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Variant: NM_000277.3(PAH):c.32T>A (p.Leu11Ter)

Version: 1.0

CA386303850

625287 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 7eef4555-98b1-448b-99e1-a6686ee78092
Approved on: 2020/4/9
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HGVS expressions

NM_000277.3:c.32T>A
NM_000277.3(PAH):c.32T>A (p.Leu11Ter)
NC_000012.12:g.102917099A>T
CM000674.2:g.102917099A>T
NC_000012.11:g.103310877A>T
CM000674.1:g.103310877A>T
NC_000012.10:g.101835007A>T
NG_008690.1:g.5504T>A
NG_008690.2:g.46312T>A
ENST00000553106.6:c.32T>A
ENST00000307000.7:c.-116T>A
ENST00000546844.1:c.32T>A
ENST00000547319.1:n.343T>A
ENST00000549111.5:n.128T>A
ENST00000550978.6:c.16T>A
ENST00000551337.5:c.32T>A
ENST00000551988.5:n.121T>A
ENST00000553106.5:c.32T>A
ENST00000635500.1:n.29-4201T>A
NM_000277.1:c.32T>A
NM_000277.2:c.32T>A
NM_001354304.1:c.32T>A
NM_001354304.2:c.32T>A

Pathogenic

Met criteria codes 4

PVS1 PP4_Moderate PM3 PM2

Evidence Links 0

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The p.L11* variant in PAH is a null variant (nonsense variant) in a gene where LOF is a known mechanism of disease, leading to premature truncation and NMD (PVS1). It is absent from ethnically diverse control databases, including gnomAD/ExAC, 1000 Genomes, and ESP (PM2). It has been previously reported in one Ugyur proband (PMID: 31355225) with classic PKU; BH4 deficiency was formally excluded by urinary pterin analysis (PP4_Moderate). The patient was compound heterozygous for the variant (confirmed by parental testing) and carried it in trans with the p.R413P variant (known pathogenic per PAH ClinGen working group) (PM3). It is also reported in ClinVar (ID 625287) as a de novo variant by one lab, in a case with PKU; no further information is given.

Met criteria codes

PVS1	✔	The p.L11* variant in PAH is a null variant (nonsense variant) in a gene where LOF is a known mechanism of disease, leading to premature truncation and NMD.
PP4_Moderate	✔	It has been previously reported in one Ugyur proband (PMID: 31355225) with classic PKU; BH4 deficiency was formally excluded by urinary pterin analysis (PP4_Moderate).
PM3	✔	It has been previously reported in one Ugyur proband (PMID: 31355225) with classic PKU; BH4 deficiency was formally excluded by urinary pterin analysis (PP4_Moderate). The patient was compound heterozygous for the variant (confirmed by parental testing) and carried it in trans with the p.R413P variant (known pathogenic per PAH ClinGen working group) (PM3).
PM2	✔	It is absent from ethnically diverse control databases, including gnomAD/ExAC, 1000 Genomes, and ESP (PM2).

Curation History

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