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_000203.5(IDUA):c.1163C>A (p.Thr388Lys)

Version: 1.0

CA247499

198696 (ClinVar)

Gene: IDUA (HGNC:3425)
Condition: mucopolysaccharidosis type 1 (MONDO:0001586)
Inheritance Mode: Autosomal recessive inheritance
UUID: 748dede1-7d86-40ee-ac1f-025f33b5cbf3
Approved on: 2025-08-08
Published on: 2025-12-05

HGVS expressions

NM_000203.5:c.1163C>A
NM_000203.5(IDUA):c.1163C>A (p.Thr388Lys)
NC_000004.12:g.1002459C>A
CM000666.2:g.1002459C>A
NC_000004.11:g.996247C>A
CM000666.1:g.996247C>A
NC_000004.10:g.986247C>A
NG_008103.1:g.20463C>A
ENST00000247933.9:c.1163C>A
ENST00000514224.2:c.1163C>A
ENST00000652070.1:n.1219C>A
ENST00000247933.8:c.1163C>A
ENST00000514224.1:c.767C>A
ENST00000514698.5:n.1270C>A
NM_000203.4:c.1163C>A
NR_110313.1:n.1251C>A
NM_001363576.1:c.767C>A

Likely Pathogenic

Met criteria codes 5

PM2_Supporting PM3_Supporting PP4_Moderate PP3 PM5_Supporting

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.1163C>A variant in IDUA is a missense variant predicted to cause substitution of threonine by lysine at amino acid 388 (p.Thr388Lys). This variant was detected in one homozygous patient with MPS I (PM3 _Supporting). This patient presented with clinical symptoms consistent with MPS I, as well as reduced IDUA activity in leukocytes and elevated total GAGs in urine (PP4_Moderate). The computational predictor REVEL gives a score of 0.756 (PP3). The highest population minor allele frequency in gnomAD v4.1.0. is 0.0000244 (1/40992 alleles) in the East Asian 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: 198696). In summary, this variant meets the criteria to be classified as likely 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): PP4_Moderate, PP3, PM2_Supporting, PM3_Supporting, PM5_Supporting (Classification approved by the ClinGen Lysosomal Diseases Variant Curation Expert Panel on August 8, 2025)

Met criteria codes

PM2_Supporting	✔	The highest population minor allele frequency in gnomAD v4.1.0. is 0.0000244 (1/40992 alleles) in the East Asian population, which is lower than the ClinGen Lysosomal Diseases VCEP's threshold for PM2_Supporting (<0.00025), meeting this criterion (PM2_Supporting).
PM3_Supporting	✔	This variant has been detected in at least 1 individual with MPS I. That individual was homozygous for the variant (0.5 points, PMID: 27520059) (PM3_Supporting)
PP4_Moderate	✔	At least 1 patient with this variant had documented IDUA deficiency within the affected range in leukocytes (2 points), and urinary GAGs expressed as total GAGs above normal range (1 point), and clinical features specific to MPS I including hepatosplenomegaly, arthropathy, corneal involvement, valvular thickening (1 point). (4 points total, PMID: 27520059, PP4_Moderate).
PP3	✔	The computational predictor REVEL gives a score of 0.756 which is in the range 0.644-0.773, evidence that correlates with impact to IDUA function at the supporting level (PMID: 36413997) (PP3).
PM5_Supporting	✔	Another variant at the same amino acid position, c.1163C>G (pThr388Arg) has been classified as likely pathogenic by the ClinGen LD VCEP (PM5_Supporting).

Curation History

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