Variant: NM_000277.2(PAH):c.355C>T (p.Pro119Ser)

Version: 1.0

CA220582

92741 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 38a183ee-7e53-4c24-a250-50958f390c78
Approved on: 2018-07-29
Published on: 2019-04-06

HGVS expressions

NM_000277.2:c.355C>T
NM_000277.2(PAH):c.355C>T (p.Pro119Ser)
NC_000012.12:g.102877548G>A
CM000674.2:g.102877548G>A
NC_000012.11:g.103271326G>A
CM000674.1:g.103271326G>A
NC_000012.10:g.101795456G>A
NG_008690.1:g.45055C>T
NG_008690.2:g.85863C>T
NM_000277.1:c.355C>T
NM_001354304.1:c.355C>T
NM_000277.3:c.355C>T
ENST00000307000.7:c.340C>T
ENST00000549111.5:n.451C>T
ENST00000550978.6:n.339C>T
ENST00000551337.5:c.355C>T
ENST00000551988.5:n.444C>T
ENST00000553106.5:c.355C>T

Likely Pathogenic

Met criteria codes 3

PP4_Moderate **PM3_Strong** **PP3**

Not Met criteria codes 1

PM2

Evidence Links 2

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

PAH-specific ACMG/AMP criteria applied: PP3: in silico analysis supportive of damaging effect; PM3_Strong: In trans with R261Q (PMID 21147011), and in trans with IVS2+1G>A (PMID 12655554) (PMID:21147011; PMID:12655554); PP4_Moderate: BH4 deficiency excluded

(PMID:21147011). In summary this variant meets criteria to be classified as likely pathogenic for phenylketonuria in an autosomal recessive manner based on the ACMG/AMP criteria applied as specified by the PAH Expert Panel: (PP3, PM3_Strong, PP4_Moderate).

Met criteria codes

PP4_Moderate	✓	BH4 deficiency excluded BH4 defect excluded at NBS and by sequencing of BH4 associated genes **PubMed:21147011**
PM3_Strong	✓	In trans with R261Q (PMID 21147011), and in trans with IVS2+1G>A (PMID 12655554) in trans with IVS2+1G>A **PubMed:12655554** in trans with R261Q **PubMed:21147011**
PP3	✓	in silico analysis supportive of damaging effect

Not Met criteria codes

PM2	✗	PAH specific specifications state PM2 criteria as 0.02% (AF=0.0002)

Curation History

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