

Variant: *NM_000132.3(F8):c.980T>C (p.Leu327Pro)*

Version: 1.0

CA255086 [↗](#)

10199 (ClinVar) [↗](#)

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

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

Inheritance Mode: X-linked inheritance

UUID: 0359c35e-8a2d-43a2-a9ba-6b9fd5c4cab8

Approved on: 2024/9/30

Published on: 2024/10/1

HGVS expressions

NM_000132.3:c.980T>C

NM_000132.3(F8):c.980T>C (p.Leu327Pro)

NC_000023.11:g.154969360A>G

CM000685.2:g.154969360A>G

NC_000023.10:g.154197635A>G

CM000685.1:g.154197635A>G

NC_000023.9:g.153850829A>G

NG_011403.1:g.58364T>C

NG_011403.2:g.58364T>C

ENST00000360256.9:c.980T>C

ENST00000647125.1:c.*856T>C

ENST00000360256.8:c.980T>C

NM_000132.4:c.980T>C

Likely Pathogenic

Met criteria codes 4

PS4_Moderate

PP3

PM5

PM2_Supporting

Not Met criteria codes 1

PP1

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>C (p.Leu327Pro) variant is absent from males in population databases (gnomAD v2.1.1/gnomAD v3). The variant has been reported in two probands with severe hemophilia A meeting phenotypic criteria for F8 in PMID: 8644728 and 26897466. This missense variant has a REVEL score of 0.926 (>0.6). A pathogenic variant, Leu327Val, is reported at the same residue 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: PP3, PS4_Moderate, PM2_Supporting, PM5.

Met criteria codes

PS4_Moderate			The c.980T>C (p.Leu327Pro) variant has been reported in two probands meeting phenotypic criteria for F8 in PMID: 8644728 and 26897466.
PP3			This missense variant has a REVEL score of 0.926 (>0.6). SpliceAI predicts no splicing impact.
PM5			Leu327Val is a pathogenic variant classified by the CFD-VCEP
PM2_Supporting			The missense variant is absent from males in population databases (gnomAD v2.1.1/gnomAD v3).

Not Met criteria codes

PP1			PMID: 8644728 reports a family in which the origin of the proband's variant has been traced to the maternal grandmother (potentially 2 segregations), however, factor levels of mother and grandmother are not noted. PP1 criteria not met.
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Curation History

  

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