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Variant: NM_000277.2(PAH):c.1063C>T (p.Gln355Ter)

Version: 1.0

CA229313

102500 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: f1366fda-582c-4f0a-8563-edbc51c3599f
Approved on: 2023/10/15
Published on: 2023/10/15

HGVS expressions

NM_000277.2(PAH):c.1063C>T (p.Gln355Ter)
NM_000277.2:c.1063C>T
NC_000012.12:g.102844338G>A
CM000674.2:g.102844338G>A
NC_000012.11:g.103238116G>A
CM000674.1:g.103238116G>A
NC_000012.10:g.101762246G>A
NG_008690.1:g.78265C>T
NG_008690.2:g.119073C>T
ENST00000553106.6:c.1063C>T
ENST00000307000.7:c.1048C>T
ENST00000549247.6:n.822C>T
ENST00000551114.2:n.725C>T
ENST00000553106.5:c.1063C>T
ENST00000635477.1:c.167C>T
ENST00000635528.1:n.578C>T
NM_000277.1:c.1063C>T
NM_001354304.1:c.1063C>T
NM_000277.3:c.1063C>T
NM_001354304.2:c.1063C>T

Pathogenic

Met criteria codes 3

PVS1 PP4 PM2_Supporting

Evidence Links 1

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

- **Criteria Specification:** *ClinGen PAH Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 1*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.1063C>T (p.Gln355Ter) variant in PAH has been reported in a German PKU patient. (PP4; PMID: 10394930). This variant is absent from population databases (PM2_supporting). It is a null variant (nonsense) in exon 10/13 (NMD predicted) in PAH, a gene where loss of function is a known mechanism of disease (PVS1). In summary, this variant meets criteria to be classified as pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PVS1, PM2_supporting, PP4.

Met criteria codes

PVS1	✔	Null variant (nonsense) in a gene where LOF in exon 10/13 (NMD predicted)
PP4	✔	Detected in a cohort of German PKU patients
		Novel “Q355X” mutation studied in group of 546 alleles in Germany PubMed:10394930
PM2_Supporting	✔	Absent from controls in ExAC, gnomAD v2.1.1, 1000 Genomes, ESP

Curation History

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