

Variant: *NM_000132.4(F8):c.248C>G (p.Pro83Arg)*

Version: 1.0

CA10568618 [↗](#)

1684385 (ClinVar) [↗](#)

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

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

Inheritance Mode: X-linked inheritance

UUID: a24495d5-1a17-4ad0-8ac0-74979c4cc0b6

Approved on: 2025/11/7

Published on: 2025/11/7

HGVS expressions

NM_000132.4:c.248C>G

NM_000132.4(F8):c.248C>G (p.Pro83Arg)

NC_000023.11:g.154999496G>C

CM000685.2:g.154999496G>C

NC_000023.10:g.154227771G>C

CM000685.1:g.154227771G>C

NC_000023.9:g.153880965G>C

NG_011403.1:g.28228C>G

NG_011403.2:g.28228C>G

ENST00000360256.9:c.248C>G

ENST00000647125.1:c.*34C>G

ENST00000360256.8:c.248C>G

ENST00000423959.5:c.143C>G

ENST00000453950.1:c.230C>G

NM_000132.3:c.248C>G

Uncertain Significance

Met criteria codes **3**

PS4_Moderate

PP4_Moderate

PP3

Not Met criteria codes **2**

PM2

BS1

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.248C>G (p.Pro83Arg) variant is a missense variant in F8 that has been observed in multiple patients in the literature with mild hemophilia A meeting PP4_Moderate and PS4_Moderate (PMID: 29296726, PMID:18403393, PMID:18184865). This variant is predicted to have a deleterious effect with a REVEL score of 0.891, which is greater than the ClinGen CFD threshold (>0.6)

meeting PP3. In summary, this variant meets criteria to be classified as a variant of uncertain significance for hemophilia A based on the ACMG/AMP criteria applied, as specified by the ClinGen Coagulation Factor Deficiency VCEP: PP3. PP4_Moderate, PS4_Moderate.

Met criteria codes			
PS4_Moderate			The c.248C>G (p.Pro83Arg) variant has been observed in multiple patients with mild hemophilia A (PMID:18403393,PMID:18184865). Scoring 2 probands at this time.
PP4_Moderate			There is at least 1 proband with factor VIII deficiency without exclusion of type 2N VWD with deletion/duplication analysis; however, with 4 probands having decreased factor VIII activity levels this code is still applicable. (PMID:29296726).
PP3			The c.248C>G (p.Pro83Arg) missense variant has a REVEL score of 0.917 (greater than 0.6).
Not Met criteria codes			
PM2			The c.248C>G (p.Pro83Arg) variant is observed in one male in population databases (gnomAD v2.1.1/gnomAD v3).
BS1			The c.248C>G (p.Pro83Arg) variant is reported at an MAF of 0.00002725 (5/183468 alleles) in the general population in gnomAD v2.1.1, with 1 hemizygote, which does not meet BS1 criteria of MAF > 0.0000333.

Curation History



 

 

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