

Variant: *NM_000133.3(F9):c.88G>A (p.Val30Ile)*

Version: 1.0

CA414434500 [↗](#)

651569 (ClinVar) [↗](#)

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

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

Inheritance Mode: X-linked inheritance

UUID: b731a335-3a67-4702-b7ce-39076c05c72e

Approved on: 2024/5/9

Published on: 2024/7/11

HGVS expressions

NM_000133.3:c.88G>A

NM_000133.3(F9):c.88G>A (p.Val30Ile)

NC_000023.11:g.139530852G>A

CM000685.2:g.139530852G>A

NC_000023.10:g.138613011G>A

CM000685.1:g.138613011G>A

NC_000023.9:g.138440677G>A

NG_007994.1:g.5117G>A

ENST00000218099.7:c.88G>A

ENST00000218099.6:c.88G>A

ENST00000394090.2:c.88G>A

ENST00000479617.2:n.95G>A

NM_001313913.1:c.88G>A

NM_000133.4:c.88G>A

NM_001313913.2:c.88G>A

Likely Pathogenic

Met criteria codes **4**

PS4

PS3_Supporting

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 c.88G>A (NM_000133.3) variant in F9 is a missense variant predicted to cause substitution of Valine by Isoleucine at amino acid 30 (p.Val30Ile). This variant has been reported in at least 5 probands meeting the hemophilia B phenotype criteria specified by the Coagulation Factor Deficiency VCEP (PS4; PMID: 10094553, 23093250, 1680287, 11122099). This variant is absent from gnomAD v2.1.1 and

v3.1.2 (PM2_Supporting). Secreted conformation-specific reporter (SCSR) assay in HEK293T cells showed decreased SCSR level at ~60% of that of the WT, indicating that this variant impacts protein function (PMID: 32766856; the study is approved by the VCEP, applicable at the Supporting strength; PS3_Supporting). The computational predictor REVEL gives a score of 0.787, which is above the threshold of 0.6, evidence that correlates with impact to F9 function. The variant is the last amino acid of exon 1. The computational splicing predictor SpliceAI gives a score of 0.96 for donor loss, predicting that the variant disrupts the donor splice site of intron 1 of F9 (PP3). In summary, this variant meets the criteria to be classified as Likely Pathogenic for X-linked recessive hemophilia B based on the ACMG/AMP criteria applied, as specified by the ClinGen Coagulation Factor Deficiency VCEP: PS4, PP3, PS3_Supporting, PM2_Supporting. (ClinGen Coagulation Factor Deficiency Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for F9 Version 1.0.0., Released 10/5/2023)

Met criteria codes

PS4			This variant has been reported in at least 5 probands meeting the hemophilia B phenotype criteria specified by the Coagulation Factor Deficiency VCEP (PS4; PMID: 10094553, 23093250, 1680287, 11122099).
PS3_Supporting			Secreted conformation-specific reporter (SCSR) assay in HEK293T cells showed decreased SCSR level at ~60% of that of the WT, indicating that this variant impacts protein function (PMID: 32766856; the study is approved by the VCEP, applicable at the Supporting strength; PS3_Supporting).
PP3			The computational predictor REVEL gives a score of 0.787, which is above the threshold of 0.6, evidence that correlates with impact to F9 function. The variant is the last amino acid of exon 1. The computational splicing predictor SpliceAI gives a score of 0.96 for donor loss, predicting that the variant disrupts the donor splice site of intron 1 of F9 (PP3).
PM2_Supporting			This variant is absent from gnomAD v2.1.1 and v3.1.2 (PM2_Supporting).

Curation History



 ▾

 ▾

Showing 1 to 1 of 1 rows

--

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.