Variant: NM_000277.1(PAH):c.982A>G (p.Thr328Ala)

Version: 1.0

CA229891

102923 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 4081a5c6-1ea3-43ec-a823-3fd1e45d656c
Approved on: 2020-09-25
Published on: 2022-02-20

HGVS expressions

NM_000277.1:c.982A>G
NM_000277.1(PAH):c.982A>G (p.Thr328Ala)
NC_000012.12:g.102844419T>C
CM000674.2:g.102844419T>C
NC_000012.11:g.103238197T>C
CM000674.1:g.103238197T>C
NC_000012.10:g.101762327T>C
NG_008690.1:g.78184A>G
NG_008690.2:g.118992A>G
ENST00000553106.6:c.982A>G
ENST00000307000.7:c.967A>G
ENST00000549247.6:n.741A>G
ENST00000551114.2:n.644A>G
ENST00000553106.5:c.982A>G
ENST00000635477.1:c.86A>G
ENST00000635528.1:n.497A>G
NM_000277.2:c.982A>G
NM_001354304.1:c.982A>G
NM_000277.3:c.982A>G
NM_001354304.2:c.982A>G

Likely Pathogenic

Met criteria codes 4

PP3 PM2 PM3_Supporting PP4_Moderate

Not Met criteria codes 1

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.982A>G (p.Thr328Ala) variant in PAH has been reported in 1 individual with PKU (BH4 deficiency excluded), detected with pathogenic variant p.L48S (PMID: 21147011). This variant has extremely low frequency in ExAC and gnomAD (MAF=0.00003). 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_Moderate, PM2, PM3_supporting, PP3.

Met criteria codes

PP3	✓	Predicted deleterious in SIFT, Polyphen2, MutationTaster. (REVEL=0.971)
PM2	✓	Absent from 1000G, ESP. Low frequency in ExAC, gnomAD (MAF=0.00003)
PM3_Supporting	✓	Seen with L48S in 1 PKU patient. Parental analysis not performed. PMID: 21147011 0.5 pts T328A seen in trans in 1 PKU patient with L48S (VarID 608, Pathogenic). PubMed:21147011
PP4_Moderate	✓	T328A seen in 1 PKU patient. BH4 deficiency was ruled out by assessment of PAH gene and genes of the BH4 synthesis/recycling pathways (PTS and QDPR). PMID: 21147011 588 hyperphenylalaninemic patients were investigated. Assessment included PAH gene and genes of the BH4 synthesis/recycling pathways (PTS and QDPR). Seen on 1 allele. PubMed:21147011

Not Met criteria codes

PM5	✗	VarID 281073, T328I, Uncertain significance

Curation History

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