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Variant: NM_000277.1(PAH):c.728G>T (p.Arg243Leu)

Version: 1.0

CA229719

102808 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 3baf9d92-6ef7-42d6-96e7-f80bec7da14a
Approved on: 2021/2/14
Published on: 2021/6/9

HGVS expressions

NM_000277.1(PAH):c.728G>T (p.Arg243Leu)
NM_000277.1:c.728G>T
NC_000012.12:g.102852929C>A
CM000674.2:g.102852929C>A
NC_000012.11:g.103246707C>A
CM000674.1:g.103246707C>A
NC_000012.10:g.101770837C>A
NG_008690.1:g.69674G>T
NG_008690.2:g.110482G>T
ENST00000553106.6:c.728G>T
ENST00000307000.7:c.713G>T
ENST00000549247.6:n.487G>T
ENST00000553106.5:c.728G>T
NM_000277.2:c.728G>T
NM_001354304.1:c.728G>T
NM_000277.3:c.728G>T
NM_001354304.2:c.728G>T

Likely Pathogenic

Met criteria codes 5

PP3 PP4 PM3_Supporting PM5 PM2

Evidence Links 1

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.728G>T (p.Arg243Leu) variant in PAH has been reported in 1 individual with PKU detected with pathogenic variant p.R261Q (P 9 submitters) PMID: 12655553, 20217238. This variant is absent in population databases. Computational evidence supports a deleterious effect. Another missense change at the same amino acid,p .Arg243Gln, is pathogenic in ClinVar by multiple submitters (variation ID 591). In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PP4, PM2, PM3, PM5, PP3.

Met criteria codes

PP3	✔	Predicted deleterious in SIFT, PolyPhen2, MutationTaster, REVEL=0.966
PP4	✔	PMID 12655553: In footnote of Table 1. listed in one allele in a cohort of Germany PKU/MHP patients.
		In footnote of Table 1. listed in one allele in a cohort of Germany PKU/MHP patients. PubMed:12655553
PM3_Supporting	✔	detected with p.R261Q (P 9 submitters) PMID: 20217238 parental analysis not reported
PM5	✔	p.Arg243Gln pathogenic 10 submitters
PM2	✔	Absent from controls in ExAC, gnomAD, 1000 Genomes, ESP

Curation History

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