

Variant: NM_001114753.3(ENG):c.2T>G (p.Met1Arg)

Version: 1.0

CA374989708 [↗](#)

458346 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 9c37e4fd-9165-4c38-b2bb-afc7e9587d13

Approved on: 2024/3/15

Published on: 2024/3/15

HGVS expressions

NM_001114753.3:c.2T>G

NM_001114753.3(ENG):c.2T>G (p.Met1Arg)

NC_000009.12:g.127854354A>C

CM000671.2:g.127854354A>C

NC_000009.11:g.130616633A>C

CM000671.1:g.130616633A>C

NC_000009.10:g.129656454A>C

NG_009551.1:g.5415T>G

ENST00000373203.9:c.2T>G

ENST00000344849.4:c.2T>G

ENST00000373203.8:c.2T>G

NM_000118.3:c.2T>G

NM_001114753.2:c.2T>G

Pathogenic

Met criteria codes **5**

PVS1_Strong

PS4

PP4_Moderate

PM5_Strong

PM2_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 1.0.0

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

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

Evidence submitted by expert panel

Hereditary Hemorrhagic Telangiectasia VCEP

The NM_001114753.3: c.2T>G variant in ENG may cause a truncated or absent protein by altering the start codon of the coding sequence and is predicted to lead to the omission of a critical region of the protein (PVS1_Strong). This variant is absent from gnomAD v2.1.1 (PM2_Supporting). This variant has been reported in >4 probands with a phenotype consistent with HHT (PS4; PMID:12920067, 32300199, 15024723, ClinVar, 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). Four different missense variants, c.3G>A, c.1A>T, c.2T>C, c.1A>G, in the same codon have been classified as pathogenic/likely pathogenic for autosomal dominant hereditary hemorrhagic telangiectasia by the ClinGen Hereditary Hemorrhagic Telangiectasia Variant Curation Expert Panel (PM5_Strong). 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: PM2_Supporting, PVS1_Strong, PS4, PP4_Moderate, PM5_Strong (specification version 1.0.0; 1/4/2024).

Met criteria codes

PVS1_Strong			The NM_001114753.3: c.2T>G variant in ENG may cause a truncated or absent protein by altering the start codon of the coding sequence and is predicted to lead to the omission of a critical region of the protein (PVS1_Strong).
PS4			This variant has been reported in >4 probands with a phenotype consistent with HHT (PS4; PMID:12920067, 32300199, 15024723, ClinVar, Internal lab contributors).
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).
PM5_Strong			Four different missense variants, c.3G>A, c.1A>T, c.2T>C, c.1A>G, in the same codon have been classified as pathogenic/likely pathogenic for autosomal dominant hereditary hemorrhagic telangiectasia by the ClinGen Hereditary Hemorrhagic Telangiectasia Variant Curation Expert Panel (PM5_Strong).
PM2_Supporting			This variant is absent from gnomAD v2.1.1 (PM2_Supporting).

Curation History



 

 

Showing 1 to 1 of 1 rows

--

