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_001754.4(RUNX1):c.*4188G>C*

CA10644605

339794 (ClinVar)

Gene: RUNX1 (HGNC:861)
Condition: hereditary thrombocytopenia and hematologic cancer predisposition syndrome (MONDO:0011071)
Inheritance Mode: Autosomal dominant inheritance
UUID: 912add43-9404-4257-a2a6-c545861ad7ef
Approved on: 2021-05-26
Published on: 2022-07-08

HGVS expressions

NM_001754.4:c.*4188G>C
NM_001754.4(RUNX1):c.*4188G>C
NC_000021.9:g.34787947C>G
CM000683.2:g.34787947C>G
NC_000021.8:g.36160244C>G
CM000683.1:g.36160244C>G
NC_000021.7:g.35082114C>G
NG_011402.2:g.1201765G>C
ENST00000675419.1:c.*4188G>C
ENST00000300305.7:c.*4188G>C
ENST00000344691.8:c.*4188G>C
ENST00000437180.5:c.*4188G>C
NM_001001890.2:c.*4188G>C
NM_001001890.3:c.*4188G>C
NM_001754.5:c.*4188G>C
NM_001754.5(RUNX1):c.*4188G>C

Likely Benign

The Expert Panel has overridden the computationally generated classification - "*Uncertain Significance - Insufficient Evidence*"

Met criteria codes 1

BS1

Not Met criteria codes 25

PP4 PP1 PP3 PP2 PM1 PM4 PM3 PM5 PM6 PM2 PS2 PS4 PS3 PS1 BA1 PVS1 BP7 BP5 BP3 BP2 BP4 BP1 BS4 BS3 BS2

Evidence Links 0

Expert Panel

Myeloid Malignancy VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Myeloid Malignancy VCEP

This 3' UTR c.*4188G>C variant is located at a non-conserved nucleotide per an evolutionary conservation prediction algorithm (PhyloP = -0.665764 in GRCh38). The variant is present in gnomAD at an allele frequency between 0.015% and 0.15% in a general continental population (European, non-Finnish, subpopulation: 0.03528% in v3) with >5 variant alleles and a minimum of 2000 total alleles (BS1) and has not been described in the literature. In summary, this variant meets criteria to be classified as likely benign. ACMG/AMP criteria applied, as specified by the ClinGen Myeloid Malignancy Variant Curation Expert Panel for RUNX1: BS1.

Met criteria codes

BS1	✔	Variant is present in >=5 alleles in the European (non-Finnish) population (has required minimum of 2000 alleles) with an MAF of 0.03528% (v3.1.1), which is within the BS1 thresholds (0.015%-0.15%). - gnomAD v2.1.1: ALL: 0.009554% (3/31402) - NFE: 0.01297% (2/15424) - OTH: 0.09208% (1/1086) - gnomAD v3.1.1: ALL: 0.02168% (33/152196) - NFE: 0.03528% (24/38024) - AMR: 0.02616% (4/15290) - ASJ: 0.05760% (2/3472) - OTH: 0.09579% (2/2088)

Not Met criteria codes

PP4	✖	Not applicable
PP1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3	✖	No donor/acceptor gains or losses predicted with SpliceAI Δ score >= 0.38.
PP2	✖	Not applicable
PM1	✖	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
PM3	✖	Not applicable
PM5	✖	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	✖	Variant is present in >=5 alleles in the European (non-Finnish) population (has required minimum of 2000 alleles) with an MAF of 0.03528% (v3.1.1), which is within the BS1 thresholds (0.015%-0.15%). - gnomAD v2.1.1: ALL: 0.009554% (3/31402) - NFE: 0.01297% (2/15424) - OTH: 0.09208% (1/1086) - gnomAD v3.1.1: ALL: 0.02168% (33/152196) - NFE: 0.03528% (24/38024) - AMR: 0.02616% (4/15290) - ASJ: 0.05760% (2/3472) - OTH: 0.09579% (2/2088)

PS2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS4	ℹ	✖	No literature found in HGMD, Google+Google Scholar searches, or COSMIC.
PS3	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS1	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1	ℹ	✖	Variant is present in >=5 alleles in the European (non-Finnish) population (has required minimum of 2000 alleles) with an MAF of 0.03528% (v3.1.1), which is within the BS1 thresholds (0.015%-0.15%). - gnomAD v2.1.1: ALL: 0.009554% (3/31402) - NFE: 0.01297% (2/15424) - OTH: 0.09208% (1/1086) - gnomAD v3.1.1: ALL: 0.02168% (33/152196) - NFE: 0.03528% (24/38024) - AMR: 0.02616% (4/15290) - ASJ: 0.05760% (2/3472) - OTH: 0.09579% (2/2088)
PVS1	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP7	ℹ	✖	3'UTR variant that is located at a non-conserved nucleotide (PhyloP = -0.665764 in GRCh38), and the variant is the reference nucleotide in one primate and/or 3 mammals.
BP5		✖	Not applicable
BP3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP2	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4	ℹ	✖	No donor/acceptor gains or losses predicted (SpliceAI Δ score <= 0.2), but does not apply for UTR variants.
BP1		✖	Not applicable
BS4	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS2		✖	Not applicable

Curation History

See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene

No matching records found