

Variant: *NM_000277.3(PAH):c.1150C>T (p.Pro384Ser)*

Version: 1.0

CA16020950 [↗](#)

551270 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 21e9cfe6-8ef8-4eff-a4de-f844833071a0

Approved on: 2021/4/23

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HGVS expressions

NM_000277.3:c.1150C>T

NM_000277.3(PAH):c.1150C>T (p.Pro384Ser)

NC_000012.12:g.102843695G>A

CM000674.2:g.102843695G>A

NC_000012.11:g.103237473G>A

CM000674.1:g.103237473G>A

NC_000012.10:g.101761603G>A

NG_008690.1:g.78908C>T

NG_008690.2:g.119716C>T

ENST00000553106.6:c.1150C>T

ENST00000307000.7:c.1135C>T

ENST00000549247.6:n.909C>T

ENST00000551114.2:n.812C>T

ENST00000553106.5:c.1150C>T

ENST00000635477.1:c.254C>T

ENST00000635528.1:n.665C>T

NM_000277.1:c.1150C>T

NM_000277.2:c.1150C>T

NM_001354304.1:c.1150C>T

NM_001354304.2:c.1150C>T

Uncertain Significance

Met criteria codes **2**

PP3

PM2

Not Met criteria codes **2**

PS3

PP4

Evidence Links **1**

Expert Panel

Phenylketonuria VCEP [↗](#)

Criteria Specification Information **!**

[↗](#) Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.1150C>T (p.Pro384Ser) PAH variant has been reported in at least one “phenylketonuria” or “hyperphenylalaninemia” proband (PMID: 31332730). This variant is absent from 1000G, ESP, and gnomAD databases. It is a missense variant predicted deleterious by Polyphen (probably damaging), MutationTaster (disease causing), and has a REVEL score of 0.902. In summary, this variant meets criteria to be classified as uncertain significance for PAH. PAH-specific ACMG/AMP criteria applied: PM2, PP3.

Met criteria codes

PP3			This variant is predicted deleterious by Polyphen (probably damaging), MutationTaster (disease causing), and has a REVEL score of 0.902.
PM2			This variant is absent in population databases including gnomAD, ExAC, 1000 Genomes, or ESP.

Not Met criteria codes

PS3			From PMID: 26803807: Expression of a PAH plasmid with the Pro384Ser variant in COS-7 cells resulted in only modestly reduced activity (76%) which does not meet the threshold of <50% activity. Additional in vitro expression studies (PMID: 27620137 and PMID: 31102715) found similar results of 66% activity. Expression of a PAH plasmid with the Pro384Ser variant in COS-7 cells resulted in only modestly reduced activity (76%) which does not meet the threshold of <50% activity. PubMed:26803807 
PP4			PMID: 31332730 describes a proband harboring this Pro384Ser variant with “phenylketonuria” or “hyperphenylalaninemia” with no additional information.

Curation History



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