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.242C>A (p.Thr81Asn)

CA275937

208180 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 50209afd-af57-49df-9248-edd2fd6d5cab
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HGVS expressions

NM_000277.2(PAH):c.242C>A (p.Thr81Asn)
NM_000277.2:c.242C>A
NC_000012.12:g.102894845G>T
CM000674.2:g.102894845G>T
NC_000012.11:g.103288623G>T
CM000674.1:g.103288623G>T
NC_000012.10:g.101812753G>T
NG_008690.1:g.27758C>A
NG_008690.2:g.68566C>A
NM_000277.1:c.242C>A
NM_001354304.1:c.242C>A
NM_000277.3:c.242C>A
ENST00000307000.7:c.227C>A
ENST00000546844.1:c.242C>A
ENST00000548677.2:n.329C>A
ENST00000548928.1:n.164C>A
ENST00000549111.5:n.338C>A
ENST00000550978.6:n.226C>A
ENST00000551337.5:c.242C>A
ENST00000551988.5:n.331C>A
ENST00000553106.5:c.242C>A

Likely Pathogenic

Met criteria codes 4

PP3 PM3 PM2 PP4_Moderate

Evidence Links 1

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.242C>A (p.Thr81Asn) variant in PAH is reported in 1 PKU patient. PAH and BH4DH genes were sequenced. It was detected with p.V230I which is interpreted as Pathogenic/Likely Pathogenic in ClinVar. (PMID: 23942198) This variant is absent from ExAC, gnomAD,

1000G, and ESP. A deleterious effect is predicted in SIFT, MutationTaster, and Polyphen-2. In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PM2, PP4_Moderate, PM3, PP3.

Met criteria codes

PP3	✔	Deleterious effect predicted in SIFT, MutationTaster, Polyphen-2 (P when manually queried)
PM3	✔	Detected with V230I (P/LP) PMID: 23942198 Sample D10: p.T81N on allele1 and p.(V230I) on allele 2. PubMed:23942198
PM2	✔	Absent from ExAC, gnomAD, 1000G, ESP
PP4_Moderate	✔	T81N detected in 1 PKU patient sample. PAH and BH4DH genes were sequenced. PMID: 23942198 High-quality genomic DNA from 107 unrelated samples (106 PKU and BH4DH patients and one control sample) was obtained. The validation cohort included 95 patients and one control sample that had previously undergone conventional biochemical and genetic diagnosis at the Centro de Diagnóstico de Enfermedades Moleculares (CEDEM) in Madrid, Spain, and all disease-causing mutations in PAH, GCH1, PTS, and QDPR were confirmed using Sanger sequencing or multiplex ligation-dependent probe amplification (MLPA), except in the case of patient H8, for whom the second PAH allele was unknown. Sample D10: p.T81N on allele1 and p.(V230I) on allele 2. PubMed:23942198

Curation History

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