

Variant: *NM_000133.3(F9):c.880C>T (p.Arg294Ter)*

Version: 1.1

CA255344 [↗](#)

10587 (ClinVar) [↗](#)

Gene: F9 ([HGNC:2158](#))

Condition: hemophilia B ([MONDO:0010604](#))

Inheritance Mode: X-linked inheritance

UID: 0742efeb-756a-4f9c-9d90-b29a1c2a1c24

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HGVS expressions

NM_000133.3:c.880C>T

NM_000133.3(F9):c.880C>T (p.Arg294Ter)

NC_000023.11:g.139561565C>T

CM000685.2:g.139561565C>T

NC_000023.10:g.138643724C>T

CM000685.1:g.138643724C>T

NC_000023.9:g.138471390C>T

NG_007994.1:g.35830C>T

ENST00000218099.7:c.880C>T

ENST00000643157.1:n.1547C>T

ENST00000218099.6:c.880C>T

ENST00000394090.2:c.766C>T

NM_001313913.1:c.766C>T

NM_000133.4:c.880C>T

NM_001313913.2:c.766C>T

Pathogenic

Met criteria codes **4**

PM2_Supporting

PVS1

PS4

PP4_Moderate

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 F9 Version 1.0.0*

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**









Evidence submitted by expert panel

Coagulation Factor Deficiency VCEP

The F9 c.880C>T (Arg294Ter) variant occurs in exon 8/8 of the F9 gene and NMD is not predicted. However, PVS1 is applied based on truncation of the peptidase S1 domain. This variant is completely absent from gnomAD v2.1.1 and v3.1.1, meeting PM2_Supporting criteria. Over 90 patients have been reported in the literature and the EAHAD database with hemophilia B in the moderate-severe range

and history of inhibitors to factor replacement products are reported, meeting **PP4_Moderate** and **PS4_Very strong** (selected PMIDs: 29296726, 8217825, 8314564). In summary, this variant meets criteria to be classified as pathogenic. ACMG/AMP criteria applied, as specified by the Coagulation Factor Deficiency Variant Curation Expert Panel for F9: **PVS1**, **PS4_VeryStrong**, **PP4_Moderate**, **PM2_Supporting**.

Met criteria codes

PM2_Supporting	 	The c.880C>T (p.Arg294Ter) variant is completely absent from gnomAD v2.1.1 and v3.1.1
PVS1	 	The c.880C>T (Arg294Ter) variant occurs in exon 8/8 of the F9 gene and NMD is not predicted. However, PVS1 at full strength is applied based on truncation of the Peptidase S1 domain.
PS4	 	At least 39 patients are counted from the literature and internal laboratory data with the Arg294Ter variant and hemophilia B in the moderate-severe range. Several other probands are in the literature and EAHAD database reports 92 patients. However, the threshold for PS4_Very Strong (>8 probands) has been reached.
PP4_Moderate	 	Male with severe hemophilia B with an inhibitor to factor replacement product. All participants in MLOF project had F8 and F9 full gene sequencing and deletion/duplication analysis.

Curation History

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