

Variant: *NM_000277.2(PAH):c.472C>T (p.Arg158Trp)*

Version: 1.0

[CA229570](#)

[102693 \(ClinVar\)](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UID: faad1844-5076-4b6f-b671-eeb06035449a

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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**

PS3 **PP3** **PM2** **PP4_Moderate**

PM3_Strong

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

PS3	✓	2% mutant enzyme activity in BioPKU
PP3	✓	Predicted deleterious in SIFT, Polyphen-2, MutationTaster. REVEL=0.939
PM2	✓	Extremely low frequency. ExAC MAF=0.00019.
PP4_Moderate	✓	<p>Detected in at least 3 patients with PAH deficiency. BH4 deficiency ruled out in 1 patient.</p> <hr/> <p>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.</p> <p>PubMed:9634518</p> <p>A novel Arg158 (CGG)-to-Trp158 (TGG) mutation was identified in exon 5 of the PAH gene in a Chinese PKU patient.</p> <p>PubMed:1307609</p> <p>R158W was observed in the study. PubMed:10429004</p>
PM3_Strong	✓	<p>Detected with 3 pathogenic/likely pathogenic variants</p> <hr/> <p>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</p> <p>In case 2, P407S (VarID102568, clinical significance not provided) was detected in one allele and R158W in the other allele. PubMed:14681498</p>

Curation History [↗](#)

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