

Variant: *NM_000551.4(VHL):c.208G>T (p.Glu70Ter)*

Version: 1.0

CA16602179 [↗](#)

428806 (ClinVar) [↗](#)

Gene: VHL ([HGNC:7428](#))

Condition: von Hippel-Lindau disease ([MONDO:0008667](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: 07181a12-5c32-4485-89e7-605d96e35ca7

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HGVS expressions

NM_000551.4(VHL):c.208G>T (p.Glu70Ter)

NM_000551.4:c.208G>T

NC_000003.12:g.10142055G>T

CM000665.2:g.10142055G>T

NC_000003.11:g.10183739G>T

CM000665.1:g.10183739G>T

NC_000003.10:g.10158739G>T

NG_008212.3:g.5421G>T

ENST00000696142.1:c.208G>T

ENST00000696143.1:c.208G>T

ENST00000696153.1:c.208G>T

ENST00000256474.3:c.208G>T

ENST00000256474.2:c.208G>T

ENST00000345392.2:c.208G>T

NM_000551.3:c.208G>T

NM_198156.2:c.208G>T

NM_001354723.1:c.208G>T

NM_001354723.2:c.208G>T

NM_198156.3:c.208G>T

Pathogenic

Met criteria codes **3**

PS4_Moderate

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_000551.3(VHL):c.208G>T (p.Glu70Ter) variant in VHL is a truncating variant. This variant causes a premature stop codon in a biologically-relevant-exon leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1_Met). The variant has been reported in 6 unrelated probands and/or families meeting either VHL Type 1 or affected with VHL-related cancers. CIViC Evidence IDs (<https://civicdb.org>): 9266,5361,5445,5035,6059,8209 and PMIDs: 18446368, 8707293, 20660572, 9829911, 7728151, 11148816. (PS4_Moderate) There is one variant present in gnomAD v4.1.0. The GroupMax Filtering Allele Frequency (95% CI) in gnomAD v4.1.0 is not calculated. PM2_Supporting can be applied for variants with <= 0.0000015 (0.00015%) frequency in gnomAD, or if no GroupMax Filtering Allele Frequency is calculated (due to a single variant present) (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_Moderate			The variant has been reported in 6 unrelated probands and/or families meeting either VHL Type 1 or affected with VHL-related cancers. CIViC Evidence IDs (https://civicdb.org): 9266,5361,5445,5035,6059,8209 and PMIDs: 18446368, 8707293, 20660572, 9829911, 7728151, 11148816. (PS4_Moderate).
PVS1			This variant causes a premature stop codon in a biologically-relevant-exon, occurring in the 1st Beta (β) domain (63-155) and leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1_Met).
PM2_Supporting			There is one variant present in gnomAD v4.1.0. The GroupMax Filtering Allele Frequency (95% CI) in gnomAD v4.1.0 is not calculated. PM2_Supporting can be applied for variants with <= 0.0000015 (0.00015%) frequency in gnomAD, or if no GroupMax Filtering Allele Frequency is calculated (due to a single variant present) (PM2_Supporting).

Curation History

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