

Variant: *NM_000133.3(F9):c.316G>A (p.Gly106Ser)*

Version: 1.0

CA255329 [↗](#)

10579 (ClinVar) [↗](#)

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

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

Inheritance Mode: X-linked inheritance

UUID: 36950276-dd4c-48f7-ba60-d0c1aa45b4d6

Approved on: 2024/2/9

Published on: 2024/7/11

HGVS expressions

NM_000133.3(F9):c.316G>A (p.Gly106Ser)

NM_000133.3:c.316G>A

NC_000023.11:g.139541114G>A

CM000685.2:g.139541114G>A

NC_000023.10:g.138623273G>A

CM000685.1:g.138623273G>A

NC_000023.9:g.138450939G>A

NG_007994.1:g.15379G>A

ENST00000218099.7:c.316G>A

ENST00000218099.6:c.316G>A

ENST00000394090.2:c.277+3728G>A

ENST00000479617.2:n.269G>A

NM_001313913.1:c.277+3728G>A

NM_000133.4:c.316G>A

NM_001313913.2:c.277+3728G>A

Pathogenic

Met criteria codes 5

PP4_Moderate

PP1

PP3

PS4

PM1

Not Met criteria codes 3

BS1

PM5

PM2

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.316G>A (p.Gly106Ser) variant affects one of the functional domains (aa 93-129; EGF-like 1 domain) in the F9 protein, meeting the PM1 criteria. This missense variant has a REVEL score of 0.905(>0.6), meeting the PP3 criteria. It is reported at an MAF of 0.00002441 (5/204867 alleles) in the overall population in gnomAD v2.1.1, with 3 hemizygotes; however BS1 criteria of MAF >=0.0000278 is not met.

Over 60 patients with mild and moderate hemophilia B are reported in the literature meeting PS4_Very strong and PP4_Moderate criteria (PMID: 22103590, 29296726). In summary, the clinical significance of this variant is pathogenic. ACMG/AMP criteria applied, as specified by the Coagulation Factor Deficiency Variant Curation Expert Panel for F9: PS4_Very strong, PM1, PP4_Moderate, PP3.

Met criteria codes

PP4_Moderate			Male with mild hemophilia B with 16% factor IX activity level who had F8 and F9 full gene sequencing with deletion/duplication analysis.
PP1			Two brothers are reported with the Gly106Ser variant and mild hemophilia B. They have a positive family history, with an affected maternal uncle who was not genotyped.
PP3			The c.316G>A (p.Gly106Ser) missense variant has a REVEL score of 0.905(>0.6)
PS4			21 patients with mild and moderate hemophilia B reported in PMID: 22103590 meet F9 phenotype criteria and are counted towards PS4_Very Strong. Several additional probands are reported in the literature and EAHAD notes 150 patients, but the maximum threshold for PS4_Very Strong has been reached. A founder effect is suggested for this variant as several patients of European descent analyzed in the US share 3 common haplotypes (PMID: 1916816). 3 males are reported in gnomAD, so this variant current meets the criteria for application of PS4.
PM1			The c.316G>A (p.Gly106Ser) variant affects one of the functional domains (aa 93-129; EGF-like 1 domain) in the F9 protein and meets criteria for PM1.

Not Met criteria codes

BS1			The c.316G>A (p.Gly106Ser) variant is reported at an MAF of 0.00002441(5/204867 alleles) in the overall population ingnomAD v2.1.1, with 3hemizygotes; however BS1 criteria of MAF >=0.0000278 is not met.
PM5			Gly106Arg, Gly106Cys, Gly106Asp are variants at the same residue. These are not evaluated by the CFD-VCEP yet.
PM2			The variant is reported in gnomAD v2.1.1. is 3 hemizygotes and does not meet criteria for 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.