverage for RUNX1. PM2_SUPPORTING IS MET.

Not Met criteria codes

PS1			This is a synonymous variant, and no other pathogenic variants have been identified at aa position 247. Therefore, PS1 is NOT MET.
PS2			An extensive literature search, including PubMed, Google Scholar, Mastermind and other databases reveal no published literature on this variant. Therefore, no data about de novo occurrences are available. BS4 is NOT MET.
PS3			An extensive literature search, including PubMed, Google Scholar, Mastermind and other databases reveal no published literature on this variant. Therefore, PS3 is NOT MET.
PS4			An extensive literature search, including PubMed, Google Scholar, Mastermind and other databases reveal no published literature on this variant. Therefore, no case-control studies are available. PS4 is NOT MET.
BP3			This rule is not applicable for MM-VCEP
BP1			This rule is not applicable for MM-VCEP

BP2			An extensive literature search, including PubMed, Google Scholar, Mastermind and other databases reveal no published literature on this variant. Therefore, no inheritance data are available. BP2 is NOT MET.
BP5			This rule is not applicable for MM-VCEP
PP1			An extensive literature search, including PubMed, Google Scholar, Mastermind and other databases reveal no published literature on this variant. Therefore, no segregation data are available. PP1 is NOT MET.
PP2			This rule is not applicable for MM-VCEP
PP3			This variant is a SYNONYMOUS variant, which does not result in a protein codon change. As such, a REVEL score is not calculable, and there is no predicted effect on protein function. SpliceAI predicted the following: Acceptor loss 0, Donor loss 0, Acceptor gain 0, Donor gain 0. As such, there is no in silico evidence of an effect on splicing. Therefore, PP3 is NOT MET.
PP4			This rule is not applicable for MM-VCEP
BA1			This variant is completely absent from all population databases with at least 20x coverage for RUNX1. BA1 is NOT MET.
PM6			An extensive literature search, including PubMed, Google Scholar, Mastermind and other databases reveal no published literature on this variant. Therefore, no data about de novo occurrences are available. BS4 is NOT MET.
PM1			This synonymous variant occurs outside of the conserved runt homology domain (aa 89-204); therefore, PM1 is NOT MET.
PM3			This rule is not applicable for MM-VCEP
PM5			This is a synonymous variant, and no other pathogenic variants have been identified at aa position 247. Therefore, PM5 is NOT MET.
PM4			This is a synonymous variant that does not result in protein length changes. As such, PM4 is NOT MET.
BS2			This rule is not applicable for MM-VCEP
BS1			This variant is completely absent from all population databases with at least 20x coverage for RUNX1. BS1 is NOT MET.
BS4			An extensive literature search, including PubMed, Google Scholar, Mastermind and other databases reveal no published literature on this variant. Therefore, no segregation data are available. BS4 is NOT MET.
BS3			An extensive literature search, including PubMed, Google Scholar, Mastermind and other databases reveal no published literature on this variant. Therefore, BS3 is NOT MET.

PVS1

This is a synonymous variant, and not a null variant. Therefore, PVS1 is NOT MET.

Curation History [↗](#)

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