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.1A>T (p.Met1Leu)

Version: 2.0

CA224496

97131 (ClinVar)

Gene: OTC (HGNC:5009)
Condition: ornithine carbamoyltransferase deficiency (MONDO:0010703)
Inheritance Mode: X-linked inheritance
UUID: 2adf0ef5-c341-479a-9a57-a80bf8429d33
Approved on: Tue, 15 Sep 2026 00:00:00 +0000
Published on: Tue, 15 Sep 2026 00:00:00 +0000

HGVS expressions

NM_000531.6(OTC):c.1A>T (p.Met1Leu)
NM_000531.6:c.1A>T
NC_000023.11:g.38352697A>T
CM000685.2:g.38352697A>T
NC_000023.10:g.38211950A>T
CM000685.1:g.38211950A>T
NC_000023.9:g.38096894A>T
NG_008471.1:g.5215A>T
ENST00000039007.5:c.1A>T
ENST00000643344.1:c.1A>T
ENST00000039007.4:c.1A>T
ENST00000465127.1:c.172-313424A>T
ENST00000488812.1:n.93A>T
NM_000531.5:c.1A>T

Likely Pathogenic

Met criteria codes 2

PVS1 PM2_Supporting

Not Met criteria codes 1

PM5

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_000156.6:c.1A>T (p.Met1Leu) variant in OTC may cause a truncated or absent protein by altering the start codon of the coding sequence and is predicted to lead to the omission of a critical region of the protein (PVS1). This variant has been detected in 1 individual with neonatal-onset OTC deficiency (PMID:16786505), however biochemical evidence was not available for review. This variant is absent in gnomAD v4.1.0 (PM2_Supporting). In summary, this variant meets the criteria to be classified as likely pathogenic 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): PVS1 (+8), PM2_Supporting (+1)

Met criteria codes

PVS1	✔	The NM_000156.6:c.1A>T (p.Met1Leu) variant in OTC may cause a truncated or absent protein by altering the start codon of the coding sequence and is predicted to lead to the omission of a critical region of the protein (PVS1).
PM2_Supporting	✔	This variant is absent in gnomAD v4.1.0 (PM2_Supporting).

Not Met criteria codes

PM5	✖	A different amino acid change at the same amino acid (p.Met1Ile) is Pathogenic (PM5; PMID:9143919, 33272297, 34014557; ClinVarID:97189), however this variant has not been formally curated by the UCD VCEP (09/15/26).

Curation History

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