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Variant: NM_000552.5(VWF):c.1451A>G (p.His484Arg)

Version: 1.0

CA6403395

256654 (ClinVar)

Gene: VWF (HGNC:7450)
Condition: hereditary von Willebrand disease (MONDO:0019565)
Inheritance Mode: Undetermined mode of inheritance
UUID: 1bab323b-11d1-4b76-8ae4-010d404e4fdc
Approved on: 2026/3/3
Published on: 2026/4/6

HGVS expressions

NM_000552.5(VWF):c.1451A>G (p.His484Arg)
NM_000552.5:c.1451A>G
NC_000012.12:g.6063036T>C
CM000674.2:g.6063036T>C
NC_000012.11:g.6172202T>C
CM000674.1:g.6172202T>C
NC_000012.10:g.6042463T>C
NG_009072.1:g.66635A>G
NG_009072.2:g.66635A>G
ENST00000261405.10:c.1451A>G
ENST00000261405.9:c.1451A>G
ENST00000538635.5:n.420+47479A>G
NM_000552.3:c.1451A>G
NM_000552.4:c.1451A>G

Benign

Met criteria codes 2

BP4 BA1

Evidence Links 0

Expert Panel

von Willebrand Disease VCEP

Criteria Specification Information

Criteria Specification: *ClinGen von Willebrand Disease Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for VWF Version 1.0.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

von Willebrand Disease VCEP

The NM_000552.5:c.1451A>G variant in VWF is a missense variant predicted to cause substitution of histidine by arginine at amino acid 484. The Grpmax filtering allele frequency in gnomAD v4.1 is 0.7007 (based on 64214/91042 alleles in the south Asian population, including 22835 homozygotes), which is higher than the ClinGen VWD VCEP threshold of >0.1 for BA1. The computational predictor REVEL gives a score of 0.0630, which is below the ClinGen VWD VCEP threshold of <0.290 and does not predict a damaging effect on VWF

function (BP4). Additionally, the computational splicing predictor SpliceAI indicated that the variant has no impact on splicing. This variant is also referenced as a polymorphic variant in several reports (PMIDs 38308883, 37017006). In summary, this variant meets the criteria to be classified as benign for hereditary von Willebrand disease based on the ACMG/AMP criteria applied, as specified by the ClinGen VWD VCEP: BA1, BP4

Met criteria codes

BP4	✔	The computational predictor REVEL gives a score of 0.0630, which is below the ClinGen VWD VCEP threshold of <0.290 and does not predict a damaging effect on VWF function (BP4). Additionally, the computational splicing predictor SpliceAI indicated that the variant has no impact on splicing.
BA1	✔	The Grpmax filtering allele frequency in gnomAD v4.1 is 0.7007 (based on 64214/91042 alleles in the south Asian population, including 22835 homozygotes), which is higher than the ClinGen VWD VCEP threshold of >0.1 for BA1.

Curation History

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See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_000552.5(VWF):c.1451A>G (p.His4...	Benign	Hereditary Von Willebrand Disease	2026-04-06	1.0	ClinGen von Willebrand Disease Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for VWF Version 1.0.0	VWF

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