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Variant: NM_000132.3:c.5488G>T

Version: 1.0

CA414908714

2775447 (ClinVar)

Gene: F8 (HGNC:2157)
Condition: hemophilia A (MONDO:0010602)
Inheritance Mode: X-linked inheritance
UUID: 0d2036b6-1d6d-4816-9b31-cf27fc6d6a86
Approved on: 2024/2/2
Published on: 2024/7/11

HGVS expressions

NM_000132.3:c.5488G>T
NC_000023.11:g.154904909C>A
CM000685.2:g.154904909C>A
NC_000023.10:g.154133184C>A
CM000685.1:g.154133184C>A
NC_000023.9:g.153786378C>A
NG_011403.1:g.122815G>T
NG_011403.2:g.122815G>T
ENST00000360256.9:c.5488G>T
ENST00000360256.8:c.5488G>T
NM_000132.4:c.5488G>T

Pathogenic

Met criteria codes 3

PM2_Supporting PS4_Supporting PVS1

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.5488G>T (p.Glu1830Ter) variant is a nonsense variant that is predicted to introduce a premature stop codon in exon 16/26 and expected to result in nonsense-mediated mRNA decay, so PVS1 criteria is met. This variant is absent from males in population databases (gnomAD v2.1.1/gnomAD v3), which meets PM2_Supporting criteria. The c.5488G>T (p.Glu1830Ter) variant is not reported in patients with Hemophilia A in the literature to the best of our knowledge; however 1 patient with severe hemophilia A is reported from internal laboratory data. 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: PVS1, PM2_Supporting, PS4_Supporting.

Met criteria codes

PM2_Supporting	✔	The c.5488G>T (p.Glu1830Ter) variant is absent from males in population databases (gnomAD v2.1.1/gnomAD v3).
PS4_Supporting	✔	The c.5488G>T (p.Glu1830Ter) variant is not reported in patients with Hemophilia A in the literature to the best of our knowledge. One male patient with severe hemophilia A and baseline FVIII:C <1% (most recent FVIII:C = 4% with continuous prophylaxis) is noted in the internal laboratory data.
PVS1	✔	The c.5488G>T (p.Glu1830Ter) variant is a nonsense variant that is predicted to introduce a premature stop codon in exon 16/26 and expected to result in nonsense-mediated mRNA decay.

Curation History

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