

Variant: NM_134425.4:c.576+3888G>T

Version: 1.2

CA355945699 [↗](#)

3906898 (ClinVar) [↗](#)

Gene: SLC26A1 ([HGNC:10861](#))

Condition: mucopolysaccharidosis type 1 ([MONDO:0001586](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: ba7c0f48-b483-48dd-8618-5a64f8045f72

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HGVS expressions

NM_134425.4:c.576+3888G>T

NC_000004.12:g.987240C>A

CM000666.2:g.987240C>A

NC_000004.11:g.981028C>A

CM000666.1:g.981028C>A

NC_000004.10:g.971028C>A

NG_008103.1:g.5244C>A

NG_033042.1:g.11197G>T

ENST00000247933.9:c.156C>A

ENST00000514224.2:c.156C>A

ENST00000247933.8:c.156C>A

ENST00000398520.6:c.576+3888G>T

ENST00000502910.5:c.156C>A

ENST00000504568.5:c.154C>A

ENST00000506561.5:n.165C>A

ENST00000508168.5:n.175C>A

ENST00000514698.5:n.197C>A

ENST00000622731.4:c.576+3888G>T

NM_000203.4:c.156C>A

NM_134425.2:c.576+3888G>T

NR_110313.1:n.244C>A

NM_000203.5:c.156C>A

NM_134425.3:c.576+3888G>T

Likely Pathogenic

Met criteria codes 4

PP4_Moderate

PP3

PM3

PM2_Supporting

Not Met criteria codes 1

PS1

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**

Lysosomal Diseases VCEP

The NM_000203.5: c.156C>A variant in IDUA is a missense variant predicted to cause substitution of phenylalanine by Leucine at amino acid 52 (p.Phe52Leu). This variant has been detected in at least one individual with MPS I. This individual is compound heterozygous for the variant and c.1037T>G p.(Leu346Arg), which is classified as likely pathogenic by the ClinGen Lysosomal Diseases VCEP (PMID 21480867, phase confirmed in trans, 1 point) (PM3). This individual has documented IDUA deficiency within the affected range (0.2 nmol/h/mg, reference range 27.2-52), increased excretion of urinary dermatan sulfate and heparin sulfate, and clinical features specific to MPS I including hepatosplenomegaly, joint stiffness and airway obstruction (PMID 21480867) (PP4_moderate). This variant is absent in gnomAD v4.1.0. (PM2_Supporting). The computational predictor REVEL gives a score of 0.669 which is in the range 0.644-0.773, evidence that correlates with impact to IDUA function at the supporting level (PMID: 36413997) (PP3_supporting). Another variant resulting in the same missense change (c.156C>G, p.Phe52Leu) is in ClinVar (Variation ID: 554280) with a low frequency in gnomAD; reported in Abdulelah et al, Iraqi J Pharm Sci, Vol.33(4) 2024). This variant has not yet been classified by the ClinGen LD VCEP. There is no ClinVar entry for this variant. 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.): PM3, PP4_moderate, PP3, PM2_supporting. (Classification approved by the ClinGen Lysosomal Diseases Variant Curation Expert Panel on April 7, 2025)

Met criteria codes

PP4_Moderate			This individual has documented IDUA deficiency within the affected range (0.2 nmol/h/mg, reference range 27.2-52), increased excretion of urinary dermatan sulfate and heparin sulfate, and clinical features specific to MPS I including hepatosplenomegaly, joint stiffness and airway obstruction ((PMID 21480867) (PP4_supporting).
PP3			The computational predictor REVEL gives a score of 0.669 which is in the range 0.644-0.773, evidence that correlates with impact to IDUA function at the supporting level (PMID: 36413997) (PP3_supporting).
PM3			This individual is compound heterozygous for the variant and c.1037T>G p.(Leu346Arg), which is classified as likely pathogenic by the ClinGen Lysosomal Diseases VCEP (PMID 21480867, phase confirmed in trans, 1 point) (PM3).
PM2_Supporting			This variant is absent in gnomAD v4.1.0. (PM2_Supporting).

Not Met criteria codes

PS1			Another variant resulting in the same missense change (c.156C>G, p.Phe52Leu) is in ClinVar (Variation ID: 554280) with a low frequency in gnomAD; reported in "Genetic Study of Mucopolysaccharidosis in A Sample of Iraqi Children", Abdulelah et al, Iraqi J Pharm Sci, Vol.33(4) 2024. This variant has not yet been classified by the ClinGen LD VCEP.
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