

Variant: NM_000152.5(GAA):c.1054C>T (p.Gln352Ter)

Version: 1.0

CA294891876 [↗](#)

2138114 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 1ba2a6fe-570b-464b-9efe-efee32bd4d67

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HGVS expressions

NM_000152.5(GAA):c.1054C>T (p.Gln352Ter)

NM_000152.5:c.1054C>T

NC_000017.11:g.80108388C>T

CM000679.2:g.80108388C>T

NC_000017.10:g.78082187C>T

CM000679.1:g.78082187C>T

NC_000017.9:g.75696782C>T

NG_009822.1:g.11833C>T

ENST00000570803.6:c.1054C>T

ENST00000572080.2:c.1054C>T

ENST00000577106.6:c.1054C>T

ENST00000302262.8:c.1054C>T

ENST00000302262.7:c.1054C>T

ENST00000390015.7:c.1054C>T

NM_000152.3:c.1054C>T

NM_001079803.1:c.1054C>T

NM_001079804.1:c.1054C>T

NM_000152.4:c.1054C>T

NM_001079803.2:c.1054C>T

NM_001079804.2:c.1054C>T

NM_001079803.3:c.1054C>T

NM_001079804.3:c.1054C>T

Likely Pathogenic

Met criteria codes **2**

PVS1

PM2_Supporting

Not Met criteria codes **2**

PP4

PM3

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 2.0

[↗](#) **PDF**

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

Lysosomal Diseases VCEP

The NM_000152.5:c.1054C>T (p.Gln352Ter) variant in GAA is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 6/20, leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). At least one individual with this variant identified by newborn screening had documented GAA activity in the affected range in dried blood spot and was compound heterozygous for the variant and c.[752C>T;761C>T] (p.[Ser251Leu;Ser254Leu]), which has not yet been evaluated by the ClinGen Lysosomal Diseases VCEP, phase unconfirmed (PMID: 24513544). However, in the absence of clinical symptoms to support that the variant causes Pompe disease, PP4 and PM3 will not be applied. The highest population minor allele frequency in gnomAD v4.1.0. is 8.474e-7 (1/1180028 alleles) in the European (non-Finnish) population, which is lower than the ClinGen Lysosomal Diseases VCEP’s threshold for PM2_Supporting (<0.001), meeting this criterion (PM2_Supporting). In summary, this variant meets the criteria to be classified as Likely Pathogenic for Pompe disease. 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). 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 July 10, 2026)

Met criteria codes

PVS1			The NM_000152.5:c.1054C>T (p.Gln352Ter) variant in GAA is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 6/20, leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).
PM2_Supporting			The highest population minor allele frequency in gnomAD v4.1.0. is 8.474e-7 (1/1180028 alleles) in the European (non-Finnish) population, which is lower than the ClinGen Lysosomal Diseases VCEP’s threshold for PM2_Supporting (<0.001), meeting this criterion (PM2_Supporting).

Not Met criteria codes

PP4			At least one patient with this variant identified through newborn screening had documented GAA activity in the affected range in dried blood spot (PMID: 24513544). However, in the absence of clinical symptoms to support that the variant causes Pompe disease, PP4 was not applied.
PM3			This variant has been detected in at least one individual with low GAA activity who was compound heterozygous for the variant and c.[752C>T;761C>T] (p.[Ser251Leu;Ser254Leu]), which has not yet been evaluated by the ClinGen Lysosomal Diseases VCEP, phase unconfirmed (PMID: 24513544). In the absence of a confirmed diagnosis and clinical symptoms to support that the variant causes Pompe disease, PM3 is not met.

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