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Variant: NM_000277.1:c.196G>A

Version: 1.0

CA16020744

1693243 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 53f9d1a2-46ec-4f4e-847b-d6425aaa650f
Approved on: 2022/6/28
Published on: 2022/6/28

HGVS expressions

NM_000277.1:c.196G>A
NC_000012.12:g.102894891C>T
CM000674.2:g.102894891C>T
NC_000012.11:g.103288669C>T
CM000674.1:g.103288669C>T
NC_000012.10:g.101812799C>T
NG_008690.1:g.27712G>A
NG_008690.2:g.68520G>A
ENST00000553106.6:c.196G>A
ENST00000307000.7:c.181G>A
ENST00000546844.1:c.196G>A
ENST00000548677.2:n.283G>A
ENST00000548928.1:n.118G>A
ENST00000549111.5:n.292G>A
ENST00000550978.6:c.180G>A
ENST00000551337.5:c.196G>A
ENST00000551988.5:n.285G>A
ENST00000553106.5:c.196G>A
ENST00000635500.1:n.164G>A
NM_000277.2:c.196G>A
NM_001354304.1:c.196G>A
NM_000277.3:c.196G>A
NM_001354304.2:c.196G>A

Likely Pathogenic

Met criteria codes 4

PM3_Supporting PP4_Moderate PM2 PP3

Evidence Links 0

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.196G>A (p.Glu66Lys) variant in PAH has been reported in 1 individual with mild PKU (BH4 deficiency excluded). (PP4_Moderate; PMID: 22921945). This variant is absent in population databases (PM2). This variant was detected with the pathogenic variant p.S349P (PM3_supporting; PMID: 22921945). Multiple lines of computational evidence support a deleterious effect (PP3). In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PP4_Moderate, PM2, PM3_supporting, PP3.

Met criteria codes

PM3_Supporting	✔	Detected with p.S349P (VarID615, P/LP) parental analysis not confirmed PMID: 22921945
PP4_Moderate	✔	Reported in 1 patient with mild PKU. BH4 deficiency excluded. PMID: 22921945
PM2	✔	Absent from controls in ExAC, gnomAD, 1000 Genomes, ESP
PP3	✔	Multiple lines of computational evidence support a deleterious effect (SIFT, PolyPhen-2, MutationTaster). REVEL=0.869.

Curation History

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