

Variant: NM_000152.5(GAA):c.1924G>T (p.Val642Phe)

Version: 1.0

CA401369892 [↗](#)

2675763 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 3aff7972-13bd-4a43-b58c-e918dbd25494

Approved on: 2026/4/7

Published on: 2026/4/8

HGVS expressions

NM_000152.5(GAA):c.1924G>T (p.Val642Phe)

NM_000152.5:c.1924G>T

NC_000017.11:g.80112911G>T

CM000679.2:g.80112911G>T

NC_000017.10:g.78086710G>T

CM000679.1:g.78086710G>T

NC_000017.9:g.75701305G>T

NG_009822.1:g.16356G>T

ENST00000570803.6:c.1924G>T

ENST00000572080.2:c.*62G>T

ENST00000577106.6:c.1924G>T

ENST00000302262.8:c.1924G>T

ENST00000302262.7:c.1924G>T

ENST00000390015.7:c.1924G>T

ENST00000570716.1:n.364G>T

ENST00000572080.1:c.343G>T

ENST00000572803.1:n.538G>T

NM_000152.3:c.1924G>T

NM_001079803.1:c.1924G>T

NM_001079804.1:c.1924G>T

NM_000152.4:c.1924G>T

NM_001079803.2:c.1924G>T

NM_001079804.2:c.1924G>T

NM_001079803.3:c.1924G>T

NM_001079804.3:c.1924G>T

Uncertain Significance

Met criteria codes **4**

PM2_Supporting

PP3

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

[↗](#) PDF

Evidence submitted by expert panel

Lysosomal Diseases VCEP

The NM_000152.5:c.1924G>T variant in GAA is a missense variant predicted to cause substitution of valine by phenylalanine at amino acid 642 (p.Val642Phe). One proband with symptoms consistent with infantile-onset Pompe disease has been reported (PMID: 26310554). A second proband with a reported diagnosis of infantile-onset Pompe disease has also been reported, but clinical features were not documented (PMID: 29122469). Both probands are compound heterozygous for the variant and a variant classified as pathogenic by the ClinGen Lysosomal Diseases VCEP, c.2105G>A (p.Arg702His) (PMID: 26310554) and c.1210G>A (p.Asp404Asn) (PMID: 29122469) (PM3). The highest population minor allele frequency for this variant in gnomAD v4.1.0. is 0.0000008483 (1/1178846 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). The computational predictor REVEL gives a score of 0.946 which is above the threshold of 0.7, evidence that correlates with impact to GAA function (PP3). There is a ClinVar entry for this variant (Variation ID: 2675763). In summary, this variant meets the criteria to be classified as uncertain significance for Pompe disease. GAA-specific ACMG/AMP criteria met, based on the specifications of the ClinGen Lysosomal Diseases Variant Curation Expert Panel (Specifications Version 2.0): PM3, PP3, PP4, PM2_Supporting. (Classification approved by the ClinGen Lysosomal Diseases Variant Curation Expert Panel, April 7, 2026)

Met criteria codes

PM2_Supporting		The highest population minor allele frequency in gnomAD v4.1.0. is 0.0000008483 (1/1178846 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).
PP3		The computational predictor REVEL gives a score of [0.X] which is above the threshold of 0.946, evidence that correlates with impact to GAA function (PP3).
PP4		One individual who harbors this variant was identified via carrier screening. One patient with this variant was diagnosed with Pompe disease but GAA activity levels and documentation of symptoms were not reported. A second patient with this variant was diagnosed with Pompe disease and reported to have cardiomyopathy, hepatosplenomegaly, and respiratory insufficiency (PP4).
PM3		This variant has been detected in three individuals with Pompe disease. One individual who harbors this variant was identified via carrier screening. Two individuals were compound heterozygous for the variant and a pathogenic variant but phase was not confirmed for either patient (PM3_Supporting).

Curation History [↗](#)

▾

▾

Showing 1 to 1 of 1 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.