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_000277.3(PAH):c.157C>T (p.Arg53Cys)

Version: 1.0

CA229445

102600 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: a11b5555-6d5e-430a-80a6-ceb313b847c1
Approved on: 2021/5/29
Published on: 2021/7/9

HGVS expressions

NM_000277.3(PAH):c.157C>T (p.Arg53Cys)
NM_000277.3:c.157C>T
NC_000012.12:g.102912802G>A
CM000674.2:g.102912802G>A
NC_000012.11:g.103306580G>A
CM000674.1:g.103306580G>A
NC_000012.10:g.101830710G>A
NG_008690.1:g.9801C>T
NG_008690.2:g.50609C>T
ENST00000553106.6:c.157C>T
ENST00000307000.7:c.142C>T
ENST00000546844.1:c.157C>T
ENST00000548677.2:n.244C>T
ENST00000548928.1:n.79C>T
ENST00000549111.5:n.253C>T
ENST00000550978.6:c.141C>T
ENST00000551337.5:c.157C>T
ENST00000551988.5:n.246C>T
ENST00000553106.5:c.157C>T
ENST00000635500.1:n.125C>T
NM_000277.1:c.157C>T
NM_000277.2:c.157C>T
NM_001354304.1:c.157C>T
NM_001354304.2:c.157C>T

Likely Pathogenic

Met criteria codes 4

PP3 PP4 PM3 PM2

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.157C>T (p.Arg53Cys) variant in PAH was reported in trans with pathogenic variant p.Arg158Gln in 1 patient with PAH deficiency (324 uMol/L Phe) (PMID: 28982351). This variant was found at an amino acid residue where p.Arg53His, a missense variant of uncertain significance, has been seen before. Computational evidence for this missense variant supports a deleterious effect (REVEL=0.766). This variant is found at an extremely low frequency in gnomAD and ExAC (MAF=0.00012), and absent from 1000 Genomes, and ESP. In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PM2, PM3, PP3, PP4.

Met criteria codes

PP3	✔	REVEL=0.766
PP4	✔	detected in a patient with mHP (324 uMol/L Phe) Patients with BH4 cofactor deficiency were excluded by BH4 loading. PMID: 28982351
PM3	✔	detected in trans with p.Arg158Gln (P) 1.0 pts PMID: 28982351
PM2	✔	extremely low frequency in gnomAD and ExAC (MAF=0.00012), absent from 1000 Genomes, ESP

Not Met criteria codes

PM5	✖	R53H is classified as uncertain significance

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.