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# *Variant: NM_000551.4(VHL):c.583C>T (p.Gln195Ter)*

Version: 1.0

*CA70052558*

*428794 (ClinVar)*

**Gene**: VHL (HGNC:7428)
**Condition**: von Hippel-Lindau disease (MONDO:0008667)
**Inheritance Mode**: Autosomal dominant inheritance
**UUID:** 506678db-35be-41e0-9c07-5feac64181ec
**Approved on**: 2024/6/25
**Published on**: 2024/6/25

## *HGVS expressions*

**NM_000551.4(VHL):c.583C>T (p.Gln195Ter)**
**NM_000551.4:c.583C>T**
NC_000003.12:g.10149906C>T
CM000665.2:g.10149906C>T
NC_000003.11:g.10191590C>T
CM000665.1:g.10191590C>T
NC_000003.10:g.10166590C>T
NG_008212.3:g.13272C>T
ENST00000696142.1:c.*260C>T
ENST00000696143.1:c.719C>T
ENST00000696153.1:c.694C>T
ENST00000256474.3:c.583C>T
ENST00000256474.2:c.583C>T
ENST00000345392.2:c.460C>T
ENST00000477538.1:n.719C>T
NM_000551.3:c.583C>T
NM_198156.2:c.460C>T
NM_001354723.1:c.*137C>T
NM_001354723.2:c.*137C>T
NM_198156.3:c.460C>T

**Pathogenic**

**Met criteria codes** 3

PS4_Moderate PVS1 PM2_Supporting

**Not Met criteria codes** 2

BA1 BS1

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 NM_000551.3(VHL):c.583C>T (p.Gln195Ter) variant in VHL is a truncating mutation that terminates the VHL protein at position 195, which resides in the second Beta domain (PVS1). A total of 13 probands or families have been identified with this variant, and they have clinical features of VHL (some Type 1, some Type 2A). 11 probands or families were identified in the following PMIDs: 20660572, 8707293, 23298237, 21463266, 9408111, 17661816, 25867206, 17024664. CIViC EIDs (https://civicdb.org) are: 5472, 5360, 5691, 8693, 9255, 5097, 6623, 5134. Two additional affected cases were contributed by a commercial laboratory, with VHL phenotypes and one case has segregation data. The case total of 13 equates to moderate evidence (PS4_Moderate). 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 disease (VHL disease) 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** | ✔ | A total of 13 probands or families have been identified with this variant, and they have clinical features of VHL (some Type 1, some Type 2A). 11 probands or families were identified in the following PMIDs: 20660572, 8707293, 23298237, 21463266, 9408111, 17661816, 25867206, 17024664. CIViC EIDs (https://civicdb.org) are: 5472, 5360, 5691, 8693, 9255, 5097, 6623, 5134. 2 additional affected cases were contributed by a commercial laboratory. The case total of 13 equates to moderate evidence (PS4_Moderate). |
| **PVS1** | ✔ | This variant terminates the VHL protein at position 195, which resides in the second Beta domain. |
| **PM2_Supporting** | ✔ | This variant is absent from gnomAD v4.1.0 (PM2_Supporting). |

**Not Met criteria codes**

| | | |
|---|---|---|
| **BA1** | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **BS1** | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |

Curation History

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