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Variant: NM_000277.3(PAH):c.907T>G (p.Ser303Ala)

Version: 1.0

CA229842

102890 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: fcbcb1f0-42ce-42c6-8beb-c2791db424ef
Approved on: 2021/1/18
Published on: 2021/4/9

HGVS expressions

NM_000277.3(PAH):c.907T>G (p.Ser303Ala)
NM_000277.3:c.907T>G
NC_000012.12:g.102851692A>C
CM000674.2:g.102851692A>C
NC_000012.11:g.103245470A>C
CM000674.1:g.103245470A>C
NC_000012.10:g.101769600A>C
NG_008690.1:g.70911T>G
NG_008690.2:g.111719T>G
ENST00000553106.6:c.907T>G
ENST00000307000.7:c.892T>G
ENST00000549247.6:n.666T>G
ENST00000551114.2:n.569T>G
ENST00000553106.5:c.907T>G
ENST00000635477.1:c.68T>G
NM_000277.1:c.907T>G
NM_000277.2:c.907T>G
NM_001354304.1:c.907T>G
NM_001354304.2:c.907T>G

Likely Pathogenic

Met criteria codes 4

PP3 PM2 PP4_Moderate PM3_Strong

Not Met criteria codes 1

PM5

Evidence Links 0

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.907T>G (p.Ser303Ala) variant in PAH has been reported in 3 individuals with PAH deficiency (BH4 deficiency excluded). (PP4_Moderate; PMID: 23430859, 23500595, 24941924, 27121329). This variant is absent in population databases (PM2). This variant was detected in 2 patients in trans with p.G46S (PMID: 27121329) (this variant is Pathogenic in ClinVar by 5 submitters, ID G46S) and with c.673C>A p.(Pro225Thr) (PMID: 24941924, parental analysis not described) (this variant is Pathogenic in ClinVar by 4 submitters, ID 102779). Computational evidence predicts a deleterious effect. In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PM3_strong, PP4_Moderate, PM2, PP3.

Met criteria codes

PP3	✔	Predicted deleterious in SIFT, PolyPhen2, MutationTaster. REVEL=0.954
PM2	✔	Absent from controls in ExAC, gnomAD, 1000 Genomes, ESP
PP4_Moderate	✔	reported in 3 patients with mild PKU, BH4 deficiency ruled out (PMID: 23430859, 23500595, 24941924, 27121329).
PM3_Strong	✔	Detected in 2 patients in trans with p.G46S (P, 2 submitters) PMID: 27121329 (segregation analysis done) and with c.673C>A, p.(Pro225Thr) (P, 1 submitter) PMID: 24941924 parental analysis not described

Not Met criteria codes

PM5	✖	p.Ser303Pro: no interpretation provided

Curation History

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