

Variant: *NM_001354304.2:c.1084C>T*

Version: 1.0

CA6748745 [↗](#)

1810381 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: e6f92dc4-515e-4f21-a00a-a068781a7c73

Approved on: 2022/12/9

Published on: 2022/12/9

HGVS expressions

NM_001354304.2:c.1084C>T
NC_000012.12:g.102843761G>A
CM000674.2:g.102843761G>A
NC_000012.11:g.103237539G>A
CM000674.1:g.103237539G>A
NC_000012.10:g.101761669G>A
NG_008690.1:g.78842C>T
NG_008690.2:g.119650C>T
ENST00000553106.6:c.1084C>T
ENST00000307000.7:c.1069C>T
ENST00000549247.6:n.843C>T
ENST00000551114.2:n.746C>T
ENST00000553106.5:c.1084C>T
ENST00000635477.1:c.188C>T
ENST00000635528.1:n.599C>T
NM_000277.1:c.1084C>T
NM_000277.2:c.1084C>T
NM_001354304.1:c.1084C>T
NM_000277.3:c.1084C>T

Likely Pathogenic

Met criteria codes **4**

PP3 PP4 PM2 PM3

Not Met criteria codes **1**

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.1084C>T (p.Pro362Ser) variant in PAH was reported in a patient with classic PKU in trans with the pathogenic variant p.Arg413Pro (PMID: 28982351). This variant was present at an extremely low frequency in ExAC and absent in the gnomAD population database.

Multiple lines of computational evidence support a deleterious effect. In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PM3, PM2, PP3, PP4.

Met criteria codes

PP3			Predicted to be damaging (SIFT), probably damaging (PolyPhen2), Disease causing (MutationTaster). REVEL=0.796
PP4			Variant was detected in a patient affected with cPKU. Variable sites in patient genes were aligned with the corresponding sites from the respective parents. This was seen in trans with a pathogenic variant listed in ClinVar. Those with BH4 cofactor deficiency were excluded PMID: 28982351
PM2			Present in European (non-Finnish) populations at a frequency of 0.00001 (ExAC). This variant is absent from the population database gnomAD.
PM3			This variant was detected in trans with the ClinVar reported pathogenic variant p.Arg413Pro in a patient with cPKU (PMID: 28982351). points=1.

Not Met criteria codes

PM5			Tother variants one likely pathogenic (p.P362R) and one uncategorized (p.P362T) have been documented in ClinVar at this amino acid residue.
-----	---	---	---

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.