The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

# *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
**Approved on**: 2019-04-26
**Published on**: 2019-04-26

## *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

PP4_Moderate PM3_Supporting PM2

**Not Met criteria codes** 1

PP3

Evidence Links 1

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

**Criteria Specifications for this VCEP**

Evidence submitted by expert panel

***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**

| | | |
|---|---|---|
| **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 |
| **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. |

**Not Met criteria codes**

| | | |
|---|---|---|
| **PP3** | ✖ | Conflicting interpretations of pathogenicity: SIFT, tolerated; Polyphen-2, benign; MutationTaster, disease causing. |

Curation History

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