

Variant: NM_000152.5(GAA):c.276C>A (p.Cys92Ter)

Version: 1.1

CA401360590 [↗](#)

654482 (ClinVar) [↗](#)

Gene: GAA ([HGNC:2548](#))

Condition: glycogen storage disease II ([MONDO:0009290](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: c94287b0-819c-42f9-931c-1aabe0fe0d45

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HGVS expressions

NM_000152.5(GAA):c.276C>A (p.Cys92Ter)

NM_000152.5:c.276C>A

NC_000017.11:g.80104862C>A

CM000679.2:g.80104862C>A

NC_000017.10:g.78078661C>A

CM000679.1:g.78078661C>A

NC_000017.9:g.75693256C>A

NG_009822.1:g.8307C>A

ENST00000570803.6:c.276C>A

ENST00000572080.2:c.276C>A

ENST00000577106.6:c.276C>A

ENST00000302262.8:c.276C>A

ENST00000302262.7:c.276C>A

ENST00000390015.7:c.276C>A

ENST00000570803.5:c.276C>A

ENST00000577106.5:c.276C>A

NM_000152.3:c.276C>A

NM_001079803.1:c.276C>A

NM_001079804.1:c.276C>A

NM_000152.4:c.276C>A

NM_001079803.2:c.276C>A

NM_001079804.2:c.276C>A

NM_001079803.3:c.276C>A

NM_001079804.3:c.276C>A

Likely Pathogenic

Met criteria codes **2**

PVS1

PM2_Supporting

Evidence Links **0**

Expert Panel

[Lysosomal Diseases VCEP](#) [↗](#)

Criteria Specification Information

[↗](#) **Criteria Specification:** ClinGen Lysosomal Storage Disorders Variant Curation Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 2

[↗](#) PDF

[↗](#) Criteria Specification Approval History

Evidence submitted by expert panel

Lysosomal Diseases VCEP

The NM_000152.5:c.276C>A (p.Cys92Ter) variant in GAA is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 2 of 20, 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 v2.1.1. and v4.1.0. (PM2_Supporting). To our knowledge, this variant has not been reported in individuals with Pompe disease in the literature and functional studies are unavailable. There is a ClinVar entry for this variant (Variation ID: 654482). 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 Pompe disease. GAA-specific ACMG/AMP criteria applied, as specified by the ClinGen Lysosomal Diseases Variant Curation Expert Panel (Specifications Version 2.0): PVS1, PM2_Supporting. (Classification approved by the ClinGen Lysosomal Diseases Variant Curation Expert Panel on October 29, 2024).

Met criteria codes

PVS1	 	The NM_000152.5:c.276C>A (p.Cys92Ter) variant in GAA is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 2 of 20, leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).
PM2_Supporting		This variant is absent in gnomAD v2.1.1. and v4.1.0. (PM2_Supporting).

Curation History [↗](#)

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