Variant: NM_000132.4(F8):c.2212T>G (p.Tyr738Asp)

Version: 1.0

CA10568350

913260 (ClinVar)

Gene: F8 (HGNC:2157)
Condition: hemophilia A (MONDO:0010602)
Inheritance Mode: X-linked inheritance
UUID: 2f568b2d-be66-4264-823e-5948b836375b
Approved on: 2025-04-04
Published on: 2025-04-04

HGVS expressions

NM_000132.4:c.2212T>G
NM_000132.4(F8):c.2212T>G (p.Tyr738Asp)
NC_000023.11:g.154931578A>C
CM000685.2:g.154931578A>C
NC_000023.10:g.154159853A>C
CM000685.1:g.154159853A>C
NC_000023.9:g.153813047A>C
NG_011403.1:g.96146T>G
NG_011403.2:g.96146T>G
ENST00000360256.9:c.2212T>G
ENST00000647125.1:c.*1878T>G
ENST00000360256.8:c.2212T>G
NM_000132.3:c.2212T>G

Benign

Met criteria codes 1

BA1

Not Met criteria codes 2

PP3 BP4

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.2212T>G variant in F8 is a missense variant predicted to cause substitution of Tyrosine by Asparagine at amino acid 738 (p.Tyr738Asp). The highest population minor allele frequency in gnomAD v2.1.1 is 0.002225 (17/7641 alleles) in the Ashkenazi Jewish population, which is higher than the ClinGen Coagulation Factor Deficiency VCEP threshold (>=0.000333) for BA1, and therefore meets this criterion (BA1). In summary, this variant meets the criteria to be classified as Benign for Hemophilia A based on the ACMG/AMP criteria

applied, as specified by the ClinGen Coagulation Factor Deficiency Variant Curation Expert Panel for F8 (version 1.0.0, released 10/5/2023): BA1.

Met criteria codes

BA1	✔	The highest population minor allele frequency in gnomAD v2.1.1 is 0.002225 (17/7641 alleles) in the Ashkenazi Jewish population, which is higher than the ClinGen Coagulation Factor Deficiency VCEP threshold (>=0.000333) for BA1, and therefore meets this criterion (BA1). Grpmax filtering AF exomes is 0.00002397 and genomes is 0.00003236.

Not Met criteria codes

PP3	✖	The computational predictor REVEL gives a score of 0.408, which is neither above nor below the thresholds predicting a damaging (>=0.6) or benign (<=0.3) impact on F8 function. Splice AI scores = 0.00, 0.00. 0.01, 0.00.
BP4	✖	The computational predictor REVEL gives a score of 0.408, which is neither above nor below the thresholds predicting a damaging (>=0.6) or benign (<=0.3) impact on F8 function. Splice AI scores = 0.00, 0.00. 0.01, 0.00.

Curation History

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