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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

PM5_Strong PVS1_Strong PM2_Supporting PP4_Moderate PS4

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

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).
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).
PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1 (PM2_Supporting).
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).
PS4	✔	This variant has been reported in >4 probands with a phenotype consistent with HHT (PS4; PMID:12920067, 32300199, 15024723, ClinVar, Internal lab contributors).

Curation History

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See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_001114753.3(ENG):c.2T>G (p.Met...	Pathogenic	Telangiectasia, Hereditary Hemorrhagic, Type 1	2024-03-15	1.0	ClinGen Hereditary Hemorrhagic Telangiectasia Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for ENG Version 1.0.0	ENG

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