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Variant: NM_000203.5(IDUA):c.439C>T (p.Gln147Ter)

Version: 1.0

CA355961461

984179 (ClinVar)

Gene: IDUA (HGNC:3425)
Condition: mucopolysaccharidosis type 1 (MONDO:0001586)
Inheritance Mode: Autosomal recessive inheritance
UUID: a1bbb46f-f9f8-4458-92f1-c03a31c770bc
Approved on: 2024/12/5
Published on: 2025/3/19

HGVS expressions

NM_000203.5(IDUA):c.439C>T (p.Gln147Ter)
NM_000203.5:c.439C>T
NC_000004.12:g.1000935C>T
CM000666.2:g.1000935C>T
NC_000004.11:g.994723C>T
CM000666.1:g.994723C>T
NC_000004.10:g.984723C>T
NG_008103.1:g.18939C>T
ENST00000247933.9:c.439C>T
ENST00000514224.2:c.439C>T
ENST00000652070.1:n.495C>T
ENST00000247933.8:c.439C>T
ENST00000502910.5:c.298C>T
ENST00000504568.5:c.399C>T
ENST00000506561.5:n.448C>T
ENST00000508168.5:n.317C>T
ENST00000509948.5:c.232C>T
ENST00000514192.5:c.256C>T
ENST00000514224.1:c.43C>T
ENST00000514698.5:n.339C>T
NM_000203.4:c.439C>T
NR_110313.1:n.527C>T
NM_001363576.1:c.43C>T

Likely Pathogenic

Met criteria codes 2

PVS1 PM2_Supporting

Not Met criteria codes 2

PM3 PP4

Evidence Links 0

Expert Panel

Lysosomal Diseases VCEP

Criteria Specification Information

Criteria Specification: *ClinGen Lysosomal Diseases Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for IDUA Version 1.0.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Lysosomal Diseases VCEP

The NM_000203.5:c.439C>T (p.Gln147Ter) variant in IDUA is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 4 of 14 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). This variant has not been reported in the literature, but has been reported in ClinVar (Variation ID: 984179). This variant is absent from gnomAD v4.1.0. (PM2_Supporting). The ClinGen SVI recommendation for absence/rarity (PM2) suggests that the combination of PVS1 and PM2 should be considered as 'likely pathogenic'. Therefore this variant meets the criteria to be classified as likely pathogenic for MPS I based on the ACMG/AMP criteria applied, as specified by the ClinGen Lysosomal Diseases Variant Curation Expert Panel (Specifications Version 1.0.0.): PVS1, PM2_Supporting. (Classification approved by the ClinGen Lysosomal Diseases Variant Curation Expert Panel on December 5, 2024)

Met criteria codes

PVS1	✔	The NM_000203.5:c.439C>T (p.Gln147Ter) variant in IDUA is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 4 out of 14, leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1; PMIDs: 11735025, 21480867).
PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0. (PM2_Supporting).

Not Met criteria codes

PM3	✖	This variant has not been reported in the literature to-date. There are two submissions regarding this variant in ClinVar, however neither confirm the patient's status as being affected by MPS I. Hence this criterion is not met.
PP4	✖	There is insufficient detail provided in the two ClinVar submissions in order to apply this criterion.

Curation History

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