

Variant: *NM\_000132.4(F8):c.7021G>A (p.Glu2341Lys)*

Version: 2.0

CA414896766 [↗](#)

993916 (ClinVar) [↗](#)

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

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

**Inheritance Mode:** X-linked inheritance

**UUID:** 2688b738-ba27-4952-af05-269db4e4de11

**Approved on:** 2025/5/2

**Published on:** 2025/5/2

### *HGVS expressions*

**NM\_000132.4(F8):c.7021G>A (p.Glu2341Lys)**

**NM\_000132.4:c.7021G>A**

NC\_000023.11:g.154837632C>T

CM000685.2:g.154837632C>T

NC\_000023.10:g.154065907C>T

CM000685.1:g.154065907C>T

NC\_000023.9:g.153719101C>T

NG\_011403.1:g.190092G>A

NG\_033065.1:g.2031G>A

NG\_011403.2:g.190092G>A

ENST00000360256.9:c.7021G>A

ENST00000644698.1:c.754G>A

ENST00000330287.10:c.616G>A

ENST00000360256.8:c.7021G>A

NM\_000132.3:c.7021G>A

NM\_019863.2:c.616G>A

NM\_019863.3:c.616G>A

**Likely Pathogenic**

**Met criteria codes** **4**

PP4\_Moderate

PP3

PM2\_Supporting

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 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.7021G>A (p.Glu2341Lys) missense variant is absent from males in population databases (gnomAD v2.1.1/gnomAD v3) meeting PM2\_Supporting. This missense variant has a REVEL score of 0.864 (>0.6) meeting PP3. This variant has been reported in at least five probands in the literature (PMID: 31829478, 21070499, 18691168, 33706050, 16879218) meeting phenotypic criteria for F8 (PP4\_Moderate & PS4). In summary, based on the evidence available at this time, the clinical significance of this variant is likely pathogenic. ACMG/AMP criteria applied, as specified by the Coagulation Factor Deficiency Variant Curation Expert Panel for F8/F9: PS4, PP4\_Moderate, PP3, PM2\_Supporting.

Met criteria codes

|                |                                                                                   |                                                                                   |                                                                                                                                                                                                                                                             |
|----------------|-----------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| PP4_Moderate   |  |  | 1 West African proband (from Côte d'Ivoire) reported with moderate hemophilia A and the Glu2341Lys variant. Variant was identified using NGS platform to detect SNV and CNV.                                                                                |
| PP3            |  |  | This missense variant has a REVEL score of 0.864 and meets PP3 criteria (threshold >0.6)                                                                                                                                                                    |
| PM2_Supporting |  |  | The c.7021G>A (p.Glu2341Lys) missense variant is completely absent from gnomAD v2.1.1 and v3.1.2                                                                                                                                                            |
| PS4            |  |  | At least six probands with hemophilia A are reported with the Glu2341Lys variant with varying severities. One proband was excluded for caution due to not being peer reviewed publication. One moderate proband is being used for PP4 (PS4 total 4 points). |

Curation History 

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