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_000277.2(PAH):c.472C>T (p.Arg158Trp)

CA229570

102693 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: faad1844-5076-4b6f-b671-eeb06035449a
Approved on: 2018-08-10
Published on: 2018-12-10

HGVS expressions

NM_000277.2:c.472C>T
NM_000277.2(PAH):c.472C>T (p.Arg158Trp)
NC_000012.12:g.102866633G>A
CM000674.2:g.102866633G>A
NC_000012.11:g.103260411G>A
CM000674.1:g.103260411G>A
NC_000012.10:g.101784541G>A
NG_008690.1:g.55970C>T
NG_008690.2:g.96778C>T
NM_000277.1:c.472C>T
NM_001354304.1:c.472C>T
NM_000277.3:c.472C>T
ENST00000307000.7:c.457C>T
ENST00000549111.5:n.568C>T
ENST00000551988.5:n.530+10829C>T
ENST00000553106.5:c.472C>T

Pathogenic

Met criteria codes 5

PP4_Moderate PM3_Strong PP3 PM2 PS3

Evidence Links 5

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

PAH-specific ACMG/AMP criteria applied: PM2: Extremely low frequency. ExAC MAF=0.00019.; PP3: Predicted deleterious in SIFT, Polyphen-2, MutationTaster. REVEL=0.939; PS3: 2% mutant enzyme activity in BioPKU; PP4_Moderate: Detected in at least 3 patients with PAH deficiency. BH4 deficiency ruled out in 1 patient. (PMID:1307609; PMID:10429004; PMID:9634518); PM3_Strong: Detected with 3 pathogenic/likely pathogenic variants (PMID:14681498; PMID:23430918). In summary this variant meets criteria to be classified as pathogenic for phenylketonuria in an autosomal recessive manner based on the ACMG/AMP criteria applied as specified by the PAH Expert Panel: (PM2, PP3, PS3, PP4_Moderate, PM3_Strong).

Met criteria codes

PP4_Moderate	✔	Detected in at least 3 patients with PAH deficiency. BH4 deficiency ruled out in 1 patient. R158W was detected. In all patients, hyperphenylalaninemia had been detected by national mass screening programs, and PAH deficiency had been assessed after exclusion of a defect in tetrahydrobiopterin metabolism. PubMed:9634518 A novel Arg158 (CGG)-to-Trp158 (TGG) mutation was identified in exon 5 of the PAH gene in a Chinese PKU patient. PubMed:1307609 R158W was observed in the study. PubMed:10429004
PM3_Strong	✔	Detected with 3 pathogenic/likely pathogenic variants Table 2. Mutant Genotypes. p.R158W: p.R261P (VarID102832, LP). p.R158W: p.R408W (VarID577, Path). p.I65T (VarID:636, P/LP): p.R158W. PubMed:23430918 In case 2, P407S (VarID102568, clinical significance not provided) was detected in one allele and R158W in the other allele. PubMed:14681498
PP3	✔	Predicted deleterious in SIFT, Polyphen-2, MutationTaster. REVEL=0.939
PM2	✔	Extremely low frequency. ExAC MAF=0.00019.
PS3	✔	2% mutant enzyme activity in BioPKU

Curation History

Showing 1 to 1 of 1 rows

See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_000277.2(PAH):c.472C>T (p.Arg15...	Pathogenic	Phenylketonuria	2019-04-06	1.0	-	PAH

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.