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# *Variant: NM_000277.3(PAH):c.1102G>A (p.Glu368Lys)*

Version: 1.0

*CA386493305*

*625289 (ClinVar)*

**Gene**: PAH (HGNC:5053)
**Condition**: phenylketonuria (MONDO:0009861)
**Inheritance Mode**: Autosomal recessive inheritance
**UUID:** f131a516-cf1e-4b4c-b85d-6ab00c72ed7b
**Approved on**: 2020/6/26
**Published on**: 2020/6/26

## *HGVS expressions*

**NM_000277.3(PAH):c.1102G>A (p.Glu368Lys)**
**NM_000277.3:c.1102G>A**
NC_000012.12:g.102843743C>T
CM000674.2:g.102843743C>T
NC_000012.11:g.103237521C>T
CM000674.1:g.103237521C>T
NC_000012.10:g.101761651C>T
NG_008690.1:g.78860G>A
NG_008690.2:g.119668G>A
ENST00000553106.6:c.1102G>A
ENST00000307000.7:c.1087G>A
ENST00000549247.6:n.861G>A
ENST00000551114.2:n.764G>A
ENST00000553106.5:c.1102G>A
ENST00000635477.1:c.206G>A
ENST00000635528.1:n.617G>A
NM_000277.1:c.1102G>A
NM_000277.2:c.1102G>A
NM_001354304.1:c.1102G>A
NM_001354304.2:c.1102G>A

**Likely Pathogenic**

**Met criteria codes** 3
PM3 PM2 PP4_Moderate

**Not Met criteria codes** 2
PP3 PM5

Evidence Links 1

Expert Panel
Phenylketonuria VCEP

Criteria Specification Information

**Criteria Specifications for this VCEP**

Evidence submitted by expert panel

***Phenylketonuria VCEP***

**The c.1102G>A (p.Glu368Lys) variant in PAH has been reported in 1 individual with moderate PKU (BH4 deficiency excluded). (PP4_Moderate; PMID: 31355225). This variant has extremely low frequency in gnomAD: MAF=0.00001 (PM2). This variant was detected in trans with pathogenic variant c.1066-11G>A. Parents were also investigated to confirm their carrier status. (PM3). Computational evidence is conflicting. In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PP4_Moderate, PM2, PM3.**

**Met criteria codes**

| | | |
|---|---|---|
| **PM3** | ✔ | Detected in trans with pathogenic variant c.1066-11G>A. Parents were also investigated to confirm their carrier status. |
| **PM2** | ✔ | extremely low frequency in gnomAD. MAF=0.00001 |
| **PP4_Moderate** | ✔ | Detected in a patient with moderate PKU (Phe levels 9.5 mg/dL), Bh4 deficiency ruled out with urinary pterin analysis, and determination of DHPR activity. PMID: 31355225 |

PubMed:31355225

**Not Met criteria codes**

| | | |
|---|---|---|
| **PP3** | ✖ | Computational evidence is conflicting: deleterious in SIFT, MutationTaster; benign in PolyPhen2, REVEL=0.711. |
| **PM5** | ✖ | The current variant is the only variant found in this codon in ClinVar. |

Curation History

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