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.490A>G (p.Ile164Val)

CA229576

102698 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 6daf45cd-bc30-4517-8391-4c64f38bea84
Approved on: 2018-08-13
Published on: 2018-12-10

HGVS expressions

NM_000277.2(PAH):c.490A>G (p.Ile164Val)
NM_000277.2:c.490A>G
NC_000012.12:g.102866615T>C
CM000674.2:g.102866615T>C
NC_000012.11:g.103260393T>C
CM000674.1:g.103260393T>C
NC_000012.10:g.101784523T>C
NG_008690.1:g.55988A>G
NG_008690.2:g.96796A>G
NM_000277.1:c.490A>G
NM_001354304.1:c.490A>G
NM_000277.3:c.490A>G
ENST00000307000.7:c.475A>G
ENST00000549111.5:n.586A>G
ENST00000551988.5:n.530+10847A>G
ENST00000553106.5:c.490A>G

Likely Pathogenic

Met criteria codes 3

PM2 PP4_Moderate PM3_Strong

Not Met criteria codes 1

PP3

Evidence Links 2

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: ExAC MAF: 0.00012; PP4_Moderate: Detected in patients with PKU/HPA. BH4 deficiency excluded. (PMID:11244681; PMID:23942198); PM3_Strong: Detected with D145V, A403V (Pathogenic) (PMID:11244681; PMID:23942198). In summary this variant meets criteria to be classified as likely pathogenic for phenylketonuria in an autosomal recessive manner based on the ACMG/AMP criteria applied as specified by the PAH Expert Panel: (PM2, PP4_Moderate, PM3_Strong).

Met criteria codes

PM2	✔	ExAC MAF: 0.00012
PP4_Moderate	✔	Detected in patients with PKU/HPA. BH4 deficiency excluded. All disease-causing mutations in PAH, GCH1, PTS, and QDPR were confirmed using Sanger sequencing or multiplex ligation-dependent probe amplification. Patient with HPA had 2 PAH mutations: I164V and A403V. PubMed:23942198 We evaluated the clinical data obtained from a multidisciplinary trial of 11 patients with PKU/HPA. I164V was identified in a patient with non-PKU HPA. PubMed:11244681
PM3_Strong	✔	Detected with D145V, A403V (Pathogenic) Patient/Sample 36: PAH variants: I164V and A403V (VarID 92731, Pathogenic) PubMed:23942198 Detected with D145V (VarID 102667, Pathogenic). PubMed:11244681

Not Met criteria codes

PP3	✖	Conflicting predictions for pathogenicity

Curation History

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