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Variant: NM_000277.3(PAH):c.226G>T (p.Glu76Ter)

Version: 1.0

CA16020752

495789 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 848a19e1-be21-4d94-b0f8-1c6fd86f2e1b
Approved on: 2023/10/15
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HGVS expressions

NM_000277.3(PAH):c.226G>T (p.Glu76Ter)
NM_000277.3:c.226G>T
NC_000012.12:g.102894861C>A
CM000674.2:g.102894861C>A
NC_000012.11:g.103288639C>A
CM000674.1:g.103288639C>A
NC_000012.10:g.101812769C>A
NG_008690.1:g.27742G>T
NG_008690.2:g.68550G>T
ENST00000553106.6:c.226G>T
ENST00000307000.7:c.211G>T
ENST00000546844.1:c.226G>T
ENST00000548677.2:n.313G>T
ENST00000548928.1:n.148G>T
ENST00000549111.5:n.322G>T
ENST00000550978.6:c.210G>T
ENST00000551337.5:c.226G>T
ENST00000551988.5:n.315G>T
ENST00000553106.5:c.226G>T
NM_000277.1:c.226G>T
NM_000277.2:c.226G>T
NM_001354304.1:c.226G>T
NM_001354304.2:c.226G>T

Pathogenic

Met criteria codes 3

PVS1 PP4 PM2_Supporting

Not Met criteria codes 1

BP2

Evidence Links 0

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The NM_000277.3(PAH):c.226G>T (p.Glu76Ter) is a nonsense variant in exon 3/13 of PAH, and is predicted to result in PTC with removal of >10% of the protein and NMD (PVS1). The variant is absent from population databases, including gnomAD, ExAC, 1000 Genomes, or ESP (PM2_supporting). The variant has been previously reported in a patient with classic PKU (plasma Phe >1200 uM) (PMID: 17096675) with BH4 deficiency not noted to have been formally excluded (PP4), in cis with the c.1089delG variant (ClinVar Pathogenic, see ID 102518). 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	✔	nonsense variant in exon 3/13 of PAH, , and is predicted to result in PTC with removal of >10% of the protein and NMD (PVS1).
PP4	✔	Complex allele p.E76X* + c.1089delG has been previously reported in a patient with classic PKU (plasma Phe >1200 uM) (PMID: 17096675) with BH4 deficiency not noted to have been formally excluded (PP4)
PM2_Supporting	✔	The variant is absent from population databases, including gnomAD, ExAC, 1000 Genomes, or ESP (PM2).

Not Met criteria codes

BP2	✖	The variant has been previously reported in a patient with classic PKU (plasma Phe >1200 uM) (PMID: 17096675) with BH4 deficiency not noted to have been formally excluded (PP4), in cis with the c.1089delG variant (ClinVar Pathogenic, see ID 102518) and no further details regarding the patient's genotype appear to be included

Curation History

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