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Variant: NM_000133.4(F9):c.520G>A (p.Val174Met)

Version: 1.0

CA414439515

811516 (ClinVar)

Gene: F9 (HGNC:2158)
Condition: hemophilia B (MONDO:0010604)
Inheritance Mode: X-linked inheritance
UUID: 057e3f28-6e3a-42f3-91c9-53d21cc20e9d
Approved on: 2024/11/5
Published on: 2025/1/7

HGVS expressions

NM_000133.4(F9):c.520G>A (p.Val174Met)
NM_000133.4:c.520G>A
NC_000023.11:g.139548491G>A
CM000685.2:g.139548491G>A
NC_000023.10:g.138630650G>A
CM000685.1:g.138630650G>A
NC_000023.9:g.138458316G>A
NG_007994.1:g.22756G>A
ENST00000218099.7:c.520G>A
ENST00000643157.1:n.1187G>A
ENST00000218099.6:c.520G>A
ENST00000394090.2:c.406G>A
NM_000133.3:c.520G>A
NM_001313913.1:c.406G>A
NM_001313913.2:c.406G>A

Likely Pathogenic

Met criteria codes 4

PM1 PS4 PP3 PM2_Supporting

Evidence Links 0

Expert Panel

Coagulation Factor Deficiency VCEP

Criteria Specification Information

Criteria Specification: *ClinGen Coagulation Factor Deficiency Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for F9 Version 1.0.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Coagulation Factor Deficiency VCEP

The NM_000133.4(F9):c.520G>A (p.Val174Met) missense variant is completely absent from gnomAD v2.1.1 and v3.1.2 meeting criteria for PM2_Supporting. The variant has a REVEL score of 0.811 (>0.6) meeting criteria for PP3. The variant changes the last nucleotide of exon 5 and SpliceAI predicts a donor loss of intron 5 (delta score of 0.66) meeting criteria for PM1. At least four probands with moderate or

severe hemophilia B are reported in the literature and internal laboratory data (PMID: 1680287; doi: 10.5336/medsci.2020-75066), meeting criteria for PS4. In summary, this variant meets criteria to be classified as likely pathogenic. ACMG/AMP criteria applied, as specified by the Coagulation Factor Deficiency Variant Curation Expert Panel for F9 (Released 10/5/2023): PM1, PS4_Moderate, PP3, PM2_Supporting.

Met criteria codes

PM1	✔	The variant affects the last nucleotide of exon 5. PM1 criteria met as variant occurs within exon 3 through 5.
PS4	✔	At least four probands with moderate or severe hemophilia B are reported in the literature and internal laboratory data (PMID: 1680287; doi: 10.5336/medsci.2020-75066), meeting criteria for PS4.
PP3	✔	The c.520G>A (p.Val174Met) variant has a REVEL score of 0.811 (>0.6). The variant changes the last nucleotide of exon 5 and SpliceAI predicts a donor loss of intron 5 (delta score of 0.66)
PM2_Supporting	✔	The c.520G>A (p.Val174Met) missense variant is completely absent from gnomAD v2.1.1 and v3.1.2

Curation History

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