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Variant: NM_001754.4(RUNX1):c.654C>T (p.Ser218=)

Version: 1.0

CA10014384

239052 (ClinVar)

Gene: RUNX1 (HGNC:861)
Condition: hereditary thrombocytopenia with normal platelets-hematological cancer predisposition syndrome (MONDO:0011071)
Inheritance Mode: Autosomal dominant inheritance
UUID: 4b6d6bcb-da2e-42b4-886e-38565501ee4a
Approved on: 2019/8/2
Published on: 2019/8/2

HGVS expressions

NM_001754.4:c.654C>T
NM_001754.4(RUNX1):c.654C>T (p.Ser218=)
NC_000021.9:g.34834561G>A
CM000683.2:g.34834561G>A
NC_000021.8:g.36206858G>A
CM000683.1:g.36206858G>A
NC_000021.7:g.35128728G>A
NG_011402.2:g.1155151C>T
ENST00000675419.1:c.654C>T
ENST00000300305.7:c.654C>T
ENST00000344691.8:c.573C>T
ENST00000358356.9:c.573C>T
ENST00000399237.6:c.618C>T
ENST00000399240.5:c.532+24913C>T
ENST00000437180.5:c.654C>T
ENST00000469087.1:n.190C>T
ENST00000482318.5:c.*244C>T
NM_001001890.2:c.573C>T
NM_001122607.1:c.573C>T
NM_001001890.3:c.573C>T
NM_001122607.2:c.573C>T
NM_001754.5:c.654C>T

Likely Benign

Met criteria codes 2

BS1 BP4

Not Met criteria codes 24

PS1 PS2 PS3 PS4 BA1 PP1
PP2 PP3 PP4 PM6 PM2
PM1 PM3 PM5 PM4 BS2
BS4 BS3 BP5 BP7 BP3 BP1
BP2 PVS1

Evidence Links 0

Expert Panel

Myeloid Malignancy VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Myeloid Malignancy VCEP

The MAF of the synonymous variant, NM_001754.4:c.654C>T (p.Ser218=), is 0.00105 (0.1%, 36/34418 alleles) in the Latino subpopulation of the gnomAD cohort, which is between 0.00015 (0.015%) and 0.0015 (0.15%) (BS1). This synonymous variant is predicted by SSF and MES to lead to an increase in the canonical splice site score or a decrease of the canonical splice site score by no more than 10% AND no putative cryptic splice sites are created (BP4). 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: BS1, BP4.

Met criteria codes

BS1	✔	gnomAD Allele Frequency of Latino Subpopulation: 0.00105 (36 out of 34418 Alleles) > 0.00015
BP4	✔	Synonymous variant for which SSF and MES predict either an increase in the canonical splice site score or a decrease of the canonical splice site score by no more than 10% AND no putative cryptic splice sites are created.

Not Met criteria codes

PS1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS3	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS4	✖	PMID: 27106701, mutational analysis from peripheral blood cells, not confirmed germline variants. PS4 can not apply in combined with BS1.
BA1	✖	gnomAD Allele Frequency of Latino Subpopulation: 0.00105 (36 out of 34418 Alleles) < 0.0015
PP1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP2	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP4	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

PM6	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM2	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM3	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM5	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM4	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS2	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS4	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP5	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP7	✖	phyloP100way: 4.58487 >0.1
BP3	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP2	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PVS1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_001754.4(RUNX1):c.654C>T (p.Ser...	Likely Benign	Hereditary Thrombocytopenia With Normal Platelets-Hematological Cancer Predisposition Syndrome	2019-08-02	1.0	-	RUNX1

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