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_000277.1:c.1076C>T

Version: 1.0

CA16020934

1327561 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: d606fba6-3c95-470e-9df8-21a67044448a
Approved on: 2020/6/19
Published on: 2021/9/19

HGVS expressions

NM_000277.1:c.1076C>T
NC_000012.12:g.102843769G>A
CM000674.2:g.102843769G>A
NC_000012.11:g.103237547G>A
CM000674.1:g.103237547G>A
NC_000012.10:g.101761677G>A
NG_008690.1:g.78834C>T
NG_008690.2:g.119642C>T
ENST00000553106.6:c.1076C>T
ENST00000307000.7:c.1061C>T
ENST00000549247.6:n.835C>T
ENST00000551114.2:n.738C>T
ENST00000553106.5:c.1076C>T
ENST00000635477.1:c.180C>T
ENST00000635528.1:n.591C>T
NM_000277.2:c.1076C>T
NM_001354304.1:c.1076C>T
NM_000277.3:c.1076C>T
NM_001354304.2:c.1076C>T

Likely Pathogenic

Met criteria codes 4

PP3 PM2 PP4_Moderate PM3_Strong

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.1076C>T (p.Ser359Leu) variant in PAH has been reported in multiple individuals with classic PKU (BH4 deficiency excluded). (PMID: 26503515). This variant is absent in population databases. This variant was detected in trans with pathogenic variant p.T278I in 2 patients (PMID: 30050108). 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

PP3	✔	Multiple lines of evidence (MutationTaster, SIFT, Polyphen) predict damaging effect.
PM2	✔	Absent from controls
PP4_Moderate	✔	Seen in 4 individuals with PKU. 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. PMID: 26503515 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. PubMed:26503515
PM3_Strong	✔	2 patients with p.T278I (P 2 submitters)/p.S359L The validation tests on parents were performed using Sanger sequencing. PMID: 30050108

Not Met criteria codes

PM5	✖	No other missense change at this amino acid

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.