

Variant: *NM_000132.3:c.980T>A*

Version: 1.0

CA414917674 [↗](#)

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

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

Inheritance Mode: X-linked inheritance

UUID: 8c3efe31-9d6b-433e-bd87-e9d10335ed14

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HGVS expressions

NM_000132.3:c.980T>A

NC_000023.11:g.154969360A>T

CM000685.2:g.154969360A>T

NC_000023.10:g.154197635A>T

CM000685.1:g.154197635A>T

NC_000023.9:g.153850829A>T

NG_011403.1:g.58364T>A

NG_011403.2:g.58364T>A

ENST00000360256.9:c.980T>A

ENST00000647125.1:c.*856T>A

ENST00000360256.8:c.980T>A

NM_000132.4:c.980T>A

Likely Pathogenic

Met criteria codes **5**

PM5

PM2_Supporting

PP1

PP3

PP4_Moderate

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.980T>A (p.Leu327Gln) variant is absent from males in population databases (gnomAD v2.1.1/gnomAD v3) meeting the PM2_Supporting criteria. The missense variant has a REVEL score of 0.868 (>0.6) meeting PP3. The variant has been reported in a proband with severe hemophilia A in the EAHAD Database genotyped through the My Life Our Future program (PP4_Moderate). This information was confirmed by a VCEP member who also reported a similarly affected nephew also found to harbor this variant meeting PP1 criteria. A pathogenic variant, Leu327Val, is reported at the same residue meeting PM5 criteria meeting PM5. 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: PM5, PP4_Moderate, PP1, PP3, PM2_Supporting

Met criteria codes

PM5			p.Leu327Val is a pathogenic variant that has been evaluated by the Coagulation Factor Deficiency VCEP
PM2_Supporting			The c.980T>A (p.Leu327Gln) variant is absent from males in population databases (gnomAD v2.1.1/gnomAD v3).
PP1			Proband and nephew with severe hemophilia A and harbor the F8 c.980T>A (p.Leu327Gln) variant.
PP3			The c.980T>A (p.Leu327Gln) missense variant has a REVEL score of 0.868 (>0.6).
PP4_Moderate			1 proband with severe hemophilia A genotyped through the My Life Our Future program.

Curation History

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