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# *Variant: NM_001354304.2:c.1016C>T*

Version: 1.0

*CA386493446*

*1810387 (ClinVar)*

**Gene**: PAH (HGNC:5053)
**Condition**: phenylketonuria (MONDO:0009861)
**Inheritance Mode**: Autosomal recessive inheritance
**UUID:** 51ea6579-cf3b-43d0-89ad-226c776fe307
**Approved on**: 2022/7/30
**Published on**: 2022/7/30

## *HGVS expressions*

**NM_001354304.2:c.1016C>T**
NC_000012.12:g.102844385G>A
CM000674.2:g.102844385G>A
NC_000012.11:g.103238163G>A
CM000674.1:g.103238163G>A
NC_000012.10:g.101762293G>A
NG_008690.1:g.78218C>T
NG_008690.2:g.119026C>T
ENST00000553106.6:c.1016C>T
ENST00000307000.7:c.1001C>T
ENST00000549247.6:n.775C>T
ENST00000551114.2:n.678C>T
ENST00000553106.5:c.1016C>T
ENST00000635477.1:c.120C>T
ENST00000635528.1:n.531C>T
NM_000277.1:c.1016C>T
NM_000277.2:c.1016C>T
NM_001354304.1:c.1016C>T
NM_000277.3:c.1016C>T

**Likely Pathogenic**

**Met criteria codes** 4

PP3 PP4 PM3 PM2

**Not Met criteria codes** 1

PM5

Evidence Links 0

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

**Criteria Specifications for this VCEP**

Evidence submitted by expert panel

***Phenylketonuria VCEP***

**This c.1016 C>T (p.Ser339Phe) variant was detected in a patient with mPKU in trans with the pathogenic variant p. Ex6-96A>G (PMID: 28982351). This variant was absent in population databases. Multiple lines of computational evidence support a deleterious effect. In**

**summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PM3, PM2, PP3, PP4.**

**Met criteria codes**

| | | |
|---|---|---|
| **PP3** | ✔ | Predicted to be damaging (SIFT), possibly damaging (PolyPhen2), Disease causing (MutationTaster). REVEL=0.716 |
| **PP4** | ✔ | Variant was detected in a patient affected with mPKU. Variable sites in patient genes were aligned with the corresponding sites from the respective parents. This was seen in trans with a pathogenic variant listed in ClinVar. Those with BH4 cofactor deficiency were excluded PMID: 28982351 |
| **PM3** | ✔ | This variant was detected in trans with the pathogenic variant p. Ex6-96A>G (evaluated by an expert panel and seen in multiple entries in ClinVar) in a patient with mPKU (PMID: 28982351). points=1. |
| **PM2** | ✔ | This variant is absent from population databases gnomAD and ExAC |

**Not Met criteria codes**

| | | |
|---|---|---|
| **PM5** | ✖ | No other variants at this amino acid site were documented in ClinVar. |

Curation History

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