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Variant: NM_001754.5(RUNX1):c.300C>G (p.Ser100=)

Version: 1.0

CA512318845

463991 (ClinVar)

Gene: RUNX1 (HGNC:861)
Condition: hereditary thrombocytopenia and hematologic cancer predisposition syndrome (MONDO:0011071)
Inheritance Mode: Autosomal dominant inheritance
UUID: e9ec7bd4-3aef-416c-9b22-48d87e0afa88
Approved on: 2022/7/7
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HGVS expressions

NM_001754.5(RUNX1):c.300C>G (p.Ser100=)
NM_001754.5:c.300C>G
NC_000021.9:g.34886894G>C
CM000683.2:g.34886894G>C
NC_000021.8:g.36259191G>C
CM000683.1:g.36259191G>C
NC_000021.7:g.35181061G>C
NG_011402.2:g.1102818C>G
ENST00000675419.1:c.300C>G
ENST00000300305.7:c.300C>G
ENST00000344691.8:c.219C>G
ENST00000358356.9:c.219C>G
ENST00000399237.6:c.264C>G
ENST00000399240.5:c.219C>G
ENST00000437180.5:c.300C>G
ENST00000455571.5:c.261C>G
ENST00000482318.5:c.59-6181C>G
NM_001001890.2:c.219C>G
NM_001122607.1:c.219C>G
NM_001754.4:c.300C>G
NM_001001890.3:c.219C>G
NM_001122607.2:c.219C>G

Likely Benign

Met criteria codes 3

BP7 BP4 PM2_Supporting

Not Met criteria codes 23

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

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.300C>G (p.Ser100=) is a synonymous variant. In summary, this variant meets the criteria to be classified as likely benign. Therefore, a REVEL score is not calculable. SpliceAI prediction suggests Acceptor loss 0, Donor loss 0, Acceptor gain 0, Donor gain 0. Therefore, there appears to be no effect on splicing (BP4). Evolutionary conservation prediction algorithms predict the site as not being conserved (PhyloP score -0.302402 < 2.0)(BP7). This variant is completely absent from all population databases with at least 20x coverage for RUNX1(PM2_supporting). ACMG/AMP criteria applied, as specified by the Myeloid Malignancy Variant Curation Expert Panel for RUNX1: BP4, BP7, PM2_supporting.

Met criteria codes

BP7	✔	This is a synonymous variant with no effect on the final amino acid codon. Therefore, a REVEL score is not calculable. SpliceAI prediction suggests: Acceptor loss 0, Donor loss 0, Acceptor gain 0, Donor gain 0. Therefore, there appears to be no effect on splicing. Given the above, PP3 is NOT MET. Evolutionary conservation prediction algorithms predict the site as not being conserved (PhyloP score -0.302402 < 2.0). Therefore, BP7 IS MET.
BP4	✔	This is a synonymous variant with no effect on the final amino acid codon. Therefore, a REVEL score is not calculable. SpliceAI prediction suggests: Acceptor loss 0, Donor loss 0, Acceptor gain 0, Donor gain 0. Therefore, there appears to be no effect on splicing. Given the above, BP4 is MET.
PM2_Supporting	✔	This variant is completely absent from all population databases with at least 20x coverage for RUNX1. Therefore, PM2 is MET.

Not Met criteria codes

PVS1	✖	This is a synonymous variant, therefore PVS1 is NOT MET.
PM6	✖	An extensive literature search of PubMed, Google Scholar, and Mastermind revealed no literature on this variant. Therefore, there are no de novo data from studies available. PM6 is NOT MET.
PM1	✖	This is not applicable for a synonymous variant
PM3	✖	This rule is not applicable for MM-VCEP
PM5	✖	This is not applicable for a synonymous variant
PM4	✖	This is a synonymous variant, which not result in a protein length altering variant. Therefore, PM4 is NOT MET.
BA1	✖	This variant is completely absent from all population databases with at least 20x coverage for RUNX1. Therefore, BA1 is NOT MET.
BS1	✖	

This variant is completely absent from all population databases with at least 20x coverage for RUNX1. Therefore, BS1 is NOT MET.

BS4	✖	An extensive literature search of PubMed, Google Scholar, and Mastermind revealed no literature on this variant. Therefore, there are no segregation studies available. BS4 is NOT MET.
BS3	✖	An extensive literature search of PubMed, Google Scholar, and Mastermind revealed no literature on this variant. Therefore, there are no functional studies available. BS3 is NOT MET.
BS2	✖	This rule is not applicable for MM-VCEP
BP5	✖	This rule is not applicable for MM-VCEP
BP3	✖	This rule is not applicable for MM-VCEP
BP1	✖	This rule is not applicable for MM-VCEP
BP2	✖	An extensive literature search of PubMed, Google Scholar, and Mastermind revealed no literature on this variant. Therefore, there are no inheritance data from studies available. BP2 is NOT MET.
PS1	✖	This is not applicable for a synonymous variant
PS2	✖	An extensive literature search of PubMed, Google Scholar, and Mastermind revealed no literature on this variant. Therefore, there are no de novo data from studies available. PS2 is NOT MET.
PS3	✖	An extensive literature search of PubMed, Google Scholar, and Mastermind revealed no literature on this variant. Therefore, there are no functional studies available. BS3 is NOT MET.
PS4	✖	An extensive literature search of PubMed, Google Scholar, and Mastermind revealed no literature on this variant. Therefore, there are no allele burden data from studies available. PS4 is NOT MET.
PP1	✖	An extensive literature search of PubMed, Google Scholar, and Mastermind revealed no literature on this variant. Therefore, there are no segregation studies available. PP1 is NOT MET.
PP2	✖	This rule is not applicable for MM-VCEP
PP3	✖	This is a synonymous variant with no effect on the final amino acid codon. Therefore, a REVEL score is not calculable. SpliceAI prediction suggests: Acceptor loss 0, Donor loss 0, Acceptor gain 0, Donor gain 0. Therefore, there appears to be no effect on splicing. Given the above, PP3 is NOT MET.
PP4	✖	This rule is not applicable for MM-VCEP

Curation History

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