

Variant: *NM_000277.1(PAH):c.155T>C (p.Leu52Ser)*

Version: 1.0

CA229443 [↗](#)

102599 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 8a5b1fbe-e4b4-425e-a73d-0dd635feca78

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HGVS expressions

NM_000277.1(PAH):c.155T>C (p.Leu52Ser)

NM_000277.1:c.155T>C

NC_000012.12:g.102912804A>G

CM000674.2:g.102912804A>G

NC_000012.11:g.103306582A>G

CM000674.1:g.103306582A>G

NC_000012.10:g.101830712A>G

NG_008690.1:g.9799T>C

NG_008690.2:g.50607T>C

ENST00000553106.6:c.155T>C

ENST00000307000.7:c.140T>C

ENST00000546844.1:c.155T>C

ENST00000548677.2:n.242T>C

ENST00000548928.1:n.77T>C

ENST00000549111.5:n.251T>C

ENST00000550978.6:c.139T>C

ENST00000551337.5:c.155T>C

ENST00000551988.5:n.244T>C

ENST00000553106.5:c.155T>C

ENST00000635500.1:n.123T>C

NM_000277.2:c.155T>C

NM_001354304.1:c.155T>C

NM_000277.3:c.155T>C

NM_001354304.2:c.155T>C

Likely Pathogenic

Met criteria codes **5**

PP3

PM3

PM2

PP4_Moderate

PS3_Supporting

Evidence Links **0**

Expert Panel

Phenylketonuria VCEP [↗](#)

Criteria Specification Information **!**

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

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.155T>C (p.Leu52Ser) variant in PAH is reported in 2 patients with PAH deficiency, detected with pathogenic variants: Exon 5_6 deletion and p.R243Q (BH4 deficiency excluded, PMID: 15319459, 30050108). PAH activity in COS cells was 27% (PMID: 9860305). This variant is absent in population databases. Multiple lines of computational evidence support a deleterious effect. In summary, this variant meets the criteria to be classified as Likely pathogenic for PAH deficiency based on the ACMG/AMP criteria applied, as specified by the ClinGen PAH VCEP: PP4_moderate, PM2, PM3, PS3_supporting, PP3.

Met criteria codes

PP3			Predicted deleterious in SIFT, Polyphen2, MutationTaster, REVEL=0.968
PM3			L52S/E5_6 del (P), parental analysis not reported, PMID: 15319459; p.R243Q (P) /p.L52S confirmed in trans PMID: 30050108 (1.5 pts)
PM2			Absent from controls in ExAC, gnomAD, 1000 genomes, and ESP
PP4_Moderate			Detected in a patient with mild PKU BH4 assessed by pteridine analysis in urine and DHPR activity. PMID: 15319459
PS3_Supporting			PAH activity in COS cells was 27% PMID: 9860305. PS3_supp approved for use in this PMID on 2/25/22 PAH VCEP call

Curation History

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