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Variant: NM_000277.3(PAH):c.523C>G (p.Pro175Ala)

Version: 1.0

CA229605

102722 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 532e385e-584f-4484-82d6-19b38c609ef7
Approved on: 2020/1/30
Published on: 2020/1/31

HGVS expressions

NM_000277.3:c.523C>G
NM_000277.3(PAH):c.523C>G (p.Pro175Ala)
NC_000012.12:g.102855319G>C
CM000674.2:g.102855319G>C
NC_000012.11:g.103249097G>C
CM000674.1:g.103249097G>C
NC_000012.10:g.101773227G>C
NG_008690.1:g.67284C>G
NG_008690.2:g.108092C>G
ENST00000553106.6:c.523C>G
ENST00000307000.7:c.508C>G
ENST00000549111.5:n.619C>G
ENST00000551988.5:n.544C>G
ENST00000553106.5:c.523C>G
NM_000277.1:c.523C>G
NM_000277.2:c.523C>G
NM_001354304.1:c.523C>G
NM_001354304.2:c.523C>G

Uncertain Significance

Met criteria codes 4

PM2 PP3 PP4 PM3_Supporting

Evidence Links 1

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.523C>G (p.Pro175Ala) variant in PAH has been reported in a US patient with MHP (PMID: 8659548). It was detected with pathogenic variant p.A104D. This variant is absent from population databases. A deleterious effect is predicted in multiple in silico models. In summary, this variant meets criteria to be classified as uncertain significance for PAH. PAH-specific ACMG/AMP criteria applied: PP4, PM2, PM3_supporting, PP3.

Met criteria codes

PM2	✔	Absent from controls in ExAC, gnomAD, 1000 Genomes, ESP
PP3	✔	Predicted deleterious in SIFT, PolyPhen2, MutationTaster, REVEL=0.91
PP4	✔	Detected in a patient with MHP PMID: 8659548
		PubMed:8659548
PM3_Supporting	✔	Detected with A104D (pathogenic 6 submitters) parental analysis not possible

Curation History

Showing 1 to 1 of 1 rows

See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_000277.3(PAH):c.523C>G (p.Pro17…	Uncertain Significance	Phenylketonuria	2020-01-31	1.0	-	PAH

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