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Variant: NM_000277.1(PAH):c.1180G>T (p.Asp394Tyr)

Version: 1.0

CA267632

120262 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 54943624-c380-4c07-bfeb-456bda0c9aa6
Approved on: 2020/7/10
Published on: 2020/7/10

HGVS expressions

NM_000277.1(PAH):c.1180G>T (p.Asp394Tyr)
NM_000277.1:c.1180G>T
NC_000012.12:g.102843665C>A
CM000674.2:g.102843665C>A
NC_000012.11:g.103237443C>A
CM000674.1:g.103237443C>A
NC_000012.10:g.101761573C>A
NG_008690.1:g.78938G>T
NG_008690.2:g.119746G>T
ENST00000553106.6:c.1180G>T
ENST00000307000.7:c.1165G>T
ENST00000549247.6:n.939G>T
ENST00000551114.2:n.842G>T
ENST00000553106.5:c.1180G>T
ENST00000635477.1:c.284G>T
ENST00000635528.1:n.695G>T
NM_000277.2:c.1180G>T
NM_001354304.1:c.1180G>T
NM_000277.3:c.1180G>T
NM_001354304.2:c.1180G>T

Likely Pathogenic

Met criteria codes 4

PP3 PP4 PM3 PM2

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.1180G>T (p.Asp394Tyr) variant in PAH has been reported in 2 French patients with mild PKU, BH4 deficiency not ruled out PMID: 26666653. Detected with pathogenic variants p.T380M and 1066-3C > T, parental analysis not performed. This variant is absent in population databases. Multiple lines of computational evidence support a deleterious effect. In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PP4, PM2, PM3, PP3.

Met criteria codes

PP3	✔	Predicted deleterious in SIFT, PolyPhen2, MutationTaster
PP4	✔	Seen in 2 mild PKU patients. BH4 deficiency not ruled out. PMID: 26666653 364 hyperphenylalaninemic patients, including 42 siblings, were investigated. Asp394Tyr found in 2 patients. PubMed:26666653
PM3	✔	Detected with T380M (P 11 submitters) and 1066-3C > T (P 3 submitters) parental analysis not performed Asp394Tyr seen with 1066-3C > T in 1 PKU patient and Thr380Met (VarID 628, Pathogenic/Likely Pathogenic in ClinVar) in a 2nd patient. PubMed:26666653
PM2	✔	Absent from ExAC, gnomAD, 1000G, ESP

Not Met criteria codes

PM5	✖	D394A - no clinical significance in ClinVar D394H - LP 1 submitter

Curation History

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