

Variant: NM_000277.2(PAH):c.169G>A (p.Glu57Lys)

Version: 1.0

CA220578 [↗](#)

92737 (ClinVar) [↗](#)

Gene: PAH (HGNC:5053)

Condition: phenylketonuria (MONDO:0009861)

Inheritance Mode: Autosomal recessive inheritance

UUID: 1afec1b2-0d05-412d-b7b8-5253350ff838

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HGVS expressions

NM_000277.2:c.169G>A

NM_000277.2(PAH):c.169G>A (p.Glu57Lys)

NC_000012.12:g.102894918C>T

CM000674.2:g.102894918C>T

NC_000012.11:g.103288696C>T

CM000674.1:g.103288696C>T

NC_000012.10:g.101812826C>T

NG_008690.1:g.27685G>A

NG_008690.2:g.68493G>A

NM_000277.1:c.169G>A

NM_001354304.1:c.169G>A

NM_000277.3:c.169G>A

ENST00000307000.7:c.154G>A

ENST00000546844.1:c.169G>A

ENST00000548677.2:n.256G>A

ENST00000548928.1:n.91G>A

ENST00000549111.5:n.265G>A

ENST00000550978.6:n.153G>A

ENST00000551337.5:c.169G>A

ENST00000551988.5:n.258G>A

ENST00000553106.5:c.169G>A

ENST00000635500.1:n.137G>A

Uncertain Significance

Met criteria codes **3**

PM3_Supporting PM2

PP4_Moderate

Not Met criteria codes **1**

PP3

Evidence Links **1**

Expert Panel

Phenylketonuria VCEP [↗](#)

Criteria Specification Information **!**

[↗](#) Criteria Specifications for this VCEP

Phenylketonuria VCEP

PAH-specific ACMG/AMP criteria applied: **PM2: Extremely low frequency. ESP MAF=0.00012.; PP4_Moderate: Detected in a patient with mild HPA. Assessment of the PAH, PTS, and QDPR genes was performed. (PMID:21147011); PM3-supporting: Detected with V388M, pathogenic in ClinVar, but parental testing not performed. (PMID:21147011).** In summary this variant meets criteria to be classified as uncertain significance for phenylketonuria in an autosomal recessive manner based on the ACMG/AMP criteria applied as specified by the PAH Expert Panel: (PM2, PP4_Moderate, PM3_supporting).

Met criteria codes

PM3_Supporting	✓	Detected with V388M, pathogenic in ClinVar. Parental testing not reported. Genotype: p.E57K/p.V388M (VarID619, Path) from supplementary table. PubMed:21147011
PM2	✓	Extremely low frequency. ESP MAF=0.00012.
PP4_Moderate	✓	Detected in a patient with mild HPA. Assessment of the PAH, PTS, and QDPR genes was performed. c.169G>A detected on 1 allele in a patient with mild HPA. Assessment of the PAH, PTS, and QDPR genes was performed. PubMed:21147011

Not Met criteria codes

PP3	✗	Conflicting interpretations of pathogenicity: SIFT, tolerated; Polyphen-2, benign; MutationTaster, disease causing.
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Curation History [↗](#)

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