

Variant: *NM_000277.3(PAH):c.1027T>G (p.Tyr343Asp)*

Version: 1.0

CA229280 [↗](#)

102476 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: fc07dc52-569c-4021-87b5-e54628c440f9

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HGVS expressions

NM_000277.3:c.1027T>G

NM_000277.3(PAH):c.1027T>G (p.Tyr343Asp)

NC_000012.12:g.102844374A>C

CM000674.2:g.102844374A>C

NC_000012.11:g.103238152A>C

CM000674.1:g.103238152A>C

NC_000012.10:g.101762282A>C

NG_008690.1:g.78229T>G

NG_008690.2:g.119037T>G

ENST00000553106.6:c.1027T>G

ENST00000307000.7:c.1012T>G

ENST00000549247.6:n.786T>G

ENST00000551114.2:n.689T>G

ENST00000553106.5:c.1027T>G

ENST00000635477.1:c.131T>G

ENST00000635528.1:n.542T>G

NM_000277.1:c.1027T>G

NM_000277.2:c.1027T>G

NM_001354304.1:c.1027T>G

NM_001354304.2:c.1027T>G

Likely Pathogenic

Met criteria codes 4

PP4_Moderate PP3 PM2 PM3

Not Met criteria codes 2

PM1 PM5

Evidence Links 1

Expert Panel

Phenylketonuria VCEP [↗](#)

Criteria Specification Information **!**

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

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.1027T>G (p.Tyr343Asp) variant in PAH has been reported in 1 individual with mild PKU (BH4 deficiency excluded) detected in trans with p.S349P (PMID: 27121329). This variant is absent in population databases. Computational evidence supports a deleterious effect. In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PP4_Moderate, PM2, PM3, PP3.

Met criteria codes

PP4_Moderate			Seen in a patient with mPKU, not BH4 responsive. The current cutoff value for Phe is 120 μM. A defect in the synthesis or regeneration pathways of 6R-BH4 was ruled out by analyzing urinary pterin levels as well as by measuring the dihydropteridine reductase activity. PMID: 27121329
			Seen in a patient with mPKU, not BH4 responsive. PubMed:27121329 
PP3			Predicted deleterious by MutationTaster, SIFT, Polyphen2.
PM2			absent from controls.
PM3			Seen in trans with S349P, pathogenic/likely pathogenic in Clinvar (Var ID: 615). Segregation analysis was done to rule out the presence of large genomic rearrangements. PMID: 27121329
			Seen in trans with S349P, pathogenic/likely pathogenic in Clinvar (Var ID: 615) PubMed:27121329 

Not Met criteria codes

PM1			Located in catalytic domain
			Mutations was located in the catalytic domain. PubMed:27121329 
PM5			Y343C classified as likely pathogenic

Curation History

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