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Variant: NM_001354304.2:c.209C>T

Version: 1.0

CA16020747

987767 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 2f26a145-c76e-4696-9509-47d4ce44f81a
Approved on: 2020/7/24
Published on: 2020/7/24

HGVS expressions

NM_001354304.2:c.209C>T
NC_000012.12:g.102894878G>A
CM000674.2:g.102894878G>A
NC_000012.11:g.103288656G>A
CM000674.1:g.103288656G>A
NC_000012.10:g.101812786G>A
NG_008690.1:g.27725C>T
NG_008690.2:g.68533C>T
ENST00000553106.6:c.209C>T
ENST00000307000.7:c.194C>T
ENST00000546844.1:c.209C>T
ENST00000548677.2:n.296C>T
ENST00000548928.1:n.131C>T
ENST00000549111.5:n.305C>T
ENST00000550978.6:c.193C>T
ENST00000551337.5:c.209C>T
ENST00000551988.5:n.298C>T
ENST00000553106.5:c.209C>T
ENST00000635500.1:n.177C>T
NM_000277.1:c.209C>T
NM_000277.2:c.209C>T
NM_001354304.1:c.209C>T
NM_000277.3:c.209C>T

Likely Pathogenic

Met criteria codes 4

PP3 PM2 PM3 PP4_Moderate

Evidence Links 1

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.209C>T (p.Ser70Phe) variant in PAH was reported in a Spanish patient with Mild HPA. A defect in the synthesis or regeneration in the pathways of 6R-BH4 was ruled out by analyzing urinary pterin levels and by measuring the dihydropteridine reductase activity (PMID 27121329). This variant was detected in trans with pathogenic variant p.Ala300Ser. It is absent in population databases and was predicted deleterious using in silico data. In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PM2, PM3, PP4 moderate, and PP3.

Met criteria codes

PP3	✔	Predicted deleterious in SIFT, PolyPhen2, Mutation Taster, REVEL=0.832
PM2	✔	Absent from 1000G, ESP, and gnomAD.
PM3	✔	Detected in trans with pathogenic variant p.Ala300Ser. Segregation analysis was done (PMID 27121329). PubMed:21307867
PP4_Moderate	✔	Reported in a Spanish patient with Mild HPA-NT. A defect in the synthesis or regeneration in the pathways of 6R-BH4 was ruled out by analyzing urinary pterin levels as well as by measuring the dihydropteridine reductase activity (PMID 27121329).

Curation History

Showing 1 to 1 of 1 rows

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