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Variant: NM_000020.3(ACVRL1):c.706G>A (p.Glu236Lys)

Version: 1.0

CA384900118

657805 (ClinVar)

Gene: ACVRL1 (HGNC:94)
Condition: telangiectasia, hereditary hemorrhagic, type 2 (MONDO:0010880)
Inheritance Mode: Autosomal dominant inheritance
UUID: a3a12193-94e4-43f1-b3d4-cbc95920566a
Approved on: 2024/3/15
Published on: 2024/3/15

HGVS expressions

NM_000020.3(ACVRL1):c.706G>A (p.Glu236Lys)
NM_000020.3:c.706G>A
NC_000012.12:g.51914519G>A
CM000674.2:g.51914519G>A
NC_000012.11:g.52308303G>A
CM000674.1:g.52308303G>A
NC_000012.10:g.50594570G>A
NG_009549.1:g.12102G>A
ENST00000547400.6:c.436G>A
ENST00000551576.6:c.706G>A
ENST00000552678.2:c.706G>A
ENST00000388922.9:c.706G>A
ENST00000388922.8:c.706G>A
ENST00000419526.6:c.184G>A
ENST00000547400.5:c.436G>A
ENST00000550683.5:c.748G>A
NM_000020.2:c.706G>A
NM_001077401.1:c.706G>A
NM_001077401.2:c.706G>A

Pathogenic

Met criteria codes 4

PP1_Strong PM2_Supporting PS4 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 ACVRL1 Version 1.0.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Hereditary Hemorrhagic Telangiectasia VCEP

The NM_000020.3: c.706G>A variant in ACVRL1 is a missense variant predicted to cause substitution of glutamic acid by lysine at amino acid 236 (p.Glu236Lys). This variant is absent from gnomAD v2.1.1 (PM2_Supporting). This variant has been reported in at least 4 probands with a phenotype consistent of HHT (PS4; PMID: 25970827, ClinVar, Internal lab contributors). The variant has been reported to segregate with HHT in 5 affected members from 1 family, and in 2 affected siblings from a different family (PP1_Strong; PMID: 25970827, personal communication). The computational predictor REVEL gives a score of 0.668, which is above the threshold of ≥0.644, evidence that correlates with impact to ACVRL1 function (PP3). In summary, this variant meets the criteria to be classified as pathogenic for Hereditary Hemorrhagic Telangiectasia based on the ACMG/AMP criteria applied, as specified by the ClinGen Hereditary Hemorrhagic Telangiectasia Variant Curation Expert Panel: PM2_Supporting, PS4, PP1_Strong, PP3 (specification version 1.0.0; 1/04/2024).

Met criteria codes

PP1_Strong	✔	The variant has been reported to segregate with HHT in 5 affected members from 1 family, and in two affected siblings from a different family (PP1_Strong; PMID: 25970827, personal communication).
PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1 (PM2_Supporting).
PS4	✔	This variant has been reported in at least 4 probands with a phenotype consistent of HHT (PS4; PMID: 25970827, ClinVar, Internal lab contributors).
PP3	✔	The computational predictor REVEL gives a score of 0.668, which is above the threshold of ≥0.644, evidence that correlates with impact to ACVRL1 function (PP3).

Curation History

Showing 1 to 1 of 1 rows

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