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Variant: NM_001313913.2:c.854_860del

Version: 1.2

CA658820951

3390364 (ClinVar)

Gene: F9 (HGNC:2158)
Condition: hemophilia B (MONDO:0010604)
Inheritance Mode: X-linked inheritance
UUID: c7549989-d137-47b7-be33-3e2d6db9914d
Approved on: 2024/12/6
Published on: 2024/12/6

HGVS expressions

NM_001313913.2:c.854_860del
NC_000023.11:g.139561654_139561660del
CM000685.2:g.139561654_139561660del
NC_000023.10:g.138643813_138643819del
CM000685.1:g.138643813_138643819del
NC_000023.9:g.138471479_138471485del
NG_007994.1:g.35919_35925del
ENST00000218099.7:c.969_975del
ENST00000643157.1:n.1636_1642del
ENST00000218099.6:c.969_975del
ENST00000394090.2:c.855_861del
NM_000133.3:c.969_975del
NM_001313913.1:c.855_861del
NM_000133.4:c.969_975del
NM_001313913.2:c.855_861del

Pathogenic

Met criteria codes 3

PVS1 PP4_Moderate PM2_Supporting

Not Met criteria codes 1

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 NM_000133.4(F9):c.969_975del variant deletes 7bp in exon 8 of the F9 gene, causing a frameshift and premature termination of translation. NMD is not predicted to occur, but the truncation of the peptidase S1 domain is expected to be detrimental to protein function (PVS1). The variant is absent from gnomAD v2.1 (PM2_Supporting). The variant is reported in at least one individual with severe

Hemophilia B with full gene sequencing and deletion/duplication analysis in the literature (PP4_Moderate - PMID: 26612714). In summary, this variant meets criteria to be classified as pathogenic. ACMG/AMP criteria applied, as specified by the Coagulation Factor Deficiency VCEP for F9: PVS1, PP4_Moderate, PM2_Supporting.

Met criteria codes

PVS1	✔	The 7-bp deletion occurs in exon 8/8 of F9 and causes a frameshift and premature termination of translation. The variant is not predicted to undergo NMD. PVS1 is applied based on the potential truncation of the peptidase S1 domain, which is determined to be critical to protein function by the CFD-VCEP.
PP4_Moderate	✔	1 proband with severe hemophilia B. MLPA was used for deletion/duplication analysis.
PM2_Supporting	✔	The variant is absent from gnomAD v2.1 and v3.1.

Not Met criteria codes

PS4	✖	There was some concern that the proband was the same in both publications. Given this variant meets a pathogenic classification counting only one proband, we used a conservative approach to only count one proband for PP4_Moderate.

Curation History

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