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_000531.6(OTC):c.67C>T (p.Arg23Ter)

Version: 1.0

CA224742

97292 (ClinVar)

Gene: OTC (HGNC:5009)
Condition: ornithine carbamoyltransferase deficiency (MONDO:0010703)
Inheritance Mode: X-linked inheritance
UUID: c14edd18-22b7-4575-8a73-81897d3ea21e
Approved on: Tue, 03 Nov 2026 00:00:00 +0000
Published on: Tue, 03 Nov 2026 00:00:00 +0000

HGVS expressions

NM_000531.6(OTC):c.67C>T (p.Arg23Ter)
NM_000531.6:c.67C>T
NC_000023.11:g.38352763C>T
CM000685.2:g.38352763C>T
NC_000023.10:g.38212016C>T
CM000685.1:g.38212016C>T
NC_000023.9:g.38096960C>T
NG_008471.1:g.5281C>T
ENST00000039007.5:c.67C>T
ENST00000643344.1:c.67C>T
ENST00000039007.4:c.67C>T
ENST00000465127.1:c.172-313358C>T
ENST00000488812.1:n.159C>T
NM_000531.5:c.67C>T

Pathogenic

Met criteria codes 3

PVS1 PM2_Supporting PP4_Moderate

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*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Urea Cycle Disorders VCEP

The NM_000531.6(OTC):c.67C>T (p.Arg23Ter) variant in OTC is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 1 of OTC leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). One patient with this variant displayed Vomiting, Childhood onset, Hepatic failure, Hyperammonemia, Oroticaciduria, Elevated circulating alanine aminotransferase concentration, Lethargy, Elevated circulating uracil concentration, 4% OTC activity which is

highly specific for OTC deficiency (3.25pts, PP4_Moderate, PMID: 24485820). This variant is absent from gnomAD v4.1.0 (PM2_Supporting). In summary, this variant meets the criteria for being classified as Pathogenic for OTC deficiency. ACMG/AMP criteria applied, as specified by the ClinGen UCD VCEP Variant Interpretation Guidelines for OTC Version 1.0.0: PVS1, PM2_Supporting, PP4_Moderate

Met criteria codes

PVS1	✔	The NM_000531.6(OTC):c.67C>T (p.Arg23Ter) variant in OTC is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 1 for OTC leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).
PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0 (PM2_Supporting)
PP4_Moderate	✔	One patient with this variant displayed Vomiting, Childhood onset, Hepatic failure, Hyperammonemia, Oroticaciduria, Elevated circulating alanine aminotransferase concentration, Lethargy, Elevated circulating uracil concentration, 4% OTC activity which is highly specific for OTC deficiency (3.25pts, PP4_Moderate, PMID: 24485820, Pathogenic).

Curation History

owing 1 to 1 of 1 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.