

Variant: *NM\_000277.1(PAH):c.728G>T (p.Arg243Leu)*

Version: 1.0

CA229719 [↗](#)

102808 (ClinVar) [↗](#)

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

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

**Inheritance Mode:** Autosomal recessive inheritance

**UID:** 3baf9d92-6ef7-42d6-96e7-f80bec7da14a

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### HGVS expressions

**NM\_000277.1:c.728G>T**

NM\_000277.1(PAH):c.728G>T (p.Arg243Leu)

NC\_000012.12:g.102852929C>A

CM000674.2:g.102852929C>A

NC\_000012.11:g.103246707C>A

CM000674.1:g.103246707C>A

NC\_000012.10:g.101770837C>A

NG\_008690.1:g.69674G>T

NG\_008690.2:g.110482G>T

ENST00000553106.6:c.728G>T

ENST00000307000.7:c.713G>T

ENST00000549247.6:n.487G>T

ENST00000553106.5:c.728G>T

NM\_000277.2:c.728G>T

NM\_001354304.1:c.728G>T

NM\_000277.3:c.728G>T

NM\_001354304.2:c.728G>T

**Likely Pathogenic**

Met criteria codes **5**

PM3\_Supporting PP3 PP4 PM5

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.728G>T (p.Arg243Leu) variant in PAH has been reported in 1 individual with PKU detected with pathogenic variant p.R261Q (P 9 submitters) PMID: 12655553, 20217238. This variant is absent in population databases. Computational evidence supports a deleterious effect. Another missense change at the same amino acid, p.Arg243Gln, is pathogenic in ClinVar by multiple submitters (variation ID 591). In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PP4, PM2, PM3, PM5, PP3.

### Met criteria codes

<b>PM3_Supporting</b>	✓	detected with p.R261Q (P 9 submitters) PMID: 20217238 parental analysis not reported
<b>PP3</b>	✓	Predicted deleterious in SIFT, PolyPhen2, MutationTaster, REVEL=0.966
<b>PP4</b>	✓	PMID 12655553: In footnote of Table 1. listed in one allele in a cohort of Germany PKU/MHP patients. In footnote of Table 1. listed in one allele in a cohort of Germany PKU/MHP patients. <a href="#">PubMed:12655553</a>
<b>PM5</b>	✓	p.Arg243Gln pathogenic 10 submitters
<b>PM2</b>	✓	Absent from controls in ExAC, gnomAD, 1000 Genomes, ESP

### Curation History [↗](#)

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