

Variant: *NM_000277.2(PAH):c.301G>A (p.Asp101Asn)*

Version: 1.0

CA16020762 [↗](#)

553851 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: d22e7b49-130c-409a-8c8c-270cdd072c23

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HGVS expressions

NM_000277.2:c.301G>A

NM_000277.2(PAH):c.301G>A (p.Asp101Asn)

NC_000012.12:g.102894786C>T

CM000674.2:g.102894786C>T

NC_000012.11:g.103288564C>T

CM000674.1:g.103288564C>T

NC_000012.10:g.101812694C>T

NG_008690.1:g.27817G>A

NG_008690.2:g.68625G>A

ENST00000553106.6:c.301G>A

ENST00000307000.7:c.286G>A

ENST00000546844.1:c.301G>A

ENST00000548928.1:n.223G>A

ENST00000549111.5:n.397G>A

ENST00000550978.6:c.285G>A

ENST00000551337.5:c.301G>A

ENST00000551988.5:n.390G>A

ENST00000553106.5:c.301G>A

NM_000277.1:c.301G>A

NM_001354304.1:c.301G>A

NM_000277.3:c.301G>A

NM_001354304.2:c.301G>A

Likely Pathogenic

Met criteria codes 3

PM3_Strong

PP4_Moderate

PM2

Not Met criteria codes 1

PP3

Evidence Links 3

Expert Panel

Phenylketonuria VCEP [↗](#)

Criteria Specification Information **!**

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

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.301G>A (p.Asp101Asn) variant in PAH has been reported in 3 patients with PKU (BH4 deficiency excluded) (PMID: 26503515, 26600521, 28982351). This variant is absent from controls in ExAC, gnomAD, 1000 Genomes, ESP. Conflicting computational evidence: SIFT (T); PolyPhen-2 (B); MutationTaster (D); REVEL=0.465. It is detected in trans with pathogenic variants Q267E and p.Arg158Trp. 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.

Met criteria codes

PM3_Strong			Detected in trans with Q267E (P, PAH VCEP) PMID: 26600521 p.Arg158Trp (P, 4 submitters) . PMID: 28982351 variable sites in patient genes were aligned with the corresponding sites from the respective parents
Table 4. Family 86. Proband genotype: D101N/Q267E (VarID102839, no clinical significance provided)			
PubMed:26600521  PubMed:28982351 			
PP4_Moderate			p.D101N (c.301G>A) was detected in 3 patients with PKU. BH4 deficiency assessed. PMID: 26503515 A total of 796 unrelated patients from 29 separate newborn screening centres of China were enrolled. Biochemical testing data, including plasma phenylalanine (Phe) levels, dihydropteridine reductase activity, urinary biopterin and neopterin ratio, and tetrahydrobiopterin loading, were collected. p.D101N (c.301G>A) was detected in 1 patient. PubMed:26503515 
PM2			Absent from controls in ExAC, gnomAD, 1000 Genomes, ESP

Not Met criteria codes

PP3			Conflicting computational evidence: SIFT (T); PolyPhen-2 (B); MutationTaster (D); REVEL=0.465.
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Curation History

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