

Variant: *NM\_000277.2(PAH):c.561G>A (p.Trp187Ter)*

Version: 1.0

CA229624 [↗](#)

102736 (ClinVar) [↗](#)

**Gene:** PAH (HGNC:5053)

**Condition:** phenylketonuria (MONDO:0009861)

**Inheritance Mode:** Autosomal recessive inheritance

**UID:** c75a3cc6-1a5e-4837-b431-6e2b2a14c0b1

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### *HGVS expressions*

**NM\_000277.2:c.561G>A**

NM\_000277.2(PAH):c.561G>A (p.Trp187Ter)

NC\_000012.12:g.102855281C>T

CM000674.2:g.102855281C>T

NC\_000012.11:g.103249059C>T

CM000674.1:g.103249059C>T

NC\_000012.10:g.101773189C>T

NG\_008690.1:g.67322G>A

NG\_008690.2:g.108130G>A

NM\_000277.1:c.561G>A

NM\_001354304.1:c.561G>A

NM\_000277.3:c.561G>A

ENST00000307000.7:c.546G>A

ENST00000549111.5:n.657G>A

ENST00000551988.5:n.582G>A

ENST00000553106.5:c.561G>A

**Pathogenic**

Met criteria codes **3**

PM2 PVS1 PP4\_Moderate

Evidence Links **1**

Expert Panel

Phenylketonuria VCEP [↗](#)

Criteria Specification Information **!**

[↗](#) Criteria Specifications for this VCEP

Evidence submitted by expert panel

#### ***Phenylketonuria VCEP***

**PAH-specific ACMG/AMP criteria applied: PVS1: Nonsense variant; PM2: Extremely low frequency in gnomAD. MAF=0.00002.; PP4\_Moderate: Detected in 3 chromosomes of patients with PAH deficiency. BH4 deficiency ruled out. (PMID:8268925). In summary this variant meets criteria to be classified as pathogenic for phenylketonuria in an autosomal recessive manner based on the ACMG/AMP criteria applied as specified by the PAH Expert Panel: (PVS1, PM2, PP4\_Moderate).**

### Met criteria codes

<b>PM2</b>	✓	Extremely low frequency in gnomAD. MAF=0.00002.
<b>PVS1</b>	✓	Nonsense variant
<b>PP4_Moderate</b>	✓	Detected in 3 chromosomes of patients with PAH deficiency. BH4 deficiency ruled out.

W187X detected in 3 chromosomes. All patients were presenting with blood phenylalanine levels persistently above 150 umol/l, and diagnosis of PAH deficiency was made when other potential causes of hyperphenylalaninemia had been ruled out. The criteria for inclusion were: normal serum tyrosine, normal urinary excretion of biopterin and neopterin, and no indication of acquired hyperphenylalaninemia. [PubMed:8268925](#)

### Curation History [↗](#)

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