

Variant: *NM_001114753.3(ENG):c.1510G>A (p.Val504Met)*

Version: 1.0

CA211420 [↗](#)

161231 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: bdb31ba6-8241-494a-853a-41a92fa517a2

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HGVS expressions

NM_001114753.3(ENG):c.1510G>A (p.Val504Met)

NM_001114753.3:c.1510G>A

NC_000009.12:g.127818296C>T

CM000671.2:g.127818296C>T

NC_000009.11:g.130580575C>T

CM000671.1:g.130580575C>T

NC_000009.10:g.129620396C>T

NG_009551.1:g.41473G>A

ENST00000480266.6:c.964G>A

ENST00000373203.9:c.1510G>A

ENST00000344849.4:c.1510G>A

ENST00000373203.8:c.1510G>A

ENST00000480266.5:c.964G>A

NM_000118.3:c.1510G>A

NM_001114753.2:c.1510G>A

NM_001278138.1:c.964G>A

NR_136302.1:n.1378-15C>T

NM_001278138.2:c.964G>A

Likely Benign

Met criteria codes **3**

BS3_Supporting

BP2

BS1

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.1510G>A variant in ENG is a missense variant predicted to cause substitution of valine by methionine at amino acid 504 (p.Val504Met). The filtering allele frequency (the lower threshold of the 95% CI of 225/24916) of the c.1510G>A variant in ENG is 0.007757 for African/African American 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 trans with the variant c.23T>C, p.Leu8Pro (PMID: 19767588), which is classified as pathogenic by the ClinGen Hereditary Hemorrhagic Telangiectasia Variant Curation Expert Panel, in affected family members with HHT. The phase of the variants was confirmed by parental testing (BP2). The computational predictor REVEL gives a score of 0.239, 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). 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, BP2, 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).
BP2			This variant has been observed in trans with the variant c.23T>C, p.Leu8Pro (PMID: 19767588), which is classified as pathogenic by the ClinGen Hereditary Hemorrhagic Telangiectasia Variant Curation Expert Panel, in affected family members with HHT. The phase of the variants was confirmed by parental testing (BP2).
BS1			The filtering allele frequency (the lower threshold of the 95% CI of 225/24916) of the c.1510G>A variant in ENG is 0.007757 for African/African American 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).

Not Met criteria codes

PP3			The computational predictor REVEL gives a score of 0.239, 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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