

Variant: *NM_000132.4:c.1814A>G*

Version: 1.0

CA414910923 [↗](#)

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

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

Inheritance Mode: X-linked inheritance

UUID: c7daad24-04fe-40c0-926b-c07c1f87ace7

Approved on: 2025/5/2

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HGVS expressions

NM_000132.4:c.1814A>G

NC_000023.11:g.154953981T>C

CM000685.2:g.154953981T>C

NC_000023.10:g.154182256T>C

CM000685.1:g.154182256T>C

NC_000023.9:g.153835450T>C

NG_011403.1:g.73743A>G

NG_011403.2:g.73743A>G

ENST00000360256.9:c.1814A>G

ENST00000647125.1:c.*1690A>G

ENST00000360256.8:c.1814A>G

NM_000132.3:c.1814A>G

Pathogenic

Met criteria codes **5**

PP4_Moderate

PP3

PS4

PP1_Moderate

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 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.1814A>G (p.Tyr605Cys) variant is absent from population database gnomAD v2.1.1 and v3.1.2 meeting PM2_Supporting criteria. The missense variant has a REVEL score of 0.957 (>0.6), meeting criteria for PP3. Seven probands with moderate-severe hemophilia A are reported in the literature and internal laboratory data who meet F8 phenotype criteria and criteria for PS4 or PP4_Moderate (PMIDs: 18217193, 21883705, 18691168, 29296726). At least 4 related individuals with this variant were identified in the My Life Our Future Project (PMID: 29296726), meeting criteria for PP1_Moderate. 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 F8: PS4, PP4_Moderate, PP1_Moderate, PP3, PM2_Supporting.

Met criteria codes

PP4_Moderate			Proband with severe hemophilia A from the MLOF project.
PP3			The Tyr605Cys missense variant has a REVEL score of 0.957 (>0.6), meeting criteria for PP3.
PS4			At least 7 probands with moderate-severe hemophilia A are reported in the literature and internal laboratory data who meet F8 phenotype criteria and criteria for PS4 (>4 probands). One of the 7 probands was used for PP4_Moderate.
PP1_Moderate			1 proband with three relatives with variant in the MLOF Project.
PM2_Supporting			The c.1814A>G (p.Tyr605Cys) variant is absent from population database gnomAD v2.1 and v3.1.

Curation History

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