

Variant: NM_001354304.2:c.453T>A

Version: 1.0

CA16020793 [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 54974578-304b-4ce9-bb26-5f6aa31359bb

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HGVS expressions

NM_001354304.2:c.453T>A

NC_000012.12:g.102866652A>T

CM000674.2:g.102866652A>T

NC_000012.11:g.103260430A>T

CM000674.1:g.103260430A>T

NC_000012.10:g.101784560A>T

NG_008690.1:g.55951T>A

NG_008690.2:g.96759T>A

ENST00000553106.6:c.453T>A

ENST00000307000.7:c.438T>A

ENST00000549111.5:n.549T>A

ENST00000551988.5:n.530+10810T>A

ENST00000553106.5:c.453T>A

NM_000277.1:c.453T>A

NM_000277.2:c.453T>A

NM_001354304.1:c.453T>A

NM_000277.3:c.453T>A

Likely Pathogenic

Met criteria codes 4

PP4_Moderate

PP3_Strong

PM3

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.453T>A (p.Asp151Glu) variant in PAH has been reported in two patients with PAH deficiency: a patient with mild HPA, detected with pathogenic variant T380M (PMID: 11552030); and a patient with classic PKU, detected with pathogenic variant c.1066-11G>A (PMID: 23856132). This variant is absent from gnomAD. Multiple lines of computational evidence support a deleterious effect (REVEL=0.935). In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PM2_supporting, PM3, PP3_strong, PP4_moderate.

Met criteria codes

PP4_Moderate			Reported in a patient with mild HPA (180-240 mmol/L), urinary pterins and erythrocyte DHPR were normal . PMID: 11552030
PP3_Strong			Predicted deleterious in SIFT, PP-2, MutationTaster, REVEL=0.935
PM3			T380M (P), parental analysis not reported PMID: 11552030; IVS10-11G>A, parental analysis not reported PMID: 23856132
PM2_Supporting			absent from gnomAD v4.1.0

Not Met criteria codes

PM5			D151G, H no interpretation in ClinVar, US by PAH VCEP
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Curation History

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