

Variant: *NM_000132.4(F8):c.332C>T (p.Ala111Val)*

Version: 1.0

CA414919986 [↗](#)

3380944 (ClinVar) [↗](#)

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

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

Inheritance Mode: X-linked inheritance

UUID: d3a7e3f1-03d8-45a1-8c07-de0b02e6ff2c

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HGVS expressions

NM_000132.4(F8):c.332C>T (p.Ala111Val)

NM_000132.4:c.332C>T

NC_000023.11:g.154997029G>A

CM000685.2:g.154997029G>A

NC_000023.10:g.154225304G>A

CM000685.1:g.154225304G>A

NC_000023.9:g.153878498G>A

NG_011403.1:g.30695C>T

NG_011403.2:g.30695C>T

ENST00000360256.9:c.332C>T

ENST00000647125.1:c.*118C>T

ENST00000360256.8:c.332C>T

ENST00000423959.5:c.227C>T

ENST00000453950.1:c.314C>T

NM_000132.3:c.332C>T

Uncertain Significance

Met criteria codes **4**

PS4_Moderate

PM5_Supporting

PP3

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 NM_000132.4(F8):c.332C>T (p.Ala111Val) variant is a missense variant in F8 that is absent from population databases (gnomAD v2.1.1/gnomAD v3; PM2_Supporting) and is predicted to have a deleterious effect (REVEL score of 0.968), which is greater than the ClinGen CFD threshold for PP3 (>0.6). The variant has been observed in at least two probands with mild to moderate hemophilia A with type 2N

von Willebrand disease ruled out (PMID:11857744, External laboratory data; PS4_Moderate). Another missense variant (c.331G>A, p.Ala111Thr, CAID:CA414919991) in the same codon has been classified as likely pathogenic for hemophilia A by the ClinGen Coagulation Factor Deficiency VCEP (PM5_Supporting) with agreement in splicing predictors show no splicing impact. In summary, this variant meets the criteria to be classified as a variant of uncertain significance for hemophilia A. ACMG/AMP criteria applied, as specified by the Coagulation Factor Deficiency Variant Curation Expert Panel (specifications version 1.0.0) for F8: PS4_Moderate, PM5_Supporting, PM2_Supporting, PP3.

Met criteria codes

PS4_Moderate			This variant has been observed in at least two probands with mild to moderate hemophilia A with type 2N von Willebrand disease ruled out (PMID:11857744, 1 point PS4; External laboratory data, 1 Point PS4; Total 2 points PS4, PS4_Moderate).
PM5_Supporting			Another missense variant (c.331G>A, p.Ala111Thr, CAID:CA414919991) in the same codon has been classified as likely pathogenic for hemophilia A by the ClinGen Coagulation Factor Deficiency VCEP (PM5_Supporting) with agreement in splicing predictors show no splicing impact.
PP3			The c.332C>T (p.Ala111Val) missense variant has a REVEL score of 0.968 (greater than 0.6).
PM2_Supporting			The c.332C>T (p.Ala111Val) variant is from population databases (gnomAD v2.1.1/gnomAD v3).

Curation History



 

 

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