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Variant: NM_000551.4(VHL):c.263G>A (p.Trp88Ter)

Version: 1.0

CA020197

182978 (ClinVar)

Gene: VHL (HGNC:7428)
Condition: von Hippel-Lindau disease (MONDO:0008667)
Inheritance Mode: Autosomal dominant inheritance
UUID: eb3883a6-80f5-45f8-9c0f-a2928a4e24ca
Approved on: 2024/6/25
Published on: 2024/7/17

HGVS expressions

NM_000551.4(VHL):c.263G>A (p.Trp88Ter)
NM_000551.4:c.263G>A
NC_000003.12:g.10142110G>A
CM000665.2:g.10142110G>A
NC_000003.11:g.10183794G>A
CM000665.1:g.10183794G>A
NC_000003.10:g.10158794G>A
NG_008212.3:g.5476G>A
ENST00000696142.1:c.263G>A
ENST00000696143.1:c.263G>A
ENST00000696153.1:c.263G>A
ENST00000256474.3:c.263G>A
ENST00000256474.2:c.263G>A
ENST00000345392.2:c.263G>A
NM_000551.3:c.263G>A
NM_198156.2:c.263G>A
NM_001354723.1:c.263G>A
NM_001354723.2:c.263G>A
NM_198156.3:c.263G>A

Pathogenic

Met criteria codes 3

PS4 PVS1 PM2_Supporting

Evidence Links 0

Expert Panel

VHL VCEP

Criteria Specification Information

Criteria Specification: *ClinGen VHL Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for VHL Version 1.0.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

VHL VCEP

The variant NM_000551.4(VHL):c.263G>A (p.Trp88Ter) in VHL is a truncating variant. This variant causes a premature stop codon in a biologically-relevant-exon predicted to undergo nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). This variant has been identified in at least 9 unrelated probands (and other related family members not counted within each) all meeting Danish VHL criteria, from literature evaluated in both CIViC and Hypothes.is VHL datasets. CIViC EIDs (https://civicdb.org): 8292;7606;5776;9374;6806;6538. This corresponds to Strong evidence (5-15 probands) (PS4). This variant is absent from gnomAD v4.1.0 (PM2_Supporting). In summary, this variant meets the criteria to be classified as Pathogenic for autosomal-dominant von Hippel Lindau syndrome (VHL syndrome) based on the ACMG/AMP criteria applied, as specified by the ClinGen VHL VCEP Version 1.0 (Specifications approval date: 02/26/2024. Variant Approval Date 06/25/2024).

Met criteria codes

PS4	✔	This variant has been identified in at least 9 unrelated probands (and other related family members not counted within each) all meeting Danish VHL criteria, from literature evaluated in both CIViC and Hypothes.is VHL datasets. CIViC EIDs (https://civicdb.org): 8292;7606;5776;9374;6806;6538. This corresponds to Strong evidence (5-15 probands) (PS4).
PVS1	✔	This variant causes a premature stop codon in a biologically-relevant-exon, predicted to cause nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).
PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0 (PM2_Supporting).

Curation History

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