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Variant: NM_000133.4(F9):c.1106T>C (p.Leu369Pro)

Version: 1.0

CA414445922

626973 (ClinVar)

Gene: F9 (HGNC:2158)
Condition: hemophilia B (MONDO:0010604)
Inheritance Mode: X-linked inheritance
UUID: 1caeabb7-f10b-491a-8e60-9664d4b6713a
Approved on: 2025/8/15
Published on: 2025/8/21

HGVS expressions

NM_000133.4:c.1106T>C
NM_000133.4(F9):c.1106T>C (p.Leu369Pro)
NC_000023.11:g.139561791T>C
CM000685.2:g.139561791T>C
NC_000023.10:g.138643950T>C
CM000685.1:g.138643950T>C
NC_000023.9:g.138471616T>C
NG_007994.1:g.36056T>C
ENST00000218099.7:c.1106T>C
ENST00000643157.1:n.1723+50T>C
ENST00000218099.6:c.1106T>C
ENST00000394090.2:c.992T>C
NM_000133.3:c.1106T>C
NM_001313913.1:c.992T>C
NM_001313913.2:c.992T>C

Likely Pathogenic

Met criteria codes 3

PM2_Supporting PS4 PP3

Not Met criteria codes 1

PM5

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.1106T>C, p.Leu369Pro is completely absent from gnomAD v2.1.1 and v3.1.2, meeting PM2_Supporting. The computational predictor REVEL gives a score of 0.948 and has a SpliceAI score of 0, meeting PP3 criteria (>=0.6). This variant has been reported in 5 probands meeting phenotypic criteria for hemophilia B (PS4_moderate; EAHAD Database, PMID: 31064749, PMID: 19699296). In summary,

this variant meets the criteria to be classified as likely pathogenic for hemophilia B based on the ACMG/AMP criteria applied, as specified by the ClinGen Coagulation Factor Deficiency VCEP ClinGen Coagulation Factor Deficiency VCEP F9 (version 1.0.0, released 10/5/2023): PS4, PM2_Supporting, PP3.

Met criteria codes

PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1 and v3.1.2 meeting PM2_Supporting.
PS4	✔	This variant has been reported in at least 5 probands meeting phenotypic criteria for Hemophilia B (EAHAD Database, PMID: 31064749, PMID: 19699296). We are aware of at least one additional published report, but there is not enough information provided to meet phenotypic criteria.
PP3	✔	The computational predictor REVEL gives a score of 0.948, meeting PP3 criteria (>=0.6). It also has a SpliceAI score of 0.00.

Not Met criteria codes

PM5	✖	An alternate variant at this position (p.Leu369Phe) that has been curated by the CFD VCEP that will not be used to apply PM5 to avoid circularity. There is another variant (p.Leu369Val) that is lacking enough evidence to reach likely pathogenic at this time.

Curation History

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