

Variant: *NM_000277.2(PAH):c.165delT (p.Phe55Leufs)*

Version: 1.1

CA251540 [↗](#)

611 (ClinVar) [↗](#)

Gene: PAH ([HGNC:5053](#))

Condition: phenylketonuria ([MONDO:0009861](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: 71884bd5-9f73-46c5-ad77-5b47444367a9

Approved on: 2019/4/3

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HGVS expressions

NM_000277.2(PAH):c.165delT (p.Phe55Leufs)

NC_000012.12:g.102912796del

CM000674.2:g.102912796del

NC_000012.11:g.103306574del

CM000674.1:g.103306574del

NC_000012.10:g.101830704del

NG_008690.1:g.9809del

NG_008690.2:g.50617del

ENST00000553106.6:c.165del

ENST00000307000.7:c.150del

ENST00000546844.1:c.165del

ENST00000548677.2:n.252del

ENST00000548928.1:n.87del

ENST00000549111.5:n.261del

ENST00000550978.6:c.149del

ENST00000551337.5:c.165del

ENST00000551988.5:n.254del

ENST00000553106.5:c.165del

ENST00000635500.1:n.133del

NM_000277.1:c.165del

NM_000277.2:c.165del

NM_001354304.1:c.165del

NM_000277.3:c.165del

NM_001354304.2:c.165del

Pathogenic

Met criteria codes **3**

PP4 PM2 PVS1

Evidence Links **2**

Expert Panel

Phenylketonuria VCEP [↗](#)

Criteria Specification Information **!**

[↗](#) Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.165delT (p.F55Lfs*6) is a frameshift variant in exon 2 of 13 in PAH, predicted to undergo nonsense mediated decay with the truncated region critical to protein function. It has been reported in compound heterozygote state in multiple patients with PKU (BH4 deficiency not excluded) (PMID: 1682235 & 23500595). The variants in trans include: R408W, and R261Q, both confirmed pathogenic. This variant has an extremely low allele frequency in the Genome Aggregation database (3/251384) (PM2). In summary, this variant meets criteria to be classified as pathogenic for PAH. PAH-specific ACMG/AMP criteria: PM2, PP4, PVS1.

Met criteria codes

PP4			Three patients with PKU are reported who are compound heterozygotes with either R408W or intron 12 mutations. BH4 deficiency is not excluded. The mutations are segregating with disease: pedigree in figure 3. PubMed:1682235  This variant is reported in two compound heterozygote patients with PKU from the northwest region of Spain. The second variant is pathogenic R261Q, and pre-treatment phenylalanine levels are 1465, and 1382 uM (Table 2). PubMed:23500595 
PM2			gnomAD minor allele frequency: 0.00001
PVS1			Frameshift variant in exon 2 of 13 in PAH, predicted to undergo nonsense mediated decay with the truncated region critical to protein function

Curation History



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