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_000277.1(PAH):c.716G>T (p.Gly239Val)

Version: 1.0

CA229711

102800 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: fb82abb9-c0f3-4901-acad-0e2a6de4b34d
Approved on: 2020/10/23
Published on: 2020/10/23

HGVS expressions

NM_000277.1:c.716G>T
NM_000277.1(PAH):c.716G>T (p.Gly239Val)
NC_000012.12:g.102852941C>A
CM000674.2:g.102852941C>A
NC_000012.11:g.103246719C>A
CM000674.1:g.103246719C>A
NC_000012.10:g.101770849C>A
NG_008690.1:g.69662G>T
NG_008690.2:g.110470G>T
ENST00000553106.6:c.716G>T
ENST00000307000.7:c.701G>T
ENST00000549247.6:n.475G>T
ENST00000553106.5:c.716G>T
NM_000277.2:c.716G>T
NM_001354304.1:c.716G>T
NM_000277.3:c.716G>T
NM_001354304.2:c.716G>T

Likely Pathogenic

Met criteria codes 4

PP3 PP4 PM2 PM3

Not Met criteria codes 1

PM5

Evidence Links 3

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.716G>T (p.Gly239Val) variant in PAH has been reported in 2 individuals with classic PKU (PMID 10394930, 31623983) detected with pathogenic variants p.R408W and IVS10–11g>a (PMID: 32106880). This variant has extremely low frequency in gnomAD (MAF=0.00006). Computational evidence supports a deleterious effect. In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PP4, PM2, PM3, PP3.

Met criteria codes

PP3	✔	Predicted deleterious in SIFT, PolyPhen2, MutationTaster, REVEL=0.978
PP4	✔	PMID 10394930: In Table 1, listed on allele of p.Gly239Val in a cohort of Germany PKU/HPA patients. PMID: 31623983 Detected in a classic PKU patient at Boston Children's. BH4 deficiency not reportedly ruled out PMID: 32106880 In Table 1, listed on allele of p.Gly239Val in a cohort of Germany PKU/HPA patients. PubMed:10394930
PM2	✔	extremely low frequency in GnomAD (MAF=0.00006)
PM3	✔	detected with p.R408W (P 14 submitters) PMID: 31623983 IVS10–11g>a (P 7 submitters) PMID: 32106880 parental analysis not reported PubMed:32106880 PubMed:31623983

Not Met criteria codes

PM5	✖	p.Gly239Ala/Ser/Asp no interpretation in ClinVar

Curation History

Showing 1 to 1 of 1 rows

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.

ClinGen Terms of Use.
¤ Powered by BCM's Genboree.