

Variant: NM_000277.3:c.361T>G

Version: 2.0

CA16020778 [↗](#)

872832 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 30be1927-f360-4d2f-8927-b5c1a42e0b38

Approved on: 2024/9/6

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HGVS expressions

NM_000277.3:c.361T>G

NC_000012.12:g.102877542A>C

CM000674.2:g.102877542A>C

NC_000012.11:g.103271320A>C

CM000674.1:g.103271320A>C

NC_000012.10:g.101795450A>C

NG_008690.1:g.45061T>G

NG_008690.2:g.85869T>G

ENST00000553106.6:c.361T>G

ENST00000307000.7:c.346T>G

ENST00000549111.5:n.457T>G

ENST00000550978.6:c.345T>G

ENST00000551337.5:c.361T>G

ENST00000551988.5:n.450T>G

ENST00000553106.5:c.361T>G

NM_000277.1:c.361T>G

NM_000277.2:c.361T>G

NM_001354304.1:c.361T>G

NM_001354304.2:c.361T>G

Likely Pathogenic

Met criteria codes **4**

PP4_Moderate

PP3_Strong

PM2_Supporting

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.361T>G (p.Phe121Val) variant in PAH has been reported in a Chinese patient with PAH deficiency (BH4 deficiency excluded) (PP4_Moderate; PMID: 26503515) This variant is absent from 1000G, ESP, ExAC and gnomAD (PM2). A deleterious effect is predicted in SIFT, Polyphen-2, MutationTaster, and REVEL=0.99. A different pathogenic missense change (p.Phe121Leu) has been seen before. In summary, this variant meets criteria to be classified as Likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PP4_Moderate, PM2_supporting, PP3_strong, PM5.

Met criteria codes

PP4_Moderate			detected on 1 allele. Diagnosed through neonatal screening program or by clinical presentation. Phenylalanine plasma concentrations >120 µmol/L were reported for all subjects. Tetrahydrobiopterin (BH4) deficiency was excluded through a BH4 loading test, urinary pterin analysis, DHPR activity assay. PMID: 26503515
PP3_Strong			Deleterious effect predicted in SIFT, PolyPhen2, MutationTaster. REVEL=0.99.
PM2_Supporting			Absent from controls in ExAC, gnomAD, 1000 Genomes, ESP
PM5			F121L is Pathogenic by Invitae

Curation History



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