

Variant: *NM_001354304.2:c.1205T>G*

Version: 2.0

CA16020970 [↗](#)

987755 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 66e02e7e-b8c3-4033-828b-04cc081ba5c4

Approved on: 2024/11/17

Published on: 2024/11/18

HGVS expressions

NM_001354304.2:c.1205T>G
NC_000012.12:g.102840510A>C
CM000674.2:g.102840510A>C
NC_000012.11:g.103234288A>C
CM000674.1:g.103234288A>C
NC_000012.10:g.101758418A>C
NG_008690.1:g.82093T>G
NG_008690.2:g.122901T>G
ENST00000553106.6:c.1205T>G
ENST00000307000.7:c.1190T>G
ENST00000551114.2:n.867T>G
ENST00000553106.5:c.1205T>G
ENST00000635477.1:c.309T>G
ENST00000635528.1:n.720T>G
NM_000277.1:c.1205T>G
NM_000277.2:c.1205T>G
NM_001354304.1:c.1205T>G
NM_000277.3:c.1205T>G

Likely Pathogenic

Met criteria codes **3**

PP4_Moderate **PP3_Strong**
PM2_Supporting

Not Met criteria codes **1**

PM5

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.1205 (p.Phe402Cys) variant in PAH has been detected in 1 Japanese patient with mild HPA and BH4 deficiency excluded (PMID: 21307867; PP4_Moderate). This variant is absent from population databases (PM2_Supporting), and is predicted deleterious by SIFT, PolyPhen2, MutationTaster, and REVEL = 0.94 (PP3_Strong). 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, PP3_Strong, PP4.

Met criteria codes

PP4_Moderate			PMID: 21307867 - F402C detected in 1 Japanese patient with mild HPA, serum Phe = 180-600umol/l. BH4 deficiency was excluded by analysis of dihydropteridine reductase activity in red blood cells, biopterin loading test and/or pteridine analysis in urine.
PP3_Strong			Predicted deleterious by SIFT, PolyPhen2, MutationTaster, and REVEL = 0.94 (>0.932)
PM2_Supporting			Variant absent from gnomAD v4.1.0

Not Met criteria codes

PM5			At same codon as c.1204T>A (p.F402I), c.1204T>C (p.F402L), and c.1204T>G (p.F402V) - all curated as VUS by ClinGen PAH VCEP.
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Curation History

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