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_001754.5(RUNX1):c.702A>G (p.Thr234=)

Version: 1.0

CA512318619

1147528 (ClinVar)

Gene: RUNX1 (HGNC:861)
Condition: hereditary thrombocytopenia and hematologic cancer predisposition syndrome (MONDO:0011071)
Inheritance Mode: Autosomal dominant inheritance
UUID: 8f58b5ea-df99-41a3-a72f-23315c1b5196
Approved on: 2022/6/30
Published on: 2022/6/30

HGVS expressions

NM_001754.5:c.702A>G
NM_001754.5(RUNX1):c.702A>G (p.Thr234=)
NC_000021.9:g.34834513T>C
CM000683.2:g.34834513T>C
NC_000021.8:g.36206810T>C
CM000683.1:g.36206810T>C
NC_000021.7:g.35128680T>C
NG_011402.2:g.1155199A>G
ENST00000675419.1:c.702A>G
ENST00000300305.7:c.702A>G
ENST00000344691.8:c.621A>G
ENST00000358356.9:c.621A>G
ENST00000399237.6:c.666A>G
ENST00000399240.5:c.532+24961A>G
ENST00000437180.5:c.702A>G
ENST00000469087.1:n.238A>G
ENST00000482318.5:c.*292A>G
NM_001001890.2:c.621A>G
NM_001122607.1:c.621A>G
NM_001754.4:c.702A>G
NM_001001890.3:c.621A>G
NM_001122607.2:c.621A>G

Likely Benign

Met criteria codes 3

BP7 BP4 PM2_Supporting

Not Met criteria codes 18

BP3 BP1 PVS1 PS1 PS2 PS3 PS4 BA1 PP1 PP2 PP3 PP4 PM5 PM4 PM6 BS1 BS4 BS3

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

The c.702A>G (p.Thr234=) variant is a synonymous variant that is not predicted by SpliceAI to impact splicing (BP4). In addition, an evolutionary conservation algorithm predicts the site as being non-conserved (PhyloP score = -0.138811 in GRCh38), and the variant is the reference nucleotide in one primate and/or three mammal species. Although the variant is absent from gnomAD v2 and v3 (PM2_Supporting), it has not been reported in cases or the literature. In summary, this variant meets the criteria to be classified as likely benign for hereditary thrombocytopenia and hematologic cancer predisposition syndrome based on the ACMG/AMP criteria applied, as specified by the ClinGen Myeloid Malignancy VCEP: BP4, BP7, and PM2_Supporting.

Met criteria codes

BP7	✔	The c.702A>G (p.Thr234=) variant is a synonymous (silent) variant that is not predicted by SpliceAI to impact splicing. In addition, an evolutionary conservation algorithm predicts the site as being non-conserved (PhyloP score = -0.138811 in GRCh38), and the variant is the reference nucleotide in one primate and/or three mammal species.
BP4	✔	SpliceAI doesn't predict any significant splicing impact (Δ scores ≤ 0.20).
PM2_Supporting	✔	Completely absent from gnomAD with a mean coverage of at least 20X (v2 and v3).

Not Met criteria codes

BP3	✖	Not applicable
BP1	✖	Not applicable
PVS1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2	✖	No literature was found in LOVD, HGMD, ClinVar, COSMIC, Mastermind, and Google/Google Scholar searches.
PS3	✖	No literature was found in LOVD, HGMD-, ClinVar, COSMIC, Mastermind, and Google/Google Scholar searches-.
PS4	✖	No cases or literature were found in LOVD, HGMD, ClinVar, COSMIC, Mastermind, and Google/Google Scholar searches.
BA1	✖	Completely absent from gnomAD with a mean coverage of at least 20X (v2 and v3).
PP1	✖	No literature was found in LOVD, HGMD-, ClinVar, COSMIC, Mastermind, and Google/Google Scholar searches-.

PP2		✖	Not applicable
PP3	ℹ	✖	SpliceAI doesn't predict any significant splicing impact (Δ scores ≤ 0.20).
PP4		✖	Not applicable
PM5	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM4	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM6	ℹ	✖	No literature was found in LOVD, HGMD, ClinVar, COSMIC, Mastermind, and Google/Google Scholar searches.
BS1	ℹ	✖	Completely absent from gnomAD with a mean coverage of at least 20X (v2 and v3).
BS4	ℹ	✖	No literature was found in LOVD, HGMD-, ClinVar, COSMIC, Mastermind, and Google/Google Scholar searches-.
BS3	ℹ	✖	No literature was found in LOVD, HGMD-, ClinVar, COSMIC, Mastermind, and Google/Google Scholar searches-.

Curation History

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See Report	Preferred Variant Title	Classification ℹ	Condition	Published Date	Version ℹ	Criteria Specification	Gene
View	NM_001754.5(RUNX1):c.702A>G (p.Th...	Likely Benign	Hereditary Thrombocytopenia And Hematologic Cancer Predisposition Syndrome	2022-06-30	1.0	ClinGen Myeloid Malignancy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 2	RUNX1

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