

Variant: *NM_019863.3:c.137T>A*

Version: 1.0

CA414907101 [↗](#)

Gene: F8 ([HGNC:2157](#))

Condition: hemophilia A ([MONDO:0010602](#))

Inheritance Mode: X-linked inheritance

UUID: ff4d31f3-17cd-4752-b167-53383dd6a07b

Approved on: 2025/10/3

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HGVS expressions

NM_019863.3:c.137T>A

NC_000023.11:g.154863115A>T

CM000685.2:g.154863115A>T

NC_000023.10:g.154091390A>T

CM000685.1:g.154091390A>T

NC_000023.9:g.153744584A>T

NG_011403.1:g.164609T>A

NG_011403.2:g.164609T>A

ENST00000360256.9:c.6542T>A

ENST00000644698.1:c.275T>A

ENST00000330287.10:c.137T>A

ENST00000360256.8:c.6542T>A

NM_000132.3:c.6542T>A

NM_019863.2:c.137T>A

NM_000132.4:c.6542T>A

Likely Pathogenic

Met criteria codes **4**

PP4_Moderate

PS4_Moderate

PP3

PM2_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 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.6542T>A (p.Leu2181His) variant is absent from males in population databases (gnomAD v2.1.1/gnomAD v3) meeting **PM2_Supporting**. The c.6542T>A (p.Leu2181His) missense variant has a REVEL score of 0.936 (>0.6) meeting **PP3**. The variant has been reported in at least 3 probands meeting phenotypic criteria for F8 meeting **PS4_Moderate** and **PP4_Moderate** (PMID: 29296726). In

summary, this variant meets criteria to be classified as likely pathogenic. ACMG/AMP criteria applied, as specified by the Coagulation Factor Deficiency Variant Curation Expert Panel for F8/F9: PM2_Supporting, PP3, PS4_Moderate, and PP4_Moderate.

Met criteria codes

PP4_Moderate			There is at least 1 proband with severe Hemophilia A, meeting phenotypic criteria for F8.
PS4_Moderate			The c.6542T>A (p.p.Leu2181His) variant has been reported in 3 probands (1-3 probands & 0 gnomAD alleles) meeting phenotypic criteria for F8.
PP3			The c.6542T>A (p.Leu2181His) missense variant has a REVEL score of 0.936 (>0.6) and a CADD score of 26.3 (>21).
PM2_Supporting			The c.6542T>A (p.Leu2181His) variant is absent from males in population databases (gnomAD v2.1.1/gnomAD v3).

Curation History

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