

Variant: *NM_000277.3(PAH):c.563G>A (p.Gly188Asp)*

Version: 1.0

CA229628 [↗](#)

102738 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 1ebfcbe1-94c5-44ac-917b-3bb6d1edebc5

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HGVS expressions

NM_000277.3(PAH):c.563G>A (p.Gly188Asp)

NM_000277.3:c.563G>A

NC_000012.12:g.102855279C>T

CM000674.2:g.102855279C>T

NC_000012.11:g.103249057C>T

CM000674.1:g.103249057C>T

NC_000012.10:g.101773187C>T

NG_008690.1:g.67324G>A

NG_008690.2:g.108132G>A

ENST00000553106.6:c.563G>A

ENST00000307000.7:c.548G>A

ENST00000549111.5:n.659G>A

ENST00000551988.5:n.584G>A

ENST00000553106.5:c.563G>A

NM_000277.1:c.563G>A

NM_000277.2:c.563G>A

NM_001354304.1:c.563G>A

NM_001354304.2:c.563G>A

Likely Pathogenic

Met criteria codes **4**

PP4_Moderate

PP3

PM2

PM3

Evidence Links **0**

Expert Panel

Phenylketonuria VCEP [↗](#)

Criteria Specification Information **!**

[↗](#) Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.563G>A (p.Gly188Asp) variant in PAH has been reported in 3 affected individuals (BH4 deficiency excluded). (PP4_Moderate; PMID: 23430918, 26503515, 22526846). This variant is absent in population databases (PM2). This variant was detected with pathogenic variants p.F55fs (parental analysis not reported, PMID: 22526846) and p.R243Q (in trans, PMID: 26322415; PM3). Computational evidence support

a deleterious effect (PP3). In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PP4_Moderate, PM2, PM3, PP3.

Met criteria codes

PP4_Moderate			Detected in a French patient with PKU (1383 pre-treatment); BH4 assessment not reported. PMID: 23430918. Detected in a Chinese patient with PKU; Dihydropteridine reductase activity, urinary biopterin and neopterin ratio, and tetrahydrobiopterin loading were assessed. PMID: 26503515. Detected in an Austrian patient with PKU PMID: 22526846
PP3			Deleterious effect predicted in SIFT, PolyPhen2, MutationTaster. REVEL=0.84.
PM2			Absent from controls in ExAC, gnomAD, 1000 Genomes, ESP
PM3			detected with p.F55fs (P by 4 submitters, LP by 1 submitter), parental analysis not reported, PMID: 22526846. Detected in trans with p.R243Q (P by 8 submitters) PMID: 26322415

Curation History

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