

Variant: *NM_001114753.3(ENG):c.1586G>A (p.Arg529His)*

Version: 1.0

[CA321073](#)

[213212 \(ClinVar\)](#)

Gene: ENG ([HGNC:2022](#))

Condition: telangiectasia, hereditary hemorrhagic, type 1 ([MONDO:0008535](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: 59ed568c-8b34-41b1-baa2-f56a0adfb060

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HGVS expressions

NM_001114753.3:c.1586G>A

NM_001114753.3(ENG):c.1586G>A (p.Arg529His)

NC_000009.12:g.127818220C>T

CM000671.2:g.127818220C>T

NC_000009.11:g.130580499C>T

CM000671.1:g.130580499C>T

NC_000009.10:g.129620320C>T

NG_009551.1:g.41549G>A

ENST00000480266.6:c.1040G>A

ENST00000373203.9:c.1586G>A

ENST00000344849.4:c.1586G>A

ENST00000373203.8:c.1586G>A

ENST00000480266.5:c.1040G>A

NM_000118.3:c.1586G>A

NM_001114753.2:c.1586G>A

NM_001278138.1:c.1040G>A

NR_136302.1:n.1378-91C>T

NM_001278138.2:c.1040G>A

Pathogenic

Met criteria codes **4**

PS4

PM2_Supporting

PP1_Strong

PP4_Moderate

Evidence Links **0**

Expert Panel

[Hereditary Hemorrhagic Telangiectasia VCEP](#)

Criteria Specification Information

Criteria Specification: *ClinGen Hereditary Hemorrhagic Telangiectasia Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for ENG Version 1.1.0*

Criteria Specification Approval History









Criteria Specifications for this VCEP

Evidence submitted by expert panel

Hereditary Hemorrhagic Telangiectasia VCEP

The NM_001114753.3: c.1586G>A variant in ENG is a missense variant predicted to cause substitution of arginine by histidine at amino acid 529 (p.Arg529His). This variant has been reported in more than 10 probands with a phenotype consistent with HHT (PS4; PMID: 22991266, 16752392, Internal lab contributors). At least one patient's phenotype meets Curacao Criteria for HHT, and sequencing and large deletion/duplication analysis was performed for ENG and ACVRL1, which is highly specific for HHT (PP4_Moderate; Internal lab contributors). The variant has been reported to segregate with HHT in more than 20 affected family members from multiple families (PP1_Strong; Internal lab contributors). The overall minor allele frequency in gnomAD v2.1.1 is 0.000004 (1/251282 alleles), which is lower than the ClinGen Hereditary Hemorrhagic Telangiectasia VCEP threshold (<6 total alleles) for PM2_Supporting, meeting this criterion (PM2_Supporting). The computational predictor REVEL gives a score of 0.579, which is neither above nor below the thresholds predicting a damaging or benign impact on ENG function. In summary, this variant meets the criteria to be classified as pathogenic for autosomal dominant hereditary hemorrhagic telangiectasia based on the ACMG/AMP criteria applied, as specified by the ClinGen Hereditary Hemorrhagic Telangiectasia Variant Curation Expert Panel: PM2_Supporting, PS4, PP4_Moderate, PP1_Strong (specifications version 1.1.0; 09/11/2024).

Met criteria codes

PS4			This variant has been reported in more than 10 probands with a phenotype consistent with HHT (PS4; PMID: 22991266, 16752392, Internal lab contributors).
PM2_Supporting			The overall minor allele frequency in gnomAD v2.1.1 is 0.000004 (1/251282 alleles), which is lower than the ClinGen Hereditary Hemorrhagic Telangiectasia VCEP threshold (<6 total alleles) for PM2_Supporting, meeting this criterion (PM2_Supporting).
PP1_Strong			The variant has been reported to segregate with HHT in more than 20 affected family members from multiple families (PP1_Strong; Internal lab contributors).
PP4_Moderate			At least one patient's phenotype meets Curacao Criteria for HHT, and sequencing and large deletion/duplication analysis was performed for ENG and ACVRL1, which is highly specific for HHT (PP4_Moderate; Internal lab contributors).

Curation History



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