

Variant: *NM_001313913.2:c.838C>T*

Version: 1.0

CA414444915 [↗](#)

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

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

Inheritance Mode: X-linked inheritance

UUID: 28772313-2391-433a-85eb-86a59f7a4dd8

Approved on: 2024/10/11

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HGVS expressions

NM_001313913.2:c.838C>T

NC_000023.11:g.139561637C>T

CM000685.2:g.139561637C>T

NC_000023.10:g.138643796C>T

CM000685.1:g.138643796C>T

NC_000023.9:g.138471462C>T

NG_007994.1:g.35902C>T

ENST00000218099.7:c.952C>T

ENST00000643157.1:n.1619C>T

ENST00000218099.6:c.952C>T

ENST00000394090.2:c.838C>T

NM_000133.3:c.952C>T

NM_001313913.1:c.838C>T

NM_000133.4:c.952C>T

Pathogenic

Met criteria codes **4**

PM2_Supporting **PP3** **PS2** **PS4**

Not Met criteria codes **2**

PM1 **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 c.952C>T; p.Leu318Phe variant is completely absent from gnomAD v2.1.1 and v3.1.1. This missense variant has a REVEL score of 0.943 and meets PP3 criteria (threshold >0.6). At least 4 patients are reported in the literature with moderate-severe hemophilia B and this variant, meeting F9 phenotype criteria for PS4. There is at least 1 proband with isolated reduction in FIX activity levels meeting phenotypic criteria for F9, with confirmed de novo (maternity confirmed in an affected male) occurrence (PMID: 30648777). In summary,

this variant meets criteria to be classified as pathogenic. The ACMG/AMP criteria applied, as specified by the Coagulation Factor Deficiency Variant Curation Expert Panel, for F9: PS4, PS2, PP3, PM2_Supporting.

Met criteria codes

PM2_Supporting			Absent in gnomAD v2.1.1 and v3.1.
PP3			REVEL score is 0.943 which is above the 0.6 cutoff.
PS2			Lu, 2019 PMID: 30648777 is de novo (maternity confirmed), meets 2 points SVI PS2/PM6 chart = PS2
PS4			At least four probands have been identified with this variant and moderate/severe hemophilia B.

Not Met criteria codes

PM1			Variant is not within 3, 4 or 5.
PM5			Evidence from this curation has been used in PM5 for the classification of another variant at the same codon, Leu318Arg. Therefore, PM5 is not applied in order o avoid circularity

Curation History

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