

Variant: *NM_001114753.3(ENG):c.662T>C (p.Leu221Pro)*

Version: 1.0

CA374983528 [↗](#)

435060 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 3d717ef0-3d29-4ae8-92c1-13c6f812bf95

Approved on: 2024/3/15

Published on: 2024/3/15

HGVS expressions

NM_001114753.3(ENG):c.662T>C (p.Leu221Pro)

NM_001114753.3:c.662T>C

NC_000009.12:g.127825722A>G

CM000671.2:g.127825722A>G

NC_000009.11:g.130588001A>G

CM000671.1:g.130588001A>G

NC_000009.10:g.129627822A>G

NG_009551.1:g.34047T>C

ENST00000480266.6:c.116T>C

ENST00000373203.9:c.662T>C

ENST00000344849.4:c.662T>C

ENST00000373203.8:c.662T>C

ENST00000480266.5:c.116T>C

NM_000118.3:c.662T>C

NM_001114753.2:c.662T>C

NM_001278138.1:c.116T>C

NM_001278138.2:c.116T>C

Likely Pathogenic

Met criteria codes 4

PP4_Moderate

PM2_Supporting

PS3_Supporting

PS4

Not Met criteria codes 1

PP3

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 1.0.0*

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Hereditary Hemorrhagic Telangiectasia VCEP

The NM_001114753.3: c.662T>C variant in ENG is a missense variant predicted to cause substitution of leucine by proline at amino acid 221 (p.Leu221Pro). This variant is absent from gnomAD v2.1.1 (PM2_Supporting). This variant has been reported in >10 probands with a phenotype consistent with HHT (PS4; PMID: 10545596, 15880681, 17384219, 18498373, 20414677, 22991266, 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 computational predictor REVEL gives a score of 0.478, which is neither above nor below the thresholds predicting a damaging or benign impact on ENG function. However, protein expression assays in cell lines showed the variant causes reduced endoglin expression (PS3_Supporting; PMID: 10545596). In summary, this variant meets the criteria to be classified as likely 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, PP4_Moderate, PS3_Supporting, PM2_Supporting (specification version 1.0.0; 1/4/2024).

Met criteria codes

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).
PM2_Supporting			This variant is absent from gnomAD v2.1.1 (PM2_Supporting).
PS3_Supporting			Protein expression assays in cell lines showed the variant causes reduced endoglin expression (PS3_Supporting; PMID: 10545596).
PS4			This variant has been reported in >10 probands with a phenotype consistent with HHT (PS4; PMID: 10545596, 15880681, 17384219, 18498373, 20414677, 22991266, Internal lab contributors).

Not Met criteria codes

PP3			The computational predictor REVEL gives a score of 0.478, which is neither above nor below the thresholds predicting a damaging or benign impact on ENG function.
-----	---	---	---

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.](#)