

Variant: *NM_000132.4(F8):c.3637del (p.Ile1213fs)*

Version: 1.0

CA255146 [↗](#)

10253 (ClinVar) [↗](#)

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

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

Inheritance Mode: X-linked inheritance

UUID: 19e2feae-a2b9-46b5-aa09-71123369b1ca

Approved on: 2024/6/25

Published on: 2024/7/10

HGVS expressions

NM_000132.4(F8):c.3637del (p.Ile1213fs)

NM_000132.4:c.3637del

NM_000132.4:c.3637delA

NC_000023.11:g.154930161del

CM000685.2:g.154930161del

NC_000023.10:g.154158436del

CM000685.1:g.154158436del

NC_000023.9:g.153811630del

NG_011403.1:g.97571del

NG_011403.2:g.97571del

ENST00000360256.9:c.3637del

ENST00000647125.1:c.*3303del

ENST00000360256.8:c.3637del

NM_000132.3:c.3637del

Pathogenic

Met criteria codes **4**

PS4

PS2_Very Strong

PVS1

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 F8 c.3637del (p.Ile1213Phefs*5) variant is a frameshift variant that is predicted to introduce a premature stop codon in exon 14 and expected to result in nonsense-mediated mRNA decay. This variant is completely absent from males in gnomAD v2.1.1 and gnomAD v3. This variant has been reported in >16 probands with moderate to severe hemophilia, meeting phenotypic criteria for F8 (PMID: 15921397; PMID: 20533009; PMID: 8307558; PMID: 16601827). This variant has been reported both with and without the development of inhibitors.

This variant is reported as de novo in at least seven probands with maternilia confirmed in the affected male (PMID: 29381227). 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: PVS1, PS2_Very Strong, PS4_Very Strong, PM2_Supporting. (ClinGen Coagulation Factor Deficiency Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for F8 Version 1.0.0., Released 10/5/2023)

Met criteria codes

PS4			At least 8 individuals with severe Hemophilia A across 10 publications reported (202 cases registered in the EAHAD database) who meet F8 phenotype criteria specified by the CFD VCEP for PS4.
PS2_Very Strong			There are at least at least 7 probands meeting phenotypic criteria for F8 (>4 points), with confirmed de novo (maternity confirmed in an affected male) occurrence PMID: 29381227.
PVS1			The 1-bp deletion occurs in exon 14 which results in a PTC 5 codons downstream, within exon 14/26. NMD is predicted.
PM2_Supporting			The variant is is absent from males in population databases (gnomAD v2.1.1/gnomAD v3).

Curation History

▼

▼

Showing 1 to 1 of 1 rows

--

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.