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.1145G>A (p.Cys382Tyr)

Version: 1.0

CA374978902

430375 (ClinVar)

Gene: ENG (HGNC:2022)
Condition: telangiectasia, hereditary hemorrhagic, type 1 (MONDO:0008535)
Inheritance Mode: Autosomal dominant inheritance
UUID: 495f0389-0c66-4d9f-ab7f-f1bf5d4cfa68
Approved on: 2025/2/4
Published on: 2025/3/26

HGVS expressions

NM_001114753.3(ENG):c.1145G>A (p.Cys382Tyr)
NM_001114753.3:c.1145G>A
NC_000009.12:g.127820027C>T
CM000671.2:g.127820027C>T
NC_000009.11:g.130582306C>T
CM000671.1:g.130582306C>T
NC_000009.10:g.129622127C>T
NG_009551.1:g.39742G>A
ENST00000480266.6:c.599G>A
ENST00000373203.9:c.1145G>A
ENST00000344849.4:c.1145G>A
ENST00000373203.8:c.1145G>A
ENST00000480266.5:c.599G>A
ENST00000486329.1:n.113G>A
NM_000118.3:c.1145G>A
NM_001114753.2:c.1145G>A
NM_001278138.1:c.599G>A
NR_136302.1:n.1569-1168C>T
NM_001278138.2:c.599G>A

Pathogenic

Met criteria codes 6

PP1 PM1 PM2_Supporting PS3_Supporting PP4_Moderate PS4

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.1145G>A variant in ENG is a missense variant predicted to cause substitution of cysteine by tyrosine at amino acid 382 (p.Cys382Tyr). This variant alters amino acid C382 of ENG that is defined as a critical residue (previously reported to be likely pathogenic or pathogenic) by the ClinGen Hereditary Hemorrhagic Telangiectasia Variant Curation Expert Panel (PM1; PMID: 17786384). This variant has been reported in more than 4 probands with a phenotype consistent with HHT (PS4; 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; PMID: 30763665). The variant has been reported to segregate with HHT in 3 affected family members from a single family (PP1; PMID: 30763665, Internal lab contributors). This variant is absent from gnomAD v.2.1.1 (PM2_Supporting). The computational predictor REVEL gives a score of 0.56, which is neither above nor below the thresholds predicting a damaging or benign impact on ENG function. Functional assays showed the variant protein to have reduced protein expression in CHO-K1 cells, indicating that this variant impacts protein function (PS3_Supporting, PMID: 30763665). 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: PS4, PM1, PP4_Moderate, PM2_Supporting, PS3_Supporting, PP1 (specifications version 1.1.0; 02/04/2025).

Met criteria codes

PP1	✔	The variant has been reported to segregate with HHT in 3 affected family members from a single family (PP1; PMID: 30763665, Internal lab contributors).
PM1	✔	This variant alters amino acid C382 of ENG that is defined as a critical residue (previously reported to be likely pathogenic or pathogenic) by the ClinGen Hereditary Hemorrhagic Telangiectasia Variant Curation Expert Panel (PM1; PMID: 17786384).
PM2_Supporting	✔	This variant is absent from gnomAD v.2.1.1 (PM2_Supporting).
PS3_Supporting	✔	Functional assays showed the variant protein to have reduced protein expression in CHO-K1 cells, indicating that this variant impacts protein function (PS3_Supporting, PMID: 30763665).
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; PMID: 30763665).
PS4	✔	This variant has been reported in more than 4 probands with a phenotype consistent with HHT (PS4; Internal lab contributors).

Curation History

Showing 1 to 1 of 1 rows

See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_001114753.3(ENG):c.1145G>A (p....	Pathogenic	Telangiectasia, Hereditary Hemorrhagic, Type 1	2025-03-26	1.0	ClinGen Hereditary Hemorrhagic Telangiectasia Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for ENG Version 1.1.0	ENG

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.