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Variant: NM_000531.6(OTC):c.1052del (p.Lys351fs)

Version: 1.1

CA1139667400

915468 (ClinVar)

Gene: OTC (HGNC:5009)
Condition: ornithine carbamoyltransferase deficiency (MONDO:0010703)
Inheritance Mode: X-linked inheritance
UUID: a628fc0f-f6a4-4a34-b785-49fef665b42e
Approved on: 2026/6/11
Published on: 2026/9/10

HGVS expressions

NM_000531.6:c.1052del
NM_000531.6(OTC):c.1052del (p.Lys351fs)
NC_000023.11:g.38421069del
CM000685.2:g.38421069del
NC_000023.10:g.38280322del
CM000685.1:g.38280322del
NC_000023.9:g.38165266del
NG_008471.1:g.73587del
ENST00000039007.5:c.1052del
ENST00000039007.4:c.1052del
ENST00000465127.1:c.172-245052del
NM_000531.5:c.1052del

Likely Pathogenic

Met criteria codes 3

PM2_Supporting PVS1_Strong PS4_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*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Urea Cycle Disorders VCEP

The NM_000531.6:c.1052del (p.K351Sfs*44) variant in OTC is a frameshift variant predicted to cause a shift of the reading frame of the protein and extension beyond the Ter354 and a novel Ter395 within the last exon of the gene. While this variant is expected to escape nonsense mediated decay it is predicted to alter a region that is critical to protein function (amino acids 345-354) and per ClinGen UCD VCEP specifications, alteration including these regions is applicable at a weight of Strong (PVS1_Strong). This variant has been detected in at least 1 individual with OTC deficiency (PMID: 34014569, PMID: 34014557, ClinVar SCV001281637.1) (PS4_Supporting). This variant has been identified as a de novo occurrence with unconfirmed parental relationships in one individual with OTC deficiency (ClinVar

SCV001281637.1) (PM6_Supporting). 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_Strong, PS4_Supporting, PM2_Supporting, PM6_Supporting.

Met criteria codes

PM2_Supporting ✔	This variant is absent from controls in an ethnically-matched cohort population sample and has a PopMax frequency <0.000015 (0.0015%) in gnomAD v4.1.0 (PM2_Supporting).
PVS1_Strong ✔	The NM_000531.6:c.1052del (p.K351Sfs*44) variant in OTC is a frameshift variant predicted to cause a premature stop codon in the last exon of the gene and therefore to escape nonsense mediated decay. (PVS1_Strong).
PS4_Supporting ✔	Identified in at least 1 female proband with hyperammonemia and metabolic decompensation under physiological stress (PMID: 34014569, PMID: 34014557, ClinVar SCV001281637.1) [based on authorship of papers, may be same individual]

Curation History

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