

Variant: *NM_000133.3(F9):c.1095A>G (p.Ser365=)*

Version: 1.0

CA10529870 [↗](#)

368002 (ClinVar) [↗](#)

Gene: F9 ([HGNC:2158](#))

Condition: hemophilia B ([MONDO:0010604](#))

Inheritance Mode: X-linked inheritance

UUID: 565fc8ba-d4a0-42b7-a317-4db5d2751962

Approved on: 2024/2/9

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HGVS expressions

NM_000133.3(F9):c.1095A>G (p.Ser365=)

NM_000133.3:c.1095A>G

NC_000023.11:g.139561780A>G

CM000685.2:g.139561780A>G

NC_000023.10:g.138643939A>G

CM000685.1:g.138643939A>G

NC_000023.9:g.138471605A>G

NG_007994.1:g.36045A>G

ENST00000218099.7:c.1095A>G

ENST00000643157.1:n.1723+39A>G

ENST00000218099.6:c.1095A>G

ENST00000394090.2:c.981A>G

NM_001313913.1:c.981A>G

NM_000133.4:c.1095A>G

NM_001313913.2:c.981A>G

Benign

Met criteria codes **3**

BA1 **BP4** **BP7**

Not Met criteria codes **2**

PM1 **PS4**

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_000133.3:c.1095A>G variant predicts a synonymous change, Ser365=. It is reported at a high frequency of 0.03271 (622/19015 alleles with 172 hemizygotes) in the African subpopulation in gnomAD v2.1.1, meeting the BA1 cut-off of ≥ 0.0000556 . The variant is not predicted to impact splicing, and the nucleotide position at which this variant occurs is not highly conserved, meeting the BP4 and BP7

criteria. To the best of our knowledge, the variant has not been reported in male patients with Hemophilia B. In summary, the variant meets criteria to be classified as benign. ACMG/AMP criteria applied, as specified by the Coagulation Factor Deficiency Variant Curation Expert Panel for F9: BA1, BP4, BP7.

Met criteria codes

BA1			The variant is reported at a frequency of 0.03271 (622/19015 alleles with 172 hemizygotes) in gnomAD v2.1.1 and at a frequency of 0.03197 (1000/31280 alleles with 269 hemizygotes) in gnomAD v3, in the African population. The reported MAFs are higher than the BA1 cut-off for F9 determined by the CFD VCEP: >=0.0000556
BP4			HSF and MES predict no impact on splicing.
BP7			HSF and MES predict no impact on splicing. HSF predicts creation of cryptic splice sites, but there is no concordance with MES. The variant nucleotide is the reference in at least 3 mammals and the PhyloP score for this position is -1.77305 (from UCSC); therefore, the nucleotide is not conserved.

Not Met criteria codes

PM1			The variant occurs in the peptidase S1 region, between aa position 227-459, which is determined to be a region critical to protein function by the CFD VCEP. However, PM1 has not been applied for this high-frequency variant.
PS4			PS4 not applied when variant meets BA1 or BS1. The variant is not reported in male patients with Hemophilia B in the literature, to the best of our knowledge. From internal laboratory data: the variant was identified in a male with moderate-severe Hemophilia B, with inhibitors. An alternate pathogenic variant in F9 was also identified in this patient.

Curation History



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