The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000277.2(PAH):c.1031G>A (p.Gly344Asp)

Version: 1.0

CA229288

102481 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 916728eb-a8f7-4a52-852e-9a7b866bade4
Approved on: 2021/6/11
Published on: 2021/6/11

HGVS expressions

NM_000277.2:c.1031G>A
NM_000277.2(PAH):c.1031G>A (p.Gly344Asp)
NC_000012.12:g.102844370C>T
CM000674.2:g.102844370C>T
NC_000012.11:g.103238148C>T
CM000674.1:g.103238148C>T
NC_000012.10:g.101762278C>T
NG_008690.1:g.78233G>A
NG_008690.2:g.119041G>A
ENST00000553106.6:c.1031G>A
ENST00000307000.7:c.1016G>A
ENST00000549247.6:n.790G>A
ENST00000551114.2:n.693G>A
ENST00000553106.5:c.1031G>A
ENST00000635477.1:c.135G>A
ENST00000635528.1:n.546G>A
NM_000277.1:c.1031G>A
NM_001354304.1:c.1031G>A
NM_000277.3:c.1031G>A
NM_001354304.2:c.1031G>A

Likely Pathogenic

Met criteria codes 4

PM3_Strong PP4_Moderate 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.1031G>A (p.Gly344Asp) variant in PAH has been reported in multiple individuals with PAH deficiency (BH4 deficiency excluded, PMID: 26503515). This variant is absent in population databases. This variant was detected in with multiple pathogenic variants: p.Arg241Cys (PMID: 18985011); p.R252Q (PMID: 26322415); EX6-96A□G (PMID: 29316886); p.Q232* (PMID: 30050108). Multiple lines of computational evidence support a deleterious effect. In summary, this variant meets criteria to be classified as pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PM3_strong, PM2, PP4_Moderate, PP3.

Met criteria codes

PM3_Strong	✔	Detected with p.Arg241Cys (blood samples were collected from the patients and their family members) PMID: 18985011; p.[R252Q];[G344D]; confirmed by analyzing parental DNA. PMID: 26322415; EX6-96A□G; (variable sites in patient were aligned with the corresponding sites from the respective parents). PMID: 29316886; p.G344D/p.Q232* (validated on parents) PMID: 30050108 3.5 points
PP4_Moderate	✔	Seen in 2 individuals with PKU. Biochemical testing data, including plasma phenylalanine (Phe) levels, dihydropteridine reductase activity, urinary biopterin and neopterin ratio, and tetrahydrobiopterin loading, were collected. PMID: 26503515 Seen in 2 individuals with PKU. Biochemical testing data, including plasma phenylalanine (Phe) levels, dihydropteridine reductase activity, urinary biopterin and neopterin ratio, and tetrahydrobiopterin loading, were collected. PubMed:26503515
PP3	✔	Deleterious effect predicted by SIFT, PolyPhen, and MutationTaster
PM2	✔	Absent from controls in ExAC, 1000 Genomes, gnomAD.

Not Met criteria codes

PM5	✖	G334V curated as likely pathogenic, US in ClinVar.

Curation History

Showing 1 to 1 of 1 rows

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.

ClinGen Terms of Use.
¤ Powered by BCM's Genboree.