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Variant: NM_001363576.1:c.134T>C

Version: 1.0

CA355961706

Gene: IDUA (HGNC:3425)
Condition: mucopolysaccharidosis type 1 (MONDO:0001586)
Inheritance Mode: Autosomal recessive inheritance
UUID: 205a3748-0b3a-4ae0-ba5a-9ca116c04059
Approved on: 2025/12/21
Published on: 2025/12/29

HGVS expressions

NM_001363576.1:c.134T>C
NC_000004.12:g.1001504T>C
CM000666.2:g.1001504T>C
NC_000004.11:g.995292T>C
CM000666.1:g.995292T>C
NC_000004.10:g.985292T>C
NG_008103.1:g.19508T>C
ENST00000247933.9:c.530T>C
ENST00000514224.2:c.530T>C
ENST00000652070.1:n.586T>C
ENST00000247933.8:c.530T>C
ENST00000502910.5:c.389T>C
ENST00000504568.5:c.490T>C
ENST00000509948.5:c.323T>C
ENST00000514192.5:c.347T>C
ENST00000514224.1:c.134T>C
ENST00000514698.5:n.430T>C
NM_000203.4:c.530T>C
NR_110313.1:n.618T>C
NM_000203.5:c.530T>C

Likely Pathogenic

Met criteria codes 4

PM3_Supporting PP3_Moderate PP4_Moderate PM2_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 1.0.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Lysosomal Diseases VCEP

The NM_000203.5:c.530T>C variant in IDUA is a missense variant predicted to cause substitution of phenylalanine by serine at amino acid 177 (p.Phe177Ser). One patient from Tunisia was reported having clinical symptoms consistent with MPS I, deficient IDUA activity and increased urine GAG levels (PMID: 22074387) (PP4_Moderate). This patient is homozygous for the variant (0.5 points) (PM3_Supporting). The computational predictor REVEL gives a score of 0.942 which is above the threshold of 0.773, evidence that correlates with impact to IDUA function at the moderate level based on the specifications of the ClinGen Lysosomal Diseases VCEP (PMID: 36413997) (PP3_Moderate). SpliceAI predicts that the variant has no impact on splicing (all scores <0.1). 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 MPS I. IDUA-specific ACMG/AMP criteria applied, as specified by the ClinGen Lysosomal Diseases Variant Curation Expert Panel (Specifications Version 1.1.0): PM2_Supporting, PM3_Supporting, PP3_Moderate, PP4_Moderate. (Classification approved by the ClinGen Lysosomal Diseases Variant Curation Expert Panel on December 29, 2025)

Met criteria codes

PM3_Supporting	✔	Proband of Family E is homozygous for the variant (0.5 points) (PMID: 22074387).
PP3_Moderate	✔	The computational predictor REVEL gives a score of 0.942 which is above the threshold of 0.773, evidence that correlates with impact to IDUA function at the moderate level based on the specifications of the ClinGen Lysosomal Diseases VCEP (PMID: 36413997) (PP3_Moderate). SpliceAI predicts that the variant has no impact on splicing (all scores <0.1).
PP4_Moderate	✔	One patient from Tunisia was reported and with clinical symptoms consistent with MPS I, deficient IDUA activity, and increased urine GAG levels (PMID: 22074387) (PP4_Moderate).
PM2_Supporting	✔	This variant is absent in gnomAD v4.1.0. (PM2_Supporting).

Curation History

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