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_001363576.1:c.686del

Version: 1.0

CA2573332225

Gene: IDUA (HGNC:3425)
Condition: mucopolysaccharidosis type 1 (MONDO:0001586)
Inheritance Mode: Autosomal recessive inheritance
UUID: 84b6fe98-c34a-46c9-bae5-bb95f5e632aa
Approved on: 2025-01-03
Published on: 2025-01-03

HGVS expressions

NM_001363576.1:c.686del
NC_000004.12:g.1002378del
CM000666.2:g.1002378del
NC_000004.11:g.996166del
CM000666.1:g.996166del
NC_000004.10:g.986166del
NG_008103.1:g.20382del
ENST00000247933.9:c.1082del
ENST00000514224.2:c.1082del
ENST00000652070.1:n.1138del
ENST00000247933.8:c.1082del
ENST00000514224.1:c.686del
ENST00000514698.5:n.1189del
NM_000203.4:c.1082del
NR_110313.1:n.1170del
NM_000203.5:c.1082del

Likely Pathogenic

Met criteria codes 2

PM2_Supporting PVS1

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.1082del (p.Ala361GlyfsTer79) variant in IDUA is a frameshift variant predicted to cause a premature stop codon in exon 9 out of 14 total exons, leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism

(PVS1). This variant is absent in gnomAD v4.1.0. To our knowledge, this variant has not been reported in the literature in any individuals with mucopolysaccharidosis type 1. The classification of this variant has been upgraded from Variant of Uncertain Significance to Likely Pathogenic based on the recommendations of the ClinGen Sequence Variant Interpretation Working Group, that a variant meeting PVS1 and PM2_Supporting is classified as Likely Pathogenic (https://clinicalgenome.org/site/assets/files/5182/pm2_-_svi_recommendation_-_approved_sept2020.pdf). In summary, this variant meets the criteria to be classified as likely pathogenic for mucopolysaccharidosis type 1. IDUA-specific ACMG-AMP criteria applied, as specified by the ClinGen Lysosomal Diseases VCEP (Specifications Version 1.0.0): PVS1, PM2_Supporting. (Classification approved by the ClinGen Lysosomal Diseases Variant Curation Expert Panel on January 3, 2025)

Met criteria codes

PM2_Supporting	✔	This variant is absent in gnomAD v4.1.0.
PVS1	✔	The NM_000203.5:c.1082del (p.Ala361GlyfsTer79) variant in IDUA is a frameshift variant predicted to cause a premature stop codon in exon 9 out of 14 total exons, leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).

Curation History

See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene

No matching records found