

Variant: *NM_000277.3(PAH):c.1175T>C (p.Phe392Ser)*

Version: 2.0

CA229369 [↗](#)

102544 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 4a89f184-bab9-45d5-b0eb-0ad48c77ec55

Approved on: 2024/11/17

Published on: 2024/11/18

HGVS expressions

NM_000277.3(PAH):c.1175T>C (p.Phe392Ser)

NM_000277.3:c.1175T>C

NC_000012.12:g.102843670A>G

CM000674.2:g.102843670A>G

NC_000012.11:g.103237448A>G

CM000674.1:g.103237448A>G

NC_000012.10:g.101761578A>G

NG_008690.1:g.78933T>C

NG_008690.2:g.119741T>C

ENST00000553106.6:c.1175T>C

ENST00000307000.7:c.1160T>C

ENST00000549247.6:n.934T>C

ENST00000551114.2:n.837T>C

ENST00000553106.5:c.1175T>C

ENST00000635477.1:c.279T>C

ENST00000635528.1:n.690T>C

NM_000277.1:c.1175T>C

NM_000277.2:c.1175T>C

NM_001354304.1:c.1175T>C

NM_001354304.2:c.1175T>C

Likely Pathogenic

Met criteria codes **3**

PM2_Supporting

PP3_Strong

PM5

Not Met criteria codes **1**

PP4

Evidence Links **0**

Expert Panel

Phenylketonuria VCEP [↗](#)

Criteria Specification Information

[↗](#) **Criteria Specification:** *ClinGen Phenylketonuria Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for PAH Version 2.0.0*

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.1175T>C (p.Phe392Ser) variant in PAH was reported in one individual with PAH deficiency; however, this report was non-English article that is not accessible and thus cannot be used as case-level evidence at this time (PMID: 22333022). This variant is absent from gnomAD v2.1.1 (PM2_Supporting), and is predicted damaging by REVEL = 0.98 (PP3_Strong). A different missense variant at the same position, p.F392I, is reported as pathogenic in ClinVar (VarID: 853581) (PM5). 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_Supporting, PM5, PP3_Strong.

Met criteria codes

PM2_Supporting			Variant absent from gnomAD v4.1.0
PP3_Strong			REVEL score 0.98.
PM5			A different missense variant at the same position, p.F392I, is reported as pathogenic in ClinVar by PAH VCEP (VarID:853581)

Not Met criteria codes

PP4			F392S reported in one patient with PAH deficiency (PMID: 22333022). Not able to access full description of methods due to article being in Chinese.
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Curation History

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