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_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
Approved on: 2024/9/11
Published on: 2024/9/19

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

PM2_Supporting | PP4_Moderate | PS4 | PP1_Strong

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

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).
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).
PS4	✔	This variant has been reported in more than 10 probands with a phenotype consistent with HHT (PS4; PMID: 22991266, 16752392, Internal lab contributors).
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).

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.