

Variant: *NM_000132.4(F8):c.5703C>A (p.Ile1901=)*

Version: 1.0

CA10567943 [↗](#)

1685787 (ClinVar) [↗](#)

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

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

Inheritance Mode: X-linked inheritance

UUID: e76604d7-5270-4ce3-9b34-e95d6adfb996

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HGVS expressions

NM_000132.4(F8):c.5703C>A (p.Ile1901=)

NM_000132.4:c.5703C>A

NC_000023.11:g.154904408G>T

CM000685.2:g.154904408G>T

NC_000023.10:g.154132683G>T

CM000685.1:g.154132683G>T

NC_000023.9:g.153785877G>T

NG_011403.1:g.123316C>A

NG_011403.2:g.123316C>A

ENST00000360256.9:c.5703C>A

ENST00000360256.8:c.5703C>A

NM_000132.3:c.5703C>A

Benign

Met criteria codes **2**

BA1 **BP4**

Not Met criteria codes **2**

BP7 **PS4**

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.5703C>A variant in F8 is a synonymous (silent) variant (p.Ile1901=) that is not predicted by SpliceAI to impact splicing. This variant is located in Exon 17, within the A3 domain of FVIII. However, BP7 was not applied as the nucleotide is conserved. This variant has been reported in 1 proband with mild Hemophilia A. However, PS4_Supporting cannot be applied because VWD 2N was not ruled out (PMID: 16128892) and BA1 was met. The c.5703C>A (p.Ile1901=) variant is reported at an MAF of 0.007915 (151/19078 alleles) in the South Asian population in gnomAD v2.1.1 with 105 hemizygotes, meeting BA1 criteria of MAF >= 0.000333. The computational predictor REVEL has a score of 0 which is below the threshold of 0.3, and the splice site predictor Splice AI indicated that the variant has no impact on splicing,

evidence that does not predict a damaging effect on F8 function (BP4_Supporting). In summary, this variant meets the criteria to be classified as benign for Hemophilia A based on the ACMG/AMP criteria applied, as specified by the Coagulation Factor Deficiency Variant Curation Expert Panel for F8 (version 1.0.0, released 10/5/2023): BA1, BP4_Supporting.

Met criteria codes

BA1			The c.5703C>A (p.Ile1901=) variant is reported at an MAF of 0.007915 (151/19078 alleles) in the South Asian population in gnomAD v2.1.1 with 105 hemizygotes, meeting BA1 criteria of MAF >= 0.000333.
BP4			The computational predictor REVEL has a score of 0 which is below the threshold of 0.3, and the splice site predictor Splice AI indicated that the variant has no impact on splicing (Splice AI score of 0.01, 0.01, 0.02, 0.02, which is less than the threshold of <0.05), evidence that does not predict a damaging effect on F8 function (BP4_Supporting)

Not Met criteria codes

BP7			The c.5703C>A (p.Ile1901=) variant is a synonymous (silent) variant that is not predicted by SpliceAI to impact splicing. Splice AI scores = 0.01, 0.01, 0.02, 0.02 which is less than the threshold of 0.05. BP7 was not applied because the nucleotide is conserved as shown by PhyloP 100 vertebrates score of 1.298 (cutoff <0.1) and PhastCons 100 vertebrates score of 1 (cutoff <0.5).
PS4			This variant has been reported in 1 proband with mild Hemophilia A. However, PS4_Supporting cannot be applied because VWD 2N was not ruled out and because BA1 met (PMID: 16128892).

Curation History



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