

Variant: *NM_000277.1(PAH):c.613G>A (p.Glu205Lys)*

Version: 1.0

CA229656 [↗](#)

102759 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: a77e5c1a-429d-4442-831d-cb2df5966879

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HGVS expressions

NM_000277.1:c.613G>A

NM_000277.1(PAH):c.613G>A (p.Glu205Lys)

NC_000012.12:g.102855229C>T

CM000674.2:g.102855229C>T

NC_000012.11:g.103249007C>T

CM000674.1:g.103249007C>T

NC_000012.10:g.101773137C>T

NG_008690.1:g.67374G>A

NG_008690.2:g.108182G>A

ENST00000553106.6:c.613G>A

ENST00000307000.7:c.598G>A

ENST00000549111.5:n.709G>A

ENST00000553106.5:c.613G>A

NM_000277.2:c.613G>A

NM_001354304.1:c.613G>A

NM_000277.3:c.613G>A

NM_001354304.2:c.613G>A

Likely Pathogenic

Met criteria codes 4

PP4_Moderate

PM3_Strong

PP3

PM2

Not Met criteria codes 1

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.613G>A (p.Glu205Lys) variant in PAH has been reported in 2 individuals with mild-moderate and classic PKU, in trans with pathogenic variant p.Arg243* in both patients (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_strong, PP3.

Met criteria codes

PP4_Moderate			Detected in a patient with mild-moderate PKU (Phe 600-1200umol/L) and one classic PKU patient (Phe >1200umol/L) 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
			p.[Glu205Lys];[Arg243*] in one mild-moderate PKU (Phe 600-1200umol/L) and one classic PKU patient (Phe >1200umol/L). PubMed:27121329 
PM3_Strong			Detected in trans with p.Arg243* in 2 patients (P, 7 submitters). Segregation analysis was done to rule out the presence of large genomic rearrangements. PMID: 27121329
			p.[Glu205Lys];[Arg243*] in one mild-moderate PKU (Phe 600-1200umol/L) and one classic PKU patient (Phe >1200umol/L). PubMed:27121329 
PP3			Predicted deleterious in SIFT, PolyPhen2, MutationTaster, REVEL=0.943
PM2			Absent from controls in ExAC, gnomAD, 1000 Genomes, ESP

Not Met criteria codes

PM5			E205A and K: no interpretation in ClinVar
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Curation History



 

 

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