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Variant: NM_000203.5(IDUA):c.123G>A (p.Trp41Ter)

Version: 1.0

CA355945567

2734632 (ClinVar)

Gene: IDUA (HGNC:3425)
Condition: mucopolysaccharidosis type 1 (MONDO:0001586)
Inheritance Mode: Autosomal recessive inheritance
UUID: 9e526aa0-5e27-46f8-9ef3-5e53aed401d8
Approved on: 2025/4/7
Published on: 2025/5/4

HGVS expressions

NM_000203.5(IDUA):c.123G>A (p.Trp41Ter)
NM_000203.5:c.123G>A
NC_000004.12:g.987207G>A
CM000666.2:g.987207G>A
NC_000004.11:g.980995G>A
CM000666.1:g.980995G>A
NC_000004.10:g.970995G>A
NG_008103.1:g.5211G>A
NG_033042.1:g.11230C>T
ENST00000247933.9:c.123G>A
ENST00000514224.2:c.123G>A
ENST00000247933.8:c.123G>A
ENST00000398520.6:c.576+3921C>T
ENST00000502910.5:c.123G>A
ENST00000504568.5:c.121G>A
ENST00000506561.5:n.132G>A
ENST00000508168.5:n.142G>A
ENST00000514698.5:n.164G>A
ENST00000622731.4:c.576+3921C>T
NM_000203.4:c.123G>A
NM_134425.2:c.576+3921C>T
NR_110313.1:n.211G>A
NM_134425.3:c.576+3921C>T
NM_134425.4:c.576+3921C>T

Pathogenic

Met criteria codes 3

PM2_Supporting PVS1 PP4_Moderate

Not Met criteria codes 1

PM3

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. c.123G>A (p.Trp41Ter) variant in IDUA is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 1 out of 14, leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). This variant has been detected in at least one individual with Hurler syndrome, presenting with IDUA deficiency within the affected range, increased excretion of urinary dermatan sulfate and heparan sulfate, and clinical features specific to MPS I including Macrocephaly, joint stiffness, Mongolian macula, hepatosplenomegaly, hernia, cardiac disease, and airway obstruction (PMID 21480867) (PP4_moderate). This individual is compound heterozygous for the variant and c.300-1G>C, p.(?). The allelic data for this patient will be used to support the classification of c.300-1G>C and is not included here in order to avoid circular logic. The highest population minor allele frequency in gnomAD v4.1.0 is 8.889e-7 (1/1,124,963 alleles) in the Non-Finnish European population, which is lower than the ClinGen Lysosomal Diseases VCEP's threshold for PM2_Supporting (>0.00025), meeting this criterion (PM2_Supporting). There is a ClinVar entry for this variant (Variation ID: 2734632). In summary, this variant meets the criteria to be classified as pathogenic for MPS I based on the IDUA-specific ACMG/AMP criteria applied, as specified by the ClinGen Lysosomal Diseases Variant Curation Expert panel (Specifications Version 1.0.0): (PVS1, PP4 moderate, PM2 supporting). (Classification approved by the ClinGen Lysosomal Diseases Variant Curation Expert Panel on April 7, 2025)

Met criteria codes

PM2_Supporting	✔	The highest population minor allele frequency in gnomAD v4.1.0 is 8.889e-7 (1/1,124,963 alleles) in the Non-Finnish European population, which is lower than the ClinGen Lysosomal Diseases VCEP's threshold for PM2_Supporting (>0.00025), meeting this criterion (PM2_Supporting).
PVS1	✔	The NM_000203.5:c. c.123G>A (p.Trp41Ter) variant in IDUA is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 1 out of 14, leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).
PP4_Moderate	✔	This variant has been detected in at least one individual with Hurler syndrome, presenting with IDUA deficiency within the affected range, increased excretion of urinary dermatan sulfate and heparan sulfate, and clinical features specific to MPS I including macrocephaly, joint stiffness, Mongolian macula, hepatosplenomegaly, hernia, cardiac disease, and airway obstruction (PMID 21480867) (PP4_moderate).

Not Met criteria codes

PM3	✖	This individual is compound heterozygous for c.123G>A (p.Trp41Ter) and c.300-1G>C, p.(?). The allelic data for this patient will be used to support the classification of c.300-1G>C and is not included here in order to avoid circular logic.

Curation History



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.

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