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Variant: NM_000132.4(F8):c.766T>A (p.Tyr256Asn)

Version: 1.0

CA414918961

618107 (ClinVar)

Gene: F8 (HGNC:2157)
Condition: hemophilia A (MONDO:0010602)
Inheritance Mode: X-linked inheritance
UUID: 56810547-f2ab-47a5-8292-247dc9d7b8e4
Approved on: 2026/2/6
Published on: 2026/2/27

HGVS expressions

NM_000132.4(F8):c.766T>A (p.Tyr256Asn)
NM_000132.4:c.766T>A
NC_000023.11:g.154984708A>T
CM000685.2:g.154984708A>T
NC_000023.10:g.154212983A>T
CM000685.1:g.154212983A>T
NC_000023.9:g.153866177A>T
NG_011403.1:g.43016T>A
NG_011403.2:g.43016T>A
ENST00000360256.9:c.766T>A
ENST00000647125.1:c.*552T>A
ENST00000360256.8:c.766T>A
ENST00000423959.5:c.661T>A
NM_000132.3:c.766T>A

Likely Pathogenic

Met criteria codes 4

PP4_Moderate PP3 PS4_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 NM_000132.4(F8):c.766T>A; p.Tyr256Asn is a missense variant that is absent from gnomAD v2.1.1/gnomAD v3 meeting PM2_Supporting. The variant is predicted to have a deleterious effect with a REVEL score of 0.942, which is greater than the ClinGen CFD threshold for PP3 (>0.6) meeting PP3. This variant has been observed in at least 4 probands in the literature with mild hemophilia A (PP4_Moderate, PMID:29296726; PS4_Moderate, PMID:29296726, 16786531). In summary, this variant meets the criteria to be classified as

likely pathogenic for hemophilia A. ACMG/AMP criteria applied, as specified by the Coagulation Factor Deficiency Variant Curation Expert Panel using v1.0.0 rule specifications for F8: PS4_Moderate, PP4_Moderate, PM2_Supporting, PP3.

Met criteria codes

PP4_Moderate	✔	The c.766T>A, p.Tyr256Asn variant has been observed in a patient with mild hemophilia A without type 2N von Willebrand disease ruled out (2 points PP4, PMID:29296726, PP4_Moderate).
PP3	✔	The c.766T>A, p.Tyr256Asn variant is predicted to have a deleterious effect (REVEL score of 0.942; PP3), which is greater than the Clingen CFD threshold for PP3 (>0.6).
PS4_Moderate	✔	The c.766T>A, p.Tyr256Asn variant has been observed at least 3 patients with mild hemophilia A without type 2N von Willebrand disease ruled out (2 points PS4, PMID:29296726, 1 point PS4, PMID:16786531; PS4_Moderate).
PM2_Supporting	✔	The c.766T>A, p.Tyr256Asn variant is absent from population databases (gnomAD v2.1.1/gnomAD v3; PM2_Supporting)

Curation History

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