

Variant: NM_001313913.2:c.689G>A

Version: 1.0

CA414443541 [↗](#)

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

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

Inheritance Mode: X-linked inheritance

UUID: 6e32ad07-8030-4bf1-a955-0c857e980a91

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HGVS expressions

NM_001313913.2:c.689G>A

NC_000023.11:g.139560820G>A

CM000685.2:g.139560820G>A

NC_000023.10:g.138642979G>A

CM000685.1:g.138642979G>A

NC_000023.9:g.138470645G>A

NG_007994.1:g.35085G>A

ENST00000218099.7:c.803G>A

ENST00000643157.1:n.1470G>A

ENST00000218099.6:c.803G>A

ENST00000394090.2:c.689G>A

NM_000133.3:c.803G>A

NM_001313913.1:c.689G>A

NM_000133.4:c.803G>A

Pathogenic

Met criteria codes 4

PS4 PP3 PS2_Very Strong

PM2_Supporting

Not Met criteria codes 1

PM1

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.803G>A (NM_000133.4) variant in F9 is a missense variant predicted to cause substitution of cysteine by tyrosine at amino acid 268 (p.Cys268Tyr). This variant has been previously reported in 4 patients with severe FIX deficiency, including at least 2 probands with de novo occurrence (maternity and paternity confirmed in a carrier female/maternity confirmed in an affected male) (PMID: 30648777; PMID: 30210749; PMID: 34590426), meeting PS4 and PS2_Very strong. This variant is absent from males in population databases (gnomAD

v2.1.1/gnomAD v3.1/ gnomAD v4.1.0), meeting PM2_Supporting. The computational predictor REVEL gives a score of 0.989, which is above the threshold of 0.6, evidence that correlates with impact to F9 function, meeting PP3. In summary, this variant meets criteria to be classified as pathogenic. ACMG/AMP criteria applied, as specified by the Coagulation Factor Deficiency Variant Curation Expert Panel for F9: PS2_Very Strong, PS4, PM2_Supporting, PP3. (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 4 probands (4-7 probands & 0 gnomAD alleles) meeting phenotypic criteria for F9.
PP3			The computational predictor REVEL gives a score of 0.989, which is above the threshold of 0.6, evidence that correlates with impact to F9 function (PP3). This variant is predicted to have no impact on splicing based on SpliceAI in silico prediction scores (delta 0, 0, 0, 0).
PS2_Very Strong			There are 2 probands with isolated reduction in FIX activity levels meeting phenotypic criteria for F9, with confirmed de novo (maternity and paternity confirmed in a carrier female/maternity confirmed in an affected male) occurrence. Using the SVI point system, each proband in Lu et al counts for 2 pts (4 pts total), meeting PS2_VS.
PM2_Supporting			This variant is absent from males in population databases (gnomad v2.1.1, v3.1, and v4.1.0).

Not Met criteria codes

PM1			Variant is not within exons 3, 4 or 5.
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Curation History

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