The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

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
UUID: c75a3cc6-1a5e-4837-b431-6e2b2a14c0b1
Approved on: 2018-08-10
Published on: 2019-04-06

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

PP4_Moderate PM2 PVS1

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

PP4_Moderate	✔	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 excresion of biopterin and neopterin, and no indication of acquired hyperphenylalaninemia. PubMed:8268925
PM2	✔	Extremely low frequency in gnomAD. MAF=0.00002.
PVS1	✔	Nonsense variant

Curation History

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