

Variant: *NM_000277.3:c.461A>G*

Version: 1.0

CA16020794 [↗](#)

1185011 (ClinVar) [↗](#)

Gene: PAH ([HGNC:5053](#))

Condition: phenylketonuria ([MONDO:0009861](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: 05297303-7a45-44b7-a2cb-a6b1f25f114e

Approved on: 2021/1/15

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HGVS expressions

NM_000277.3:c.461A>G

NC_000012.12:g.102866644T>C

CM000674.2:g.102866644T>C

NC_000012.11:g.103260422T>C

CM000674.1:g.103260422T>C

NC_000012.10:g.101784552T>C

NG_008690.1:g.55959A>G

NG_008690.2:g.96767A>G

ENST00000553106.6:c.461A>G

ENST00000307000.7:c.446A>G

ENST00000549111.5:n.557A>G

ENST00000551988.5:n.530+10818A>G

ENST00000553106.5:c.461A>G

NM_000277.1:c.461A>G

NM_000277.2:c.461A>G

NM_001354304.1:c.461A>G

NM_001354304.2:c.461A>G

Likely Pathogenic

Met criteria codes **4**

PP4_Moderate

PP3

PM3_Supporting

PM2

Evidence Links **0**

Expert Panel

Phenylketonuria VCEP [↗](#)

Criteria Specification Information **!**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Phenylketonuria VCEP

This c.461A>G (p.Tyr154Cys) variant in PAH was reported in trans with pathogenic variant c.728G>A (p. Arg243Gln) in a patient with PAH deficiency (>120 µmol/L Phe) (PMID: 19915519, 23932990, 28754886). Computational evidence for this missense variant is predicted to be damaging (SIFT), probably damaging (PolyPhen2), and disease-causing (MutationTaster). This variant is absent from population databases ExAC, gnomAD, 1000 Genomes, ESP. In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PP4_moderate, PM2, PM3_supporting, PP3.

Met criteria codes

PP4_Moderate		✓	Detected in a patient with PKU. BH4 deficiency excluded through a BH4 loading test, urinary pterin analysis, and DHPR activity assay. PMID: 19915519, 23932990, 28754886
PP3		✓	Predicted deleterious in SIFT, PolyPhen2, MutationTaster, REVEL=0.977
PM3_Supporting		✓	detected with pathogenic variant c.728G>A (p.Arg243Gln). The patient was compound heterozygous for the variant. parental analysis not reported. PMID: 28754886
PM2		✓	Absent from controls in ExAC, gnomAD, 1000 Genomes, ESP

Curation History

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