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

CA220578

92737 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 1afec1b2-0d05-412d-b7b8-5253350ff838
Approved on: 2018-08-10
Published on: 2018-12-10

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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See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_000277.2(PAH):c.169G>A (p.Glu57…	Uncertain Significance	Phenylketonuria	2019-04-26	1.0	-	PAH

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