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.674C>T

Version: 1.0

CA6748883

932277 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 0fa6b404-a938-4150-bbca-e4162108d153
Approved on: 2020/3/8
Published on: 2020/3/8

HGVS expressions

NM_000277.1:c.674C>T
NC_000012.12:g.102855168G>A
CM000674.2:g.102855168G>A
NC_000012.11:g.103248946G>A
CM000674.1:g.103248946G>A
NC_000012.10:g.101773076G>A
NG_008690.1:g.67435C>T
NG_008690.2:g.108243C>T
ENST00000553106.6:c.674C>T
ENST00000307000.7:c.659C>T
ENST00000549111.5:n.770C>T
ENST00000553106.5:c.674C>T
NM_000277.2:c.674C>T
NM_001354304.1:c.674C>T
NM_000277.3:c.674C>T
NM_001354304.2:c.674C>T

Likely Pathogenic

Met criteria codes 4

PM5 PM2 PP3 PP4_Moderate

Evidence Links 2

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.674C>T (p.Pro225Leu) variant in PAH has been reported in 2 individuals with PKU (BH4 deficiency excluded (PMID: 21307867). This variant has extremely low frequency in gnomAD MAF=0.000008800. Computational evidence support a deleterious effect. The p.Pro225Thr variant is interpreted as pathogenic. In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PP4_Moderate, PM2, PM5, PP3.

Met criteria codes

PM5	✔	p.P225T Pathogenic, p.P225A/R/L no assertion
PM2	✔	extremely low frequency in gnomAD MAF=0.000008800
PP3	✔	Predicted deleterious in SIFT, PolyPhen2, MutationTaster. REVEL=0.967
PP4_Moderate	✔	PMID 21307867: This study enrolled 203 Japanese residents with a serum phenylalanine level higher than 0.18mM, absence of of neurologic deterioration on a low phenylalanine diet, analysis of dihydropteridine reductase activity in red blood cells, biopterin loading test and/or pteridine analysis in urine. Listed in Table 2, phe level not specified PubMed:31332730 PMID 21307867: This study enrolled 203 Japanese residents with a serum phenylalanine level higher than 0.18mM, absence of of neurologic deterioration on a low phenylalanine diet, analysis of dihydropteridine reductase activity in red blood cells, biopterin loading test and/or pteridine analysis in urine. Listed in Table 2, phe level not specified PubMed:21307867

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.