The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000133.4(F9):c.1105C>T (p.Leu369Phe)

Version: 1.0

CA414445918

1512896 (ClinVar)

Gene: F9 (HGNC:2158)
Condition: hemophilia B (MONDO:0010604)
Inheritance Mode: X-linked inheritance
UUID: 8a239405-afa4-4c2e-8fa0-a217aa9becce
Approved on: 2025/8/15
Published on: 2025/8/21

HGVS expressions

NM_000133.4:c.1105C>T
NM_000133.4(F9):c.1105C>T (p.Leu369Phe)
NC_000023.11:g.139561790C>T
CM000685.2:g.139561790C>T
NC_000023.10:g.138643949C>T
CM000685.1:g.138643949C>T
NC_000023.9:g.138471615C>T
NG_007994.1:g.36055C>T
ENST00000218099.7:c.1105C>T
ENST00000643157.1:n.1723+49C>T
ENST00000218099.6:c.1105C>T
ENST00000394090.2:c.991C>T
NM_000133.3:c.1105C>T
NM_001313913.1:c.991C>T
NM_001313913.2:c.991C>T

Uncertain Significance

Met criteria codes 4

PP3 PM2_Supporting PS4_Moderate PM5_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

The F9 c.1105C>T, p.Leu369Phe variant is absent from gnomAD v2.1.1 and v3.1.2 (PM2_Supporting). The computational predictor REVEL gives a score of 0.928, which is above the threshold of 0.6, evidence that correlates with impact to F9 function (PP3). This variant has been reported in 2 probands meeting phenotypic criteria for hemophilia B (PS4_Moderate; PMID: 15921378, PMID: 25929987). There is another

variant at this position (p.Leu369Pro) that has been curated by the Coagulation Factor Deficiency VCEP to be likely pathogenic, meeting PM5_Supporting. In summary, this variant meets the criteria to be classified as variant of uncertain significance for hemophilia B based on the ACMG/AMP criteria applied, as specified by the ClinGen Coagulation Factor Deficiency VCEP (version 1.0.0, released 10/5/2023): PS4_Moderate, PM2_Supporting, PP3, PM5_Supporting.

Met criteria codes

PP3	✔	The computational predictor REVEL gives a score of 0.928, which is above the threshold of 0.6, evidence that correlates with impact to F9 function (PP3).
PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1 (PM2_Supporting).
PS4_Moderate	✔	This variant has been reported in 2 probands meeting phenotypic criteria for Hemophilia B (PS4_moderate; PMID: 15921378, PMID: 25929987).
PM5_Supporting	✔	There is a variant at this position (p.Leu369Pro) has been curated by the CFD VCEP to be likely pathogenic. There is one variant at this position (p.Leu369=) that has been curated by the CFD VCEP to be likely benign. There is also one variant (p.Leu369Val) that will not be curated due to lack of evidence.

Curation History

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