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_000132.4:c.6429+2T>A

Version: 1.0

CA414899265

2775450 (ClinVar)

Gene: F8 (HGNC:2157)
Condition: hemophilia A (MONDO:0010602)
Inheritance Mode: X-linked inheritance
UUID: 46c40028-f5d9-4236-8b9c-3b05d2c95293
Approved on: 2024/2/9
Published on: 2024/7/11

HGVS expressions

NM_000132.4:c.6429+2T>A
NC_000023.11:g.154896075A>T
CM000685.2:g.154896075A>T
NC_000023.10:g.154124350A>T
CM000685.1:g.154124350A>T
NC_000023.9:g.153777544A>T
NG_011403.1:g.131649T>A
NG_011403.2:g.131649T>A
ENST00000360256.9:c.6429+2T>A
ENST00000360256.8:c.6429+2T>A
NM_000132.3:c.6429+2T>A

Pathogenic

Met criteria codes 3

PS4 PVS1_Strong 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.6429+2T>A variant causes in frame skipping of exon 22 resulting in a protein lacking 52 aa of the C2 domain (PMID: 15670040), which meets PVSS1_Strong criteria. This variant has been identified in at least 4 individuals with severe hemophilia A (PMID: 15670040, 19740093, 12195713) and is completely absent from gnomAD v2.1.1 and v3.1.1, which meets criteria for PS4_Strong and PM2_Supporting. 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_Strong, PS4, PM2_Supporting.

Met criteria codes

PS4	✔	Four probands noted to have severe hemophilia A found in literature, and variant is absent in gnomAD v2.1.1 and v3.1.
PVS1_Strong	✔	Variant causes in frame skipping of exon 22 resulting in a protein lacking 52 aa of the C2 domain.
PM2_Supporting	✔	Variant is absent in gnomAD v2.1.1 and v3.1.

Curation History

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