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Variant: NM_000277.3(PAH):c.745del (p.Leu249fs)

Version: 1.0

CA16020850

370982 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 1c9d8c70-9dfc-4355-8ef0-9cc1b939866f
Approved on: 2021/5/15
Published on: 2021/12/12

HGVS expressions

NM_000277.3:c.745del
NM_000277.3(PAH):c.745del (p.Leu249fs)
NC_000012.12:g.102852912del
CM000674.2:g.102852912del
NC_000012.11:g.103246690del
CM000674.1:g.103246690del
NC_000012.10:g.101770820del
NG_008690.1:g.69691del
NG_008690.2:g.110499del
ENST00000553106.6:c.745del
ENST00000307000.7:c.730del
ENST00000549247.6:n.504del
ENST00000553106.5:c.745del
NM_000277.1:c.745del
NM_000277.2:c.745del
NM_001354304.1:c.745del
NM_001354304.2:c.745del

Pathogenic

Met criteria codes 4

PM3_Supporting PP4 PM2 PVS1

Evidence Links 0

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.745del (p.Leu249fs) variant in PAH has been reported in 1 Chilean patient with mild PKU; Phe = 600-900umol/L (PMID: 29288420; PP4). This variant was detected with V388M - reported at Pathogenic in ClinVar (VarID:610, 7 submitters); phase not confirmed - 0.5 points (PMID: 29288420; PM3_supporting). This frameshift variant is predicted to undergo NMD, not located in last exon or last 50bp of preliminary exon (Coding exon number 7 out of 13 coding exons; 7 out of total exons) (PVS1). This variant is absent from population

databases (PM2). In summary, this variant meets criteria to be classified as pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PVS1, PM2, PP4, PM3_supporting.

Met criteria codes

PM3_Supporting	✔	PMID: 29288420 - L249fs detected with V388M - reported at Pathogenic in ClinVar (VarID:610, 7 submitters); phase not confirmed - 0.5 points
PP4	✔	PMID: 29288420 - L249fs detected in 1 Chilean patient with mild PKU; Phe = 600-900umol/L
PM2	✔	Variant absent from population databases.
PVS1	✔	Frameshift variant, predicted to undergo NMD, not located in last exon or last 50bp of preliminary exon. Coding exon number 7 out of 13 coding exons (7 out of total exons).

Curation History

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