

Variant: *NM_000132.4(F8):c.5186G>A (p.Gly1729Glu)*

Version: 1.2

CA414913556 [↗](#)

439677 (ClinVar) [↗](#)

Gene: F8 ([HGNC:2157](#))

Condition: hemophilia A ([MONDO:0010602](#))

Inheritance Mode: X-linked inheritance

UUID: b04e4205-4eab-440e-831c-2554db35fd1a

Approved on: 2024/10/11

Published on: 2026/1/26

HGVS expressions

NM_000132.4(F8):c.5186G>A (p.Gly1729Glu)

NM_000132.4:c.5186G>A

NC_000023.11:g.154928604C>T

CM000685.2:g.154928604C>T

NC_000023.10:g.154156879C>T

CM000685.1:g.154156879C>T

NC_000023.9:g.153810073C>T

NG_011403.1:g.99120G>A

NG_011403.2:g.99120G>A

ENST00000360256.9:c.5186G>A

ENST00000360256.8:c.5186G>A

NM_000132.3:c.5186G>A

Likely Pathogenic

Met criteria codes **5**

PM2_Supporting

PS4

PP1

PP3

PP4

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 F8 Version 1.0.0*

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Coagulation Factor Deficiency VCEP

The c.5186G>A variant in F8 is a missense variant predicted to cause substitution of glycine by glutamic acid at amino acid 1729 (p.Gly1729Glu). This variant is absent from males in population databases (gnomAD v2.1.1/gnomAD v3). The missense variant has a REVEL score of 0.861 (>0.6), meeting criteria for PP3. This variant has been reported in at least 5 patients with mild hemophilia A and type 2N VWD has been ruled out via sequencing of VWF exons 17-20 and 24-27 in at least 1 proband (PMID: 21883705, PMID: 19719828, PMID: 21592259, internal laboratory data). This variant was found to co-segregate with disease in affected family members, with 2 meioses observed in a family (PMID:21592259). 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 F8: PS4, PP4_moderate, PP3, PP1, PM2_Supporting. Variant Interpretation Guidelines for F8 Version 1.0.0, Released 10/5/2023).

Met criteria codes			
PM2_Supporting			The c.5186G>A (p.Gly1729Glu) variant is absent from males in population databases (gnomAD v2.1.1/gnomAD v3).
PS4			At least 4 patients with mild hemophilia A have been reported in the literature (PMID: 21592259; PMID: 19719828) or from internal laboratory data and type 2N VWD was ruled out via sequencing of VWF exons 17–20 and 24–27 of the VWF gene in at least 1 proband. PS4_Strong. Note the additional proband found in Lannoy, 2021. PMID: 21883705 is counted in PP4.
PP1			Seary, 2012: PMID: 21592259 includes of 3 male siblings (1 is currently counted under PP4), other two can be counted
PP3			The missense variant has a REVEL score of 0.861 (>0.6), meeting criteria for PP3
PP4			Lannoy, 2021. PMID: 21883705: This variant is reported in a proband with mild hemophilia A. Type 2N von Willebrand disease was excluded by analyzing exons 17–20 and 24–27 of the VWF gene. Multiplex ligation-dependent probe amplification (MLPA) assay was used to rule out large genomic rearrangements. This proband was not counted in PS4.

Curation History

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