

Variant: *NM_000277.1(PAH):c.673C>G (p.Pro225Ala)*

Version: 1.0

CA229686 [↗](#)

102780 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: a087e449-d830-49e4-bceb-5990ab49123a

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HGVS expressions

NM_000277.1(PAH):c.673C>G (p.Pro225Ala)

NM_000277.1:c.673C>G

NC_000012.12:g.102855169G>C

CM000674.2:g.102855169G>C

NC_000012.11:g.103248947G>C

CM000674.1:g.103248947G>C

NC_000012.10:g.101773077G>C

NG_008690.1:g.67434C>G

NG_008690.2:g.108242C>G

ENST00000553106.6:c.673C>G

ENST00000307000.7:c.658C>G

ENST00000549111.5:n.769C>G

ENST00000553106.5:c.673C>G

NM_000277.2:c.673C>G

NM_001354304.1:c.673C>G

NM_000277.3:c.673C>G

NM_001354304.2:c.673C>G

Likely Pathogenic

Met criteria codes **4**

PP4_Moderate

PP3

PM2

PM5

Evidence Links **0**

Expert Panel

Phenylketonuria VCEP [↗](#)

Criteria Specification Information **!**

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

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.673C>G (p.Pro225Ala) variant in PAH has been reported in 1 individual with classic PKU (BH4 deficiency excluded, PMID: 29499199). This variant is absent in population databases. Multiple lines of computational evidence support a deleterious effect. Another missense change at the same amino acid, p.Pro225Thr, is interpreted as pathogenic by multiple submitters in ClinVar (variation ID 102779). In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PP4_Moderate, PM2, PM5, PP3.

Met criteria codes

PP4_Moderate			Detected in a Chinese patient with classic PKU. urinary pterin analysis and a DHPR activity assay were also carried out to distinguish between PAH deficiency and tetrahydrobiopterin deficiency, in addition to sequencing of PAH, PTS, QDPR, GCH1 and PCBD1genes. PMID: 29499199
PP3			Predicted deleterious in SIFT, PolyPhen2, MutationTaster, REVEL=0.986
PM2			Absent from controls in ExAC, gnomAD, 1000 Genomes, ESP
PM5			p.P225T pathogenic 2 submitters

Curation History



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