

Variant: NM_001114753.3(ENG):c.1633G>A (p.Gly545Ser)

Version: 1.0

CA5252712 [↗](#)

237022 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: e5eca9a9-fff7-4c7a-b851-9568873871a7

Approved on: 2024/9/11

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HGVS expressions

NM_001114753.3:c.1633G>A

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NC_000009.12:g.127818173C>T

CM000671.2:g.127818173C>T

NC_000009.11:g.130580452C>T

CM000671.1:g.130580452C>T

NC_000009.10:g.129620273C>T

NG_009551.1:g.41596G>A

ENST00000480266.6:c.1087G>A

ENST00000373203.9:c.1633G>A

ENST00000344849.4:c.1633G>A

ENST00000373203.8:c.1633G>A

ENST00000480266.5:c.1087G>A

NM_000118.3:c.1633G>A

NM_001114753.2:c.1633G>A

NM_001278138.1:c.1087G>A

NR_136302.1:n.1378-138C>T

NM_001278138.2:c.1087G>A

Likely Benign

Met criteria codes **3**

BP5

BP2

BS1_Supporting

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.1633G>A variant in ENG is a missense variant predicted to cause substitution of glycine by serine at amino acid 545 (p.Gly545Ser). The filtering allele frequency (the lower threshold of the 95% CI of 54/35,428 alleles) of the c.1633G>A variant in ENG is 0.1% for Admixed American chromosomes by gnomAD v2.1.1, which is higher than the ClinGen Hereditary Hemorrhagic Telangiectasia Variant Curation Expert Panel threshold (>0.08%) for BS1_Supporting, and therefore meets this criterion (BS1_Supporting). This variant has been observed in trans with the variant c.391_392del, p.(Pro131Glyfs*17) (PMID: 18498373) which is classified as likely pathogenic (PMID: 18498373) in an individual with hereditary hemorrhagic telangiectasia. The phase of the variants was confirmed by family testing (BP2). This variant has been observed in at least two patients with an alternate molecular basis for disease (likely pathogenic/pathogenic variants identified in ACVRL1) (BP5; internal lab contributors). The computational predictor REVEL gives a score of 0.399, 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 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_Supporting, BP2, BP5 (specifications version 1.1.0; 09/11/2024).

Met criteria codes

BP5			This variant has been observed in at least two patients with an alternate molecular basis for disease (likely pathogenic/pathogenic variants identified in ACVRL1) (BP5; internal lab contributors).
BP2			This variant has been observed in trans with the variant c.391_392del, p.(Pro131Glyfs*17) (PMID: 18498373) which is classified as likely pathogenic (PMID: 18498373) in an individual with hereditary hemorrhagic telangiectasia. The phase of the variants was confirmed by family testing (BP2).
BS1_Supporting			The filtering allele frequency (the lower threshold of the 95% CI of 54/35,428 alleles) of the c.1633G>A variant in ENG is 0.1% for Admixed American chromosomes by gnomAD v2.1.1, which is higher than the ClinGen Hereditary Hemorrhagic Telangiectasia Variant Curation Expert Panel threshold (>0.08%) for BS1_Supporting, and therefore meets this criterion (BS1_Supporting).

Curation History



 

 

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