Variant: NM_000132.3:c.1244C>T

Version: 1.1

CA414915806

Gene: F8 (HGNC:2157)
Condition: hemophilia A (MONDO:0010602)
Inheritance Mode: X-linked inheritance
UUID: 9b972ba2-506e-4a79-84cf-b8592ad30afa
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HGVS expressions

NM_000132.3:c.1244C>T
NC_000023.11:g.154966453G>A
CM000685.2:g.154966453G>A
NC_000023.10:g.154194728G>A
CM000685.1:g.154194728G>A
NC_000023.9:g.153847922G>A
NG_011403.1:g.61271C>T
NG_011403.2:g.61271C>T
ENST00000360256.9:c.1244C>T
ENST00000647125.1:c.*1120C>T
ENST00000360256.8:c.1244C>T
ENST00000483822.2:n.64C>T
NM_000132.4:c.1244C>T

Pathogenic

Met criteria codes 3

PP3 PM2_Supporting PS4_Very Strong

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 F8 Version 1.0.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Coagulation Factor Deficiency VCEP

The c.1244C>T, p.Ala415Val variant is absent from males in population databases (gnomAD v2.1.1/gnomAD v3 - PM2_Supporting). The missense variant has a REVEL score of 0.829 (>0.6 - PP3). At least 27 patients of French origin are reported with moderate-severe hemophilia A in (PMID: 29656491 - PS4_Very strong). In summary, this variant meets criteria to be classified as pathogenic. ACMG/AMP criteria applied, as specified by the Coagulation Factor Deficiency Variant Curation Expert Panel for F8/F9: PS4_Very Strong, PP3, PM2_Supporting.

Met criteria codes

PP3	✔	The c.1244C>T (p.Ala415Val) missense variant has a REVEL score of 0.829 (>0.6). No splicing impact is predicted by spliceAI.
PM2_Supporting	✔	The c.1244C>T (p.Ala415Val) variant is absent from males in population databases (gnomAD v2.1.1/gnomAD v3).
PS4_Very Strong	✔	At least 27 patients of French origin are reported with moderate-severe hemophilia A in PMID: 29656491. A founder effect is suggested for the variant. The threshold for PS4_Very Strong is met (>8 probands).

Not Met criteria codes

PM5	✖	c.1244C>A (p.Ala415Asp) and c.1243G>A (p.Ala415Thr) are both present at this codon. c.1243G>A (p.Ala415Thr) is a VUS and c.1244C>A (p.Ala415Asp) is likely pathogenic.

Curation History

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