

Variant: NM_000152.5(GAA):c.2242G>T (p.Glu748Ter)

Version: 2.0

CA16041903 [↗](#)

370268 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: f329994e-9f5d-4121-8d8c-dc92a28f8082

Approved on: 2023/4/11

Published on: 2023/4/19

HGVS expressions

NM_000152.5(GAA):c.2242G>T (p.Glu748Ter)

NM_000152.5:c.2242G>T

NC_000017.11:g.80117020G>T

CM000679.2:g.80117020G>T

NC_000017.10:g.78090819G>T

CM000679.1:g.78090819G>T

NC_000017.9:g.75705414G>T

NG_009822.1:g.20465G>T

ENST00000570803.6:c.2242G>T

ENST00000572080.2:c.*380G>T

ENST00000577106.6:c.2242G>T

ENST00000302262.8:c.2242G>T

ENST00000302262.7:c.2242G>T

ENST00000390015.7:c.2242G>T

ENST00000572080.1:c.661G>T

ENST00000573556.1:n.195G>T

NM_000152.3:c.2242G>T

NM_001079803.1:c.2242G>T

NM_001079804.1:c.2242G>T

NM_000152.4:c.2242G>T

NM_001079803.2:c.2242G>T

NM_001079804.2:c.2242G>T

NM_001079803.3:c.2242G>T

NM_001079804.3:c.2242G>T

Pathogenic

Met criteria codes **3**

PM2_Supporting

PVS1

PM3_Supporting

Not Met criteria codes **1**

PP4

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.2242G>T (p.Glu748Ter) variant in GAA is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 16/20, leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). One patient with this variant, diagnosed with late onset Pompe disease, has been reported (PMID: 31545528). This individual is compound heterozygous for the variant and a pathogenic variant in GAA, c.-32-13T>G, phase unknown (PMID: 31545528) (PM3_Supporting). The data are insufficient to apply PP4 based on the specifications of the ClinGen Lysosomal Diseases VCEP. The variant is absent in gnomAD v2.1.1. (PM2_Supporting). There is a ClinVar entry for this variant (Variation ID 370268). In summary, this variant meets the criteria to be classified as pathogenic for Pompe disease. GAA-specific ACMG/AMP criteria applied, as specified by the ClinGen Lysosomal Diseases VCEP (Specifications Version 2.0): PVS1, PM3_Supporting, PM2_Supporting. (Classification approved by the ClinGen Lysosomal Diseases VCEP, April 11, 2023).

Met criteria codes

PM2_Supporting		This variant is absent in gnomAD v2.1.1.
PVS1		The NM_000152.5:c.2242G>T (p.Glu748Ter) variant in GAA is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 16/20, leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).
PM3_Supporting		One patient with late onset Pompe disease is compound heterozygous for the variant and a pathogenic variant in GAA, c.-32-13T>G, phase unknown (PMID: 31545528), 0.5 points (PM3_Supporting).

Not Met criteria codes

PP4		One patient with this variant, and a diagnosis of late onset Pompe disease, has been reported. However, the data are insufficient to apply PP4 based on the specifications of the ClinGen LD VCEP.
-----	--	--

Curation History [↗](#)

Showing 1 to 2 of 2 rows

See Report	Preferred Variant Title	Classification ⓘ	Condition	Published Date	Version ⓘ	Criteria Specification	Gene
View	NM_000152.5(GAA):c.2242G>T (p.Glu7...	Pathogenic	Glycogen Storage Disease II ↗	2023-04-19	2.0	ClinGen Lysosomal Storage Disorders Variant Curation Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 2 ↗	GAA ↗

View	NM_000152.5(GAA):c.2242G>T (p.Glu7...	Likely Pathogenic	Glycogen Storage Disease II ↗	2020-05-27	1.0	-	GAA ↗
----------------------	---------------------------------------	-------------------	---	------------	-----	---	-----------------------

Showing 1 to 2 of 2 rows

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.