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# *Variant: NM_000277.2(PAH):c.498C>A (p.Tyr166Ter)*

Version: 1.0

*CA229583*

*102702 (ClinVar)*

**Gene**: PAH (HGNC:5053)
**Condition**: phenylketonuria (MONDO:0009861)
**Inheritance Mode**: Autosomal recessive inheritance
**UUID:** 76342745-0175-4795-ab71-e314ef54d447
**Approved on**: 2019-04-08
**Published on**: 2019-04-08

## *HGVS expressions*

**NM_000277.2(PAH):c.498C>A (p.Tyr166Ter)**
**NM_000277.2:c.498C>A**
NC_000012.12:g.102866607G>T
CM000674.2:g.102866607G>T
NC_000012.11:g.103260385G>T
CM000674.1:g.103260385G>T
NC_000012.10:g.101784515G>T
NG_008690.1:g.55996C>A
NG_008690.2:g.96804C>A
NM_000277.1:c.498C>A
NM_001354304.1:c.498C>A
NM_000277.3:c.498C>A
ENST00000307000.7:c.483C>A
ENST00000549111.5:n.594C>A
ENST00000551988.5:n.530+10855C>A
ENST00000553106.5:c.498C>A

**Pathogenic**

**Met criteria codes** 4

PVS1 PP4 PM3 PM2

Evidence Links 1

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

**Criteria Specifications for this VCEP**

Evidence submitted by expert panel

*Phenylketonuria VCEP*

**The c.498C>A (p.Tyr166Ter) variant in PAH is a nonsense variant in exon 5 of 13 in PAH, predicted to undergo nonsense mediated decay with the truncated region critical to protein function. It has been reported in individuals with Classic PKU in German and Chinese cohorts. (PP4, PMID:16256386; 10394930). This variant is absent from ExAC/gnomAD, 1000 Genomes, and ESP (PM2). This variant was detected with multiple known pathogenic variants (PM3). In summary, this variant meets criteria to be classified as pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PVS1, PM2, PM3, PP4.**

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**Met criteria codes**

| | | |
|---|---|---|
| **PVS1** | ✔ | Nonsense variant in exon 5 of 13 in PAH, predicted to undergo nonsense mediated decay with the truncated region critical to protein function |
| **PP4** | ✔ | Y166X reported on 6 alleles in patients with classical PKU. PMID: 16256386<br>Y166X reported on 6 alleles in patients with classical PKU. PAH deficiency was diagnosed by conventional biochemical methods. Classic PKU (Phe > 1200 umol/L). PubMed:16256386 |
| **PM3** | ✔ | Detected with 5 known pathogenic variants: R111X (P, 7 submitters), IVS4+1G>A (P/LP, 4 submitters), Y204C (P/LP, 4 submitters), Y356X (c.1068C>A P, 5 submitters), V399V (P, 5 submitters)<br>Genotypes: R111X (P, 7 submitters)+ Y166X, Y166X + IVS4+1G>A (P/LP, 4 submitters), Y166X + Y204C (P/LP, 4 submitters), Y166X + Y356X (c.1068C>A P, 5 submitters), Y166X + V399V (P, 5 submitters) PubMed:16256386 |
| **PM2** | ✔ | Absent from controls ExAC, 1000 Genomes, or ESP |

Curation History

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