

Variant: *NM_000277.2(PAH):c.545A>G (p.Glu182Gly)*

Version: 1.0

CA229617 [↗](#)

102731 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: c6768475-78a0-4239-88ff-e933187bd6e6

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HGVS expressions

NM_000277.2(PAH):c.545A>G (p.Glu182Gly)

NM_000277.2:c.545A>G

NC_000012.12:g.102855297T>C

CM000674.2:g.102855297T>C

NC_000012.11:g.103249075T>C

CM000674.1:g.103249075T>C

NC_000012.10:g.101773205T>C

NG_008690.1:g.67306A>G

NG_008690.2:g.108114A>G

ENST00000553106.6:c.545A>G

ENST00000307000.7:c.530A>G

ENST00000549111.5:n.641A>G

ENST00000551988.5:n.566A>G

ENST00000553106.5:c.545A>G

NM_000277.1:c.545A>G

NM_001354304.1:c.545A>G

NM_000277.3:c.545A>G

NM_001354304.2:c.545A>G

Likely Pathogenic

Met criteria codes **5**

PP4_Moderate

PP1

PP3

PM2

PM3

Evidence Links **2**

Expert Panel

Phenylketonuria VCEP [↗](#)

Criteria Specification Information **!**

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

Evidence submitted by expert panel

Phenylketonuria VCEP

The NM_000277.3:c.545A>G (p.Glu182Gly) variant is a missense variant in exon 6/13 of PAH. The variant was reported in confirmed trans with the p.R261Q allele (Pathogenic per ClinGen PAH VCEP) among two siblings with mild hyperphenylalanemia; BH4 deficiency was not noted to have been formally excluded (PMID: 26542770) (PP1; PM3). The variant has also been previously reported among “two alleles” in a cohort of Armenian PKU patients among whom BH4 deficiency was excluded; no further detail appears to be given (PMID: 10541324)

(PP4_Moderate). It has also been noted in ClinVar (ID 102731), without a classification. Three heterozygotes and zero homozygotes for the variant are present in gnomAD, corresponding to a global AF of 0.0000119 and maximum population frequency of 0.0000264 (non-Finnish European population), under the frequency cutoff of 0.0002 for use of PM2 (PM2). The variant is predicted damaging by multiple in-silico missense predictors, including REVEL (REVEL score 0.929) (PP3). Classification: Likely Pathogenic Supporting Criteria: PM2; PM3; PP1; PP4_Moderate; PP3

Met criteria codes

PP4_Moderate			PMID:10541324. Two alleles in California population of PKU patients. "BH4 defects excluded in all patients in California"
PubMed:10541324 			
PP1			Detected in 2 siblings PMID: 26542770.
PP3			Predicted deleterious in SIFT, PolyPhen2, MutationTaster, REVEL=0.929.
PM2			extremely low frequency in gnomAD MAF=0.00003
PM3			PMID: 26542770. Two sibs with c.782G>A (p.R261Q) (pathogenic per ClinVar) Parental testing confirmed
PubMed:26542770 			

Curation History

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