

Variant: NM_000277.1:c.224A>G

CA16020750 [↗](#)

619158 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: ed279f84-6b13-4f46-a481-787bc75a8fc2

Approved on: 2018-12-10

Published on: 2018-12-10

HGVS expressions

NM_000277.1:c.224A>G

NC_000012.12:g.102894863T>C

CM000674.2:g.102894863T>C

NC_000012.11:g.103288641T>C

CM000674.1:g.103288641T>C

NC_000012.10:g.101812771T>C

NG_008690.1:g.27740A>G

NG_008690.2:g.68548A>G

NM_000277.2:c.224A>G

NM_001354304.1:c.224A>G

NM_000277.3:c.224A>G

ENST00000307000.7:c.209A>G

ENST00000546844.1:c.224A>G

ENST00000548677.2:n.311A>G

ENST00000548928.1:n.146A>G

ENST00000549111.5:n.320A>G

ENST00000550978.6:n.208A>G

ENST00000551337.5:c.224A>G

ENST00000551988.5:n.313A>G

ENST00000553106.5:c.224A>G

Likely Pathogenic

Met criteria codes **3**

PP4_Moderate

PM5

PM2

Not Met criteria codes **1**

PP3

Evidence Links **2**

Expert Panel

Phenylketonuria VCEP [↗](#)

Criteria Specification Information **!**

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

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.224A>G (p.Asp75Gly) variant in PAH is reported in 1 Chinese PKU patient. BH4 deficiency was assessed. (PMID: 26503515) It is absent from ExAC, gnomAD, 1000G, and ESP. Computational evidence is conflicting. Another missense change at this amino acid is interpreted as likely pathogenic by our PAH VCEP, c.224A>T (p.Asp75Val). In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PM2, PM5, PP4.

Met criteria codes

PP4_Moderate			Found in 1 Chinese PKU patient. BH4 deficiency assessed. PMID: 26503515
A total of 796 unrelated patients from 29 separate newborn screening centres of China were enrolled. These patients were diagnosed at birth either through a neonatal screening program or based on clinical presentation. Biochemical testing data, including plasma phenylalanine (Phe) levels, dihydropteridine reductase activity, urinary biopterin and neopterin ratio, and tetrahydrobiopterin loading, were collected. D75G reported on 1 allele. PubMed:26503515  A standard group of 15 samples with previously known DNA sequences and a test group of 37 HPA patients with unknown mutations were used for assay validation and application, respectively. All variations were confirmed by Sanger sequencing. Patient C24 with BH4D carrying p.?/IVS3 + 1G N A and p.Pro87Ser in PTS also had the heterozygous missense variation c. 224A>G (p.Asp75Gly) in PAH. PubMed:25456745 			
PM5			c.224A>T (p.Asp75Val) is interpreted as LP by our PAH VCEP.
PM2			Absent from ExAC, gnomAD, 1000G, ESP

Not Met criteria codes

PP3			Conflicting predictions of pathogenicity. SIFT, Polyphen2: benign; MutationTaster: disease causing. REVEL=0.454
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Curation History



 

 

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