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Variant: NM_000277.3(PAH):c.443G>T (p.Gly148Val)

Version: 1.0

CA16020791

552657 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 5c41ff75-cc92-448f-8fbd-6718561a4dac
Approved on: 2020/1/26
Published on: 2021/2/12

HGVS expressions

NM_000277.3:c.443G>T
NM_000277.3(PAH):c.443G>T (p.Gly148Val)
NC_000012.12:g.102866662C>A
CM000674.2:g.102866662C>A
NC_000012.11:g.103260440C>A
CM000674.1:g.103260440C>A
NC_000012.10:g.101784570C>A
NG_008690.1:g.55941G>T
NG_008690.2:g.96749G>T
ENST00000553106.6:c.443G>T
ENST00000307000.7:c.428G>T
ENST00000549111.5:n.539G>T
ENST00000551988.5:n.530+10800G>T
ENST00000553106.5:c.443G>T
NM_000277.1:c.443G>T
NM_000277.2:c.443G>T
NM_001354304.1:c.443G>T
NM_001354304.2:c.443G>T

Likely Pathogenic

Met criteria codes 4

PP4_Moderate PM3 PM2 PP3

Evidence Links 0

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.443G>T (p.Gly148Val) variant in PAH has been reported in multiple individuals with PKU (BH4 deficiency excluded). (PMID: 27121329, 26503515). This variant is absent in population databases (PM2). This variant was detected in trans with pathogenic variant p.Ser349Pro. Computational evidence supports a deleterious effect. In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PP4_Moderate, PM2, PM3, PP3.

Met criteria codes

PP4_Moderate	✔	Detected in a patient with classic PKU. A defect in the synthesis or regeneration pathways of 6R-BH4 was ruled out by analyzing urinary pterin levels and measuring dihydropteridine reductase activity. PMID: 27121329
PM3	✔	Detected in trans with p.Ser349Pro (pathogenic 5 submitters). Segregation analysis was done. PMID: 27121329
PM2	✔	Absent from controls in ExAC, gnomAD, 1000 Genomes, ESP
PP3	✔	Predicted deleterious in SIFT, Polyphen2, MutationTaster, REVEL=0.942

Curation History

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