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.355C>T (p.Pro119Ser)*

Version: 1.0

*CA220582*

*92741 (ClinVar)*

**Gene**: PAH (HGNC:5053)
**Condition**: phenylketonuria (MONDO:0009861)
**Inheritance Mode**: Autosomal recessive inheritance
**UUID:** 38a183ee-7e53-4c24-a250-50958f390c78
**Approved on**: 2018-07-29
**Published on**: 2019-04-06

## *HGVS expressions*

**NM_000277.2:c.355C>T**
NM_000277.2(PAH):c.355C>T (p.Pro119Ser)
NC_000012.12:g.102877548G>A
CM000674.2:g.102877548G>A
NC_000012.11:g.103271326G>A
CM000674.1:g.103271326G>A
NC_000012.10:g.101795456G>A
NG_008690.1:g.45055C>T
NG_008690.2:g.85863C>T
NM_000277.1:c.355C>T
NM_001354304.1:c.355C>T
NM_000277.3:c.355C>T
ENST00000307000.7:c.340C>T
ENST00000549111.5:n.451C>T
ENST00000550978.6:n.339C>T
ENST00000551337.5:c.355C>T
ENST00000551988.5:n.444C>T
ENST00000553106.5:c.355C>T

**Likely Pathogenic**

**Met criteria codes** 3

PP3 PP4_Moderate PM3_Strong

**Not Met criteria codes** 1

PM2

Evidence Links 2

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: PP3: in silico analysis supportive of damaging effect; PM3_Strong: In trans with R261Q (PMID 21147011), and in trans with IVS2+1G>A (PMID 12655554) (PMID:21147011; PMID:12655554); PP4_Moderate: BH4 deficiency excluded (PMID:21147011). In summary this variant meets criteria to be classified as likely pathogenic for phenylketonuria in an autosomal recessive manner based on the ACMG/AMP criteria applied as specified by the PAH Expert Panel: (PP3, PM3_Strong, PP4_Moderate).**

**Met criteria codes**

| | | |
|---|---|---|
| **PP3** | ✔ | in silico analysis supportive of damaging effect |
| **PP4_Moderate** | ✔ | BH4 deficiency excluded<br>BH4 defect excluded at NBS and by sequencing of BH4 associated genes PubMed:21147011 |
| **PM3_Strong** | ✔ | In trans with R261Q (PMID 21147011), and in trans with IVS2+1G>A (PMID 12655554)<br>in trans with IVS2+1G>A PubMed:12655554<br>in trans with R261Q PubMed:21147011 |

**Not Met criteria codes**

| | | |
|---|---|---|
| **PM2** | ✖ | PAH specific specifications state PM2 criteria as 0.02% (AF=0.0002) |

Curation History

Showing 1 to 1 of 1 rows