

Variant: *NM_001114753.3(ENG):c.1844C>T (p.Ser615Leu)*

Version: 1.0

CA211415 [↗](#)

161229 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 6d938fab-e9da-4a5a-b979-c3393ff46cf7

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HGVS expressions

NM_001114753.3(ENG):c.1844C>T (p.Ser615Leu)

NM_001114753.3:c.1844C>T

NC_000009.12:g.127815951G>A

CM000671.2:g.127815951G>A

NC_000009.11:g.130578230G>A

CM000671.1:g.130578230G>A

NC_000009.10:g.129618051G>A

NG_009551.1:g.43818C>T

NG_023245.1:g.18077G>A

ENST00000480266.6:c.1298C>T

ENST00000373203.9:c.1844C>T

ENST00000344849.4:c.1844C>T

ENST00000373203.8:c.1844C>T

ENST00000480266.5:c.1298C>T

NM_000118.3:c.1844C>T

NM_001114753.2:c.1844C>T

NM_001278138.1:c.1298C>T

NM_001278138.2:c.1298C>T

Likely Benign

Met criteria codes **3**

BS3_Supporting BS1 BP5

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.1844C>T variant in ENG is a missense variant predicted to cause substitution of serine by leucine at amino acid 615 (p.Ser615Leu). The filtering allele frequency (the lower threshold of the 95% CI of 285/115780) of the c.1844C>T variant in ENG is 0.002284 for European (non-Finnish) chromosomes by gnomAD v2.1.1, which is higher than the ClinGen Hereditary Hemorrhagic Telangiectasia Variant Curation Expert Panel threshold (>0.002) for BS1, and therefore meets this criterion (BS1). This variant has been observed in 1 patient with an alternate molecular basis for disease (patient also carries a likely pathogenic/pathogenic ACVRL1 variant) (BP5; PMID: 15712270). The computational predictor REVEL gives a score of 0.188, which is neither above nor below the thresholds predicting a damaging or benign impact on ENG function. However, cellular assays in NIH-3T3 cells showed that BMP9 binding and BMP9 response were all normal, indicating that this variant does not impact protein function (BS3_Supporting; PMID: 25312062, 22022569). In summary, this variant meets the criteria to be classified as likely benign 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: BS1, BP5, BS3_Supporting (specification version 1.0.0; 1/4/2024).

Met criteria codes

BS3_Supporting			Cellular assays in NIH-3T3 cells showed that BMP9 binding and BMP9 response were all normal, indicating that this variant does not impact protein function (BS3_Supporting; PMID: 25312062, 22022569).
BS1			The filtering allele frequency (the lower threshold of the 95% CI of 285/115780) of the c.1844C>T variant in ENG is 0.002284 for European (non-Finnish) chromosomes by gnomAD v2.1.1, which is higher than the ClinGen Hereditary Hemorrhagic Telangiectasia Variant Curation Expert Panel threshold (>0.002) for BS1, and therefore meets this criterion (BS1).
BP5			This variant has been observed in 1 patient with an alternate molecular basis for disease (also carriers likely pathogenic/pathogenic ACVRL1 variant) (BP5; PMID: 15712270).

Not Met criteria codes

PP3			The computational predictor REVEL gives a score of 0.188, which is neither above nor below the thresholds predicting a damaging or benign impact on ENG function.
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Curation History [↗](#)



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