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Variant: NM_000277.3:c.903G>T

Version: 1.0

CA16020890

805826 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 818a5909-77d6-409a-950b-67263a6bce83
Approved on: 2019/8/2
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HGVS expressions

NM_000277.3:c.903G>T
NC_000012.12:g.102851696C>A
CM000674.2:g.102851696C>A
NC_000012.11:g.103245474C>A
CM000674.1:g.103245474C>A
NC_000012.10:g.101769604C>A
NG_008690.1:g.70907G>T
NG_008690.2:g.111715G>T
ENST00000553106.6:c.903G>T
ENST00000307000.7:c.888G>T
ENST00000549247.6:n.662G>T
ENST00000551114.2:n.565G>T
ENST00000553106.5:c.903G>T
ENST00000635477.1:c.64G>T
NM_000277.1:c.903G>T
NM_000277.2:c.903G>T
NM_001354304.1:c.903G>T
NM_001354304.2:c.903G>T

Likely Pathogenic

Met criteria codes 4

PP3 PM2 PM5 PP4_Moderate

Not Met criteria codes 1

PM3

Evidence Links 0

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.903G>T (p.Gln301His) variant in PAH has been reported in at least 1 individual with PKU however without indication of the genotype (BH4 deficiency ruled out) (PMID: 21307867) . The p.Gln301His variant is absent in gnomAD and the ESP population databases. A deleterious effect is predicted in SIFT, Polyphen-2, MutationTaster, and REVEL=0.831. This variant is located in the C-terminal aromatic

amino acid hydroxylase domain and a different amino acid change at the same codon has been reported (PMID: 19292873). Overall, the c.903G>T variant is classified as likely pathogenic. PAH-specific ACMG/AMP criteria applied: PP3, PM2, PP4_M, PM5.

Met criteria codes

PP3	✔	Damaging by Polyphen, SIFT and REVEL 0.831
PM2	✔	absent from gnomAD
PM5	✔	p.Q301P is likely pathogenic, Q301K is pathogenic.
PP4_Moderate	✔	Q301H was found on 1 allele in Japanese PAH deficiency cohort. BH4 deficiency ruled out. PMID: 21307867

Not Met criteria codes

PM3	✖	Reported in 203 patients from Japan with PKU. The genotype information for the patient was not given.

Curation History

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