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Variant: NM_000203.5(IDUA):c.820G>T (p.Glu274Ter)

Version: 1.0

CA355962341

553227 (ClinVar)

Gene: IDUA (HGNC:3425)
Condition: mucopolysaccharidosis type 1 (MONDO:0001586)
Inheritance Mode: Autosomal recessive inheritance
UUID: e3b3d2a6-e030-46bd-bd2e-69e26f076772
Approved on: 2025/12/15
Published on: 2025/12/28

HGVS expressions

NM_000203.5(IDUA):c.820G>T (p.Glu274Ter)
NM_000203.5:c.820G>T
NC_000004.12:g.1002009G>T
CM000666.2:g.1002009G>T
NC_000004.11:g.995797G>T
CM000666.1:g.995797G>T
NC_000004.10:g.985797G>T
NG_008103.1:g.20013G>T
ENST00000247933.9:c.820G>T
ENST00000514224.2:c.820G>T
ENST00000652070.1:n.876G>T
ENST00000247933.8:c.820G>T
ENST00000514192.5:c.637G>T
ENST00000514224.1:c.424G>T
ENST00000514698.5:n.820G>T
NM_000203.4:c.820G>T
NR_110313.1:n.908G>T
NM_001363576.1:c.424G>T

Pathogenic

Met criteria codes 4

PM2_Supporting | PP4 | PVS1 | 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 1.1.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Lysosomal Diseases VCEP

The NM_000203.5:c.820G>T (p.Glu274Ter) variant in IDUA is a nonsense variant predicted to cause a premature stop codon in biologically-relevant exon 7 out of 14, leading to nonsense mediated decay in a gene in which loss-of function is an established disease mechanism (PVS1). At least 1 patient with this variant had documented IDUA deficiency within the affected range and bone marrow transplant resulted in a significant reduction in urine GAGs (PP4; PMID: 8401515). This individual was compound heterozygous for the variant and another variant in IDUA that has been classified as pathogenic by the ClinGen LD VCEP, c.208C>T (p.Gln70Ter), and confirmed in trans by parental testing (PM3; PMID: 8401515). The highest population minor allele frequency in gnomAD v4.1.0. is 0.000 (0/74926 alleles) in the African/African American 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: 553227). 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 1.1.0): PVS1, PP4, PM3, PM2_Supporting. (Classification approved by the ClinGen Lysosomal Diseases Variant Curation Expert Panel on December 15, 2025)

Met criteria codes

PM2_Supporting	✔	The highest population minor allele frequency in gnomAD v4.0. is 0.000 (0/74926 alleles) in the African/African American population, which is lower than the ClinGen Lysosomal Diseases VCEP's threshold for PM2_Supporting (<0.00025), meeting this criterion (PM2_Supporting).
PP4	✔	At least 1 patient with this variant had documented IDUA deficiency within the affected range and bone marrow transplant resulted in a significant reduction in urine GAGs (PP4; PMID: 8401515).
PVS1	✔	The NM_000203.5:c.820G>T (p.Glu274Ter) variant in IDUA is a nonsense variant predicted to cause a premature stop codon in biologically-relevant exon 7 out of 14, leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).
PM3	✔	This variant has been detected in at least 1 individual with MPS I. This individual was compound heterozygous for the variant and a pathogenic variant (c.208C>T (p.Gln70Ter)) and confirmed in trans by parental testing (PM3= 1 point; PMID: 8401515; PM3).

Curation History

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