

Variant: *NM_000133.4(F9):c.407T>C (p.Ile136Thr)*

Version: 1.0

CA414438824 [↗](#)

627177 (ClinVar) [↗](#)

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

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

Inheritance Mode: X-linked inheritance

UUID: 42c02c48-c3ed-4e7a-a05d-7d209d9c2d6c

Approved on: 2024/11/1

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HGVS expressions

NM_000133.4(F9):c.407T>C (p.Ile136Thr)

NM_000133.4:c.407T>C

NC_000023.11:g.139548378T>C

CM000685.2:g.139548378T>C

NC_000023.10:g.138630537T>C

CM000685.1:g.138630537T>C

NC_000023.9:g.138458203T>C

NG_007994.1:g.22643T>C

ENST00000218099.7:c.407T>C

ENST00000643157.1:n.1074T>C

ENST00000218099.6:c.407T>C

ENST00000394090.2:c.293T>C

ENST00000479617.2:n.360T>C

NM_000133.3:c.407T>C

NM_001313913.1:c.293T>C

NM_001313913.2:c.293T>C

Likely Pathogenic

Met criteria codes **4**

PS4

PP3

PM1

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 F9 Version 1.0.0*

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

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

Evidence submitted by expert panel

Coagulation Factor Deficiency VCEP

NM_000133.4(F9):c.407T>C (p.Ile136Thr) missense variant has a REVEL score of 0.634, which meets criteria for PP3. This variant is absent from males in population databases (gnomAD v2.1.1/gnomAD v3). The variant occurs within exon 5, a region deemed critical for the

encoded FIX protein by the CFD-VCEP, and meets criteria for PM1. The c.407T>C (p.Ile136Thr) variant is reported in at least two individuals with mild hemophilia B and two individuals with hemophilia B of unspecified severity (PMID: 8680410, 8091381, 31064749), meeting criteria for PS4. In summary, this variant meets criteria to be classified as likely pathogenic. ACMG/AMP criteria applied, as specified by the Coagulation Factor Deficiency Variant Curation Expert Panel for F9 (Released 10/5/2023): PS4, PM1, PP3, PM2_Supporting.

Met criteria codes

PS4			The c.407T>C (p.Ile136Thr) variant is reported in at least two individuals with mild hemophilia B and two individuals with hemophilia B of unspecified severity (PMID: 8680410, 8091381, 31064749), meeting criteria for PS4.
PP3			This missense variant has a REVEL score of 0.634, meeting criteria for PP3 (threshold >0.6). SpliceAI predicts an acceptor gain at -15bp with a delta score of 0.02. PP3 threshold (>0.5) for splicing not met.
PM1			The variant, c.407T>C occurs within exon 5, a region deemed critical for the encoded FIX protein by the CFD-VCEP, and meets criteria for PM1.
PM2_Supporting			The Ile136Thr missense variant is completely absent from gnomAD v2.1.1 and v3.1.2

Curation History

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