

Variant: *NM_000531.6(OTC):c.387T>C (p.Arg129_Val130=)*

Version: 1.0

CA515650395 [↗](#)

1915613 (ClinVar) [↗](#)

Gene: OTC ([HGNC:5009](#))

Condition: ornithine carbamoyltransferase deficiency ([MONDO:0010703](#))

Inheritance Mode: X-linked inheritance (recessive (HP:0001419))

UUID: c5b21332-3880-4e13-bf5a-ee895293b7c8

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HGVS expressions

NM_000531.6:c.387T>C

NM_000531.6(OTC):c.387T>C (p.Arg129_Val130=)

NC_000023.11:g.38401275T>C

CM000685.2:g.38401275T>C

NC_000023.10:g.38260528T>C

CM000685.1:g.38260528T>C

NC_000023.9:g.38145472T>C

NG_008471.1:g.53793T>C

ENST00000039007.5:c.387T>C

ENST000000643344.1:c.*137T>C

ENST00000039007.4:c.387T>C

ENST000000465127.1:c.172-264846T>C

ENST000000488812.1:n.424T>C

NM_000531.5:c.387T>C

Uncertain Significance

Met criteria codes **3**

BP7

BP4

PM2_Supporting

Evidence Links **0**

Expert Panel

Urea Cycle Disorders VCEP [↗](#)

Criteria Specification Information

[↗](#) **Criteria Specification:** ClinGen Urea Cycle Disorders
Expert Panel Specifications to the ACMG/AMP Variant
Interpretation Guidelines for OTC Version 1.0.0

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Urea Cycle Disorders VCEP

The NM_000531.6:c.387T>C variant in OTC is a synonymous (silent) variant (p.Arg129_Val130=) that is not predicted by SpliceAI to impact splicing and the nucleotide (BP4), however the nucleotide is within the first 3 bases of an exon, so BP7 is not applicable. To our knowledge, this variant has not been reported in the literature and results of functional studies are unavailable. Grpmax MAF in gnomAD v4.1.0 is 0.000009190 in the European (non-Finnish) population which is lower than the ClinGen UCD VCEP's threshold for PM2_Supporting

(<0.000015) and there are ≤ 1 hemizygotes/homozygotes across all populations, meeting this criterion (PM2_Supporting). In summary, this variant meets the criteria to be classified as a variant of uncertain significance for OTC deficiency based on the ACMG/AMP criteria applied, as specified by the ClinGen Urea Cycle Disorders Variant Curation Expert Panel (OTC specifications version 1.0.0): BP4, PM2_Supporting.

Met criteria codes

BP7			SpliceAI predicts no impact and nucleotide is not highly conserved.
BP4			The NM_000531.6(OTC):c.387T>C (p.Arg129_Val130=) meets BP4 (Splice AI predicts no impact of the on splicing) and the nucleotide is poorly conserved (phyloP score -0.107).
PM2_Supporting			Grpmax MAF in gnomAD v4.1.0 is 0.000009190 in the European (non-Finnish) population which is lower than the ClinGen UCD VCEP's threshold for PM2_Supporting (<0.000015) and there are ≤ 1 hemizygotes/homozygotes across all populations, meeting this criterion (PM2_Supporting).

Curation History



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