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Variant: NM_000133.4(F9):c.223C>T (p.Arg75Ter)

Version: 1.0

CA340993

10572 (ClinVar)

Gene: F9 (HGNC:2158)
Condition: hemophilia B (MONDO:0010604)
Inheritance Mode: X-linked inheritance
UUID: 4520dcb8-3b20-4ff8-b989-38b3fdd3354e
Approved on: 2024/2/9
Published on: 2024/7/11

HGVS expressions

NM_000133.4(F9):c.223C>T (p.Arg75Ter)
NM_000133.4:c.223C>T
NC_000023.11:g.139537144C>T
CM000685.2:g.139537144C>T
NC_000023.10:g.138619303C>T
CM000685.1:g.138619303C>T
NC_000023.9:g.138446969C>T
NG_007994.1:g.11409C>T
ENST00000218099.7:c.223C>T
ENST00000218099.6:c.223C>T
ENST00000394090.2:c.223C>T
ENST00000479617.2:n.230C>T
NM_000133.3:c.223C>T
NM_001313913.1:c.223C>T
NM_001313913.2:c.223C>T

Pathogenic

Met criteria codes 4

PVS1 PP4_Moderate PM2_Supporting PS4

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.223C>T; p.Arg75Ter causes a protein truncation that is expected to undergo NMD, meeting PVS1. The variant is completely absent from gnomAD v2.1.1 and v3.1.1, meeting PM2_Supporting. Over 75 patients are reported in the literature with moderate-severe hemophilia B, some with a history of inhibitors to factor replacement products, meeting F9 phenotype criteria for PS4_Very strong and

PP4_Moderate (EAHAD database; PMID: 29296726). 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_Very strong, PP4_Moderate, PM2_Supporting.

Met criteria codes

PVS1	✔	Truncated protein is expected to undergo NMD.
PP4_Moderate	✔	Male with severe hemophilia B with history of an inhibitor who had F8 and F9 full gene sequencing and deletion/duplication analysis.
PM2_Supporting	✔	Variant is absent from gnomAD v2.1.1 and v3.1.
PS4	✔	Greater than 8 probands reported in the literature, which is consistent with applying this code at the very strong strength.

Curation History

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