The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000132.3(F8):c.6046C>T (p.Arg2016Trp)

Version: 1.0

CA255197

10304 (ClinVar)

Gene: F8 (HGNC:2157)
Condition: hemophilia A (MONDO:0010602)
Inheritance Mode: X-linked inheritance
UUID: 3d921025-1d2e-41c3-9200-a2d11c4ad044
Approved on: 2024/2/2
Published on: 2024/7/11

HGVS expressions

NM_000132.3(F8):c.6046C>T (p.Arg2016Trp)
NM_000132.3:c.6046C>T
NC_000023.11:g.154902120G>A
CM000685.2:g.154902120G>A
NC_000023.10:g.154130395G>A
CM000685.1:g.154130395G>A
NC_000023.9:g.153783589G>A
NG_011403.1:g.125604C>T
NG_011403.2:g.125604C>T
ENST00000360256.9:c.6046C>T
ENST00000360256.8:c.6046C>T
NM_000132.4:c.6046C>T

Pathogenic

Met criteria codes 4

PP4_Moderate PS4 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.6046C>T (p.Arg2016Trp) variant is completely absent from gnomAD v2.1.1 and gnomAD v3 meeting PM2_Supporting. This missense variant has a REVEL score of 0.822 (>0.6) meeting PP3 criteria. More than 46 probands are reported with the variant and moderate-severe hemophilia A in the literature and internal laboratory data (PMID: 29296726, 20102490, 18387975), meeting F8 phenotype criteria. This variant has been associated with discrepant factor VIII activity levels (PMID: 32232366). This variant has also been reported in individuals with a history of inhibitor development to factor replacement therapy (EAHAD database). 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: PS4_Very Strong, PP4_Moderate, PP3, PM2_Supporting.

Met criteria codes

PP4_Moderate	✔	Male with severe hemophilia A who had full F8 and F9 gene sequencing and deletion/duplication analysis.
PS4	✔	More than 46 probands are reported with the variant and moderate-severe hemophilia A in the literature and internal laboratory data (PMID: 29296726, 20102490, 18387975), meeting F8 phenotype criteria. The threshold for PS4_Very Strong is met (>8).
PP3	✔	This missense variant has a REVEL score of 0.822 (>0.6) and meets criteria for PP3.
PM2_Supporting	✔	The c.6046C>T (p.Arg2016Trp) variant is completely absent from gnomAD v2.1.1 and 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.

ClinGen Terms of Use.
¤ Powered by BCM's Genboree.