Variant: NM_001754.5(RUNX1):c.1396A>G (p.Met466Val)

Version: 1.1

CA10014177

1002421 (ClinVar)

Gene: RUNX1 (HGNC:861)
Condition: hereditary thrombocytopenia and hematologic cancer predisposition syndrome (MONDO:0011071)
Inheritance Mode: Autosomal dominant inheritance
UUID: 32058939-e3a4-4a3d-8d5c-78f1fe956233
Approved on: 2025-05-02
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HGVS expressions

NM_001754.5:c.1396A>G
NM_001754.5(RUNX1):c.1396A>G (p.Met466Val)
NC_000021.9:g.34792182T>C
CM000683.2:g.34792182T>C
NC_000021.8:g.36164479T>C
CM000683.1:g.36164479T>C
NC_000021.7:g.35086349T>C
NG_011402.2:g.1197530A>G
ENST00000675419.1:c.1396A>G
ENST00000300305.7:c.1396A>G
ENST00000344691.8:c.1315A>G
ENST00000399240.5:c.1123A>G
ENST00000437180.5:c.1396A>G
ENST00000482318.5:c.*986A>G
NM_001001890.2:c.1315A>G
NM_001754.4:c.1396A>G
NM_001001890.3:c.1315A>G

Uncertain Significance

Met criteria codes 1

BP4

Not Met criteria codes 23

PP1 PP2 PP4 PM6 PM2 PM1 PM3 PM5 PM4 PVS1 BS2 BS1 BS4 BS3 PS1 PS2 PS3 PS4 BP3 BP1 BP2 BP5 BP7

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.1396A>G (p.Met466Val) is a missense variant which has a REVEL score ≤0.50 (0.203) and SpliceAI is ≤0.20 (0.00) (BP4). In summary, the clinical significance of this variant is uncertain. ACMG/AMP criteria applied, as specified by the Myeloid Malignancy Variant Curation Expert Panel for RUNX1: BP4.

Met criteria codes

BP4	✔	This missense variant has a REVEL score < 0.50 (0.203) and a SpliceAI score ≤ 0.20 (0.00) (BP4).

Not Met criteria codes

PP1	✖	No case studies found
PP2	✖	This rule is not applicable for MM-VCEP
PP4	✖	This rule is not applicable for MM-VCEP
PM6	✖	No case studies found
PM2	✖	gnomAD v.4.1.0: 5/1144916 alleles in European (non-Finish) sub-population, MAF: 0.0004376% This variant is present in at least one population database.
PM1	✖	Not located in a hotspot or a critical region
PM3	✖	This rule is not applicable for MM-VCEP
PM5	✖	Amino Acid location has been curated as Benign by MMVCEP
PM4	✖	Not an in-frame deletion/insertion
PVS1	✖	Not a null/truncating variant
BS2	✖	This rule is not applicable for MM-VCEP
BS1	✖	gnomAD v.4.1.0: 5/1144916 alleles in European (non-Finish) sub-population, MAF: 0.0004376% This variant does not have a MAF between 0.00015 (0.015%) and 0.0015 (0.15%) in any general continental dataset.
BS4	✖	No case studies found
BS3	✖	No functional studies found
PS1	✖	Amino Acid location has been curated as Benign by MMVCEP

PS2		✖	No case studies found
PS3	ℹ	✖	No functional studies found
PS4	ℹ	✖	This variant has been reported in one proband meeting at least one of the RUNX1-phenotypic criteria (PS4_ Supporting; PMID: 32855275) however not confirmed as germline
BP3		✖	This rule is not applicable for MM-VCEP
BP1		✖	This rule is not applicable for MM-VCEP
BP2	ℹ	✖	Variant only present in gnomAD v2.1.1 and does not meet code criteria
BP5		✖	This rule is not applicable for MM-VCEP
BP7	ℹ	✖	Not a synonymous or intronic variant

Curation History

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