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Variant: NM_000277.3(PAH):c.161T>C (p.Leu54Ser)

Version: 1.0

CA229448

102602 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: bfb0df54-1132-4767-9598-0268a4485799
Approved on: 2020/7/23
Published on: 2021/2/12

HGVS expressions

NM_000277.3(PAH):c.161T>C (p.Leu54Ser)
NM_000277.3:c.161T>C
NC_000012.12:g.102912798A>G
CM000674.2:g.102912798A>G
NC_000012.11:g.103306576A>G
CM000674.1:g.103306576A>G
NC_000012.10:g.101830706A>G
NG_008690.1:g.9805T>C
NG_008690.2:g.50613T>C
ENST00000553106.6:c.161T>C
ENST00000307000.7:c.146T>C
ENST00000546844.1:c.161T>C
ENST00000548677.2:n.248T>C
ENST00000548928.1:n.83T>C
ENST00000549111.5:n.257T>C
ENST00000550978.6:c.145T>C
ENST00000551337.5:c.161T>C
ENST00000551988.5:n.250T>C
ENST00000553106.5:c.161T>C
ENST00000635500.1:n.129T>C
NM_000277.1:c.161T>C
NM_000277.2:c.161T>C
NM_001354304.1:c.161T>C
NM_001354304.2:c.161T>C

Likely Pathogenic

Met criteria codes 4

PP3 PM3 PM2 PP4_Moderate

Evidence Links 0

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.161T>C (p.Leu54Ser) variant in PAH is a missense variant that is predicted to be deleterious in multiple lines of computational evidence. This variant was reported in a Spanish patient with mild/moderate PKU. A defect in the synthesis or regeneration pathways of 6R-BH4 was ruled out by analyzing urinary pterin levels and measuring the dihydropteridine reductase activity (PMID: 27121329). This variant was detected in trans with pathogenic variant c.912+1G>A. It was found in extremely low frequency in gnomAD (MAF=0.00006). In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PM2, PP4 moderate, PM3, and PP3.

Met criteria codes

PP3	✔	Predicted deleterious in SIFT, PolyPhen2, MutationTaster, REVEL=0.876
PM3	✔	Detected in trans with pathogenic variant c.912+1G>A (6 submitters) Segregation analysis was done. PMID: 27121329
PM2	✔	Extremely low frequency in gnomAD (MAF=0.00006)
PP4_Moderate	✔	Reported in a Spanish patient with mild/moderate PKU. A defect in the synthesis or regeneration 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

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