The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

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
Published on: 2019/8/16

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

PVS1 PM2 PP4

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

PVS1	✔	Frameshift variant in exon 2 of 13 in PAH, predicted to undergo nonsense mediated decay with the truncated region critical to protein function
PM2	✔	gnomAD minor allele frequency: 0.00001
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

Curation History

Showing 1 to 2 of 2 rows

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.

ClinGen Terms of Use.
¤ Powered by BCM's Genboree.