

Variant: *NM\_000132.4:c.2087C>T*

Version: 1.0

CA414909018 [↗](#)

2775445 (ClinVar) [↗](#)

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

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

**Inheritance Mode:** X-linked inheritance

**UUID:** f30a06e3-0a1c-419f-9520-c67684ffe703

**Approved on:** 2024/2/2

**Published on:** 2024/7/11

## HGVS expressions

**NM\_000132.4:c.2087C>T**

NC\_000023.11:g.154947724G>A

CM000685.2:g.154947724G>A

NC\_000023.10:g.154175999G>A

CM000685.1:g.154175999G>A

NC\_000023.9:g.153829193G>A

NG\_011403.1:g.80000C>T

NG\_011403.2:g.80000C>T

ENST00000360256.9:c.2087C>T

ENST00000647125.1:c.\*1779+6168C>T

ENST00000360256.8:c.2087C>T

NM\_000132.3:c.2087C>T

**Pathogenic**

Met criteria codes **4**

PS4

PP3

PM2\_Supporting

PP4\_Moderate

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.2087C>T (p.Thr696Ile) variant is absent from males in gnomAD v2.1.1 & gnomAD v3. 1 allele is reported in gnomAD v3.1.1 meeting PM2\_Supporting criteria. The missense variant has a REVEL score of 0.927 (>0.6) meeting PP3 criteria. The variant has been reported in at least 18 probands with mild hemophilia A meeting phenotypic criteria for F8 at the very strong evidence weight (PMID: 24845853 and My Life Our Future data - 29296726). This variant has also been associated with discrepant factor VIII activity levels (PMID: 32232366). 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\_VeryStrong, PP4\_Moderate, PP3, PM2\_Supporting.

Met criteria codes

|                |  |   |                                                                                                                                                                                                                |
|----------------|--|---|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| PS4            |  | ✓ | There are well over 8 individuals with mild hemophilia A reported in the literature and internal laboratory data meeting F8-phenotype criteria. PS4_Very strong is applied.                                    |
| PP3            |  | ✓ | The c.2087C>T (p.Thr696Ile) missense variant has a REVEL score of 0.927 (>0.6).                                                                                                                                |
| PM2_Supporting |  | ✓ | The c.2087C>T (p.Thr696Ile) variant is absent from males in gnomAD v2.1.1 & gnomAD v3. 1 allele is reported in gnomAD v3.1.1. (MAF - 0.00009480 in Latino/admixed American population). PM2_Supporting is met. |
| PP4_Moderate   |  | ✓ | Male with mild hemophilia A with 7% factor VIII activity level who had full F8 and F9 gene sequencing and deletion/duplication analysis through the MLOF study.                                                |

Curation History

Showing 1 to 1 of 1 rows

| See Report           | Preferred Variant Title | Classification | Condition    | Published Date | Version | Criteria Specification                                                                                                                   | Gene |
|----------------------|-------------------------|----------------|--------------|----------------|---------|------------------------------------------------------------------------------------------------------------------------------------------|------|
| <a href="#">View</a> | NM_000132.4:c.2087C>T   | Pathogenic     | Hemophilia A | 2024-07-11     | 1.0     | ClinGen Coagulation Factor Deficiency Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for F8 Version 1.0.0 | F8   |

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.