

Variant: NM_001354304.2:c.1096C>G

Version: 1.0

CA386493311 [↗](#)

1810389 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 5aff9fba-7c15-4ff6-87d5-4d90f4c313fd

Approved on: 2022/10/14

Published on: 2022/10/14

HGVS expressions

NM_001354304.2:c.1096C>G
NC_000012.12:g.102843749G>C
CM000674.2:g.102843749G>C
NC_000012.11:g.103237527G>C
CM000674.1:g.103237527G>C
NC_000012.10:g.101761657G>C
NG_008690.1:g.78854C>G
NG_008690.2:g.119662C>G
ENST00000553106.6:c.1096C>G
ENST00000307000.7:c.1081C>G
ENST00000549247.6:n.855C>G
ENST00000551114.2:n.758C>G
ENST00000553106.5:c.1096C>G
ENST00000635477.1:c.200C>G
ENST00000635528.1:n.611C>G
NM_000277.1:c.1096C>G
NM_000277.2:c.1096C>G
NM_001354304.1:c.1096C>G
NM_000277.3:c.1096C>G

Uncertain Significance

Met criteria codes **3**

PP4 PM2 PM3

Not Met criteria codes **2**

PP3 PM5

Evidence Links **0**

Expert Panel

Phenylketonuria VCEP [↗](#)

Criteria Specification Information **!**

[↗](#) Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

This c.1096C>G (p.Pro366Ala) variant in PAH was seen in a patient with PKU in trans with the likely pathogenic variant p.Gly247Arg (PMID: 28982351). This variant was absent in population databases. Computational evidence is conflicting. In summary, this variant meets criteria

to be classified as uncertain significance for PAH. PAH-specific ACMG/AMP criteria applied: PM2, PM3, PP4.

Met criteria codes

PP4			Variant was detected in a patient affected with PKU (plasma Phe >120 umol/L). BH4 cofactor deficiency were excluded using the loading test PMID: 28982351
PM2			This variant is absent from population databases gnomAD and ExAC
PM3			This variant was detected in trans with the ClinVar likely pathogenic variant p.Gly247Arg in a patient with PKU (PMID: 28982351). points=1.

Not Met criteria codes

PP3			Multiple lines of conflicting computation evidence predicted as benign in Polyphen, tolerated in Sift and disease causing in MutationTaster. revel score 0.608 also does not support this line of evidence.
PM5			Three other variants one of unknown significance (p.P366L) and two likely pathogenic (p.P366H) and (p.P366S) have been documented in ClinVar at this amino acid residue.

Curation History



 

 

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