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.1220C>T (p.Pro407Leu)

Version: 1.0

CA229402

635 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 0b5b1397-d24f-4369-b608-dd9d8cdb4d08
Approved on: 2020/8/28
Published on: 2021/2/11

HGVS expressions

NM_000277.2(PAH):c.1220C>T (p.Pro407Leu)
NM_000277.2:c.1220C>T
NC_000012.12:g.102840495G>A
CM000674.2:g.102840495G>A
NC_000012.11:g.103234273G>A
CM000674.1:g.103234273G>A
NC_000012.10:g.101758403G>A
NG_008690.1:g.82108C>T
NG_008690.2:g.122916C>T
ENST00000553106.6:c.1220C>T
ENST00000307000.7:c.1205C>T
ENST00000551114.2:n.882C>T
ENST00000553106.5:c.1220C>T
ENST00000635477.1:c.324C>T
ENST00000635528.1:n.735C>T
NM_000277.1:c.1220C>T
NM_001354304.1:c.1220C>T
NM_000277.3:c.1220C>T
NM_001354304.2:c.1220C>T

Likely Pathogenic

Met criteria codes 3

PP4 PM2 PM3_Strong

Not Met criteria codes 2

PP3 PM5

Evidence Links 0

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.1220C>T (p.Pro407Leu) variant in PAH has been reported in multiple individuals with PAH deficiency (PMID: 9950317, 23357515, 23792259). This variant is absent in population databases. This variant was detected with pathogenic variants: p.F55fs (PMID: 9950317);

p.Tyr414Cys (PMID: 23357515); p.Ala403Val (PMID: 23792259); and p.R408W (PMID: 24350308). Computational evidence is conflicting. In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PP4, PM2, PM3_strong.

Met criteria codes

PP4	✔	Found in one patient with Classic PKU, Phe levels >1,200 umol/L PMID: 9950317, 1 patient with Mild PKU PMID: 23357515, 1 patient with mild HPA PMID: 23792259
PM2	✔	Absent from controls in ExAC,gnomAD, 1000G, ESP.
PM3_Strong	✔	Found in trans with F55fs (pathogenic 6 submitters) maternal segregation confirmed PMID: 9950317 p.Tyr414Cys (P 13 submitters) parental analysis not reported PMID: 23357515; in trans with p.Ala403Val (P 15 submitters) PMID: 23792259; p.R408W(c.1222C>T)/p.P407L(c.1220C>T) parental testing not reported PMID: 24350308 2.5-3.0 pts

Not Met criteria codes

PP3	✖	Tolerated in SIFT. predicted deleterious in Polyphen and Automatic disease causing in MutationTaster.
PM5	✖	P407S (Var ID=102568), LP

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.