

Variant: NM_000152.5(GAA):c.2702T>A (p.Leu901Gln)

Version: 1.0

CA401326888 [↗](#)

2585303 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: eb46ae72-09d9-4f21-934d-27e157be8da1

Approved on: 2026/8/4

Published on: 2026/8/5

HGVS expressions

NM_000152.5(GAA):c.2702T>A (p.Leu901Gln)

NM_000152.5:c.2702T>A

NC_000017.11:g.80118708T>A

CM000679.2:g.80118708T>A

NC_000017.10:g.78092507T>A

CM000679.1:g.78092507T>A

NC_000017.9:g.75707102T>A

NG_009822.1:g.22153T>A

ENST00000570803.6:c.2702T>A

ENST00000572080.2:c.*840T>A

ENST00000577106.6:c.2702T>A

ENST00000302262.8:c.2702T>A

ENST00000302262.7:c.2702T>A

ENST00000390015.7:c.2702T>A

ENST00000573556.1:n.655T>A

NM_000152.3:c.2702T>A

NM_001079803.1:c.2702T>A

NM_001079804.1:c.2702T>A

NM_000152.4:c.2702T>A

NM_001079803.2:c.2702T>A

NM_001079804.2:c.2702T>A

NM_001079803.3:c.2702T>A

NM_001079804.3:c.2702T>A

Likely Pathogenic

Met criteria codes 5

PS3_Moderate

PP3

PM3

PM2_Supporting

PP4_Moderate

Not Met criteria codes 1

PM5

Evidence Links 1

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

Evidence submitted by expert panel

Lysosomal Diseases VCEP

The NM_000152.5:c.2702T>A variant in GAA is a missense variant predicted to cause substitution of leucine by glutamine at amino acid 901 (p.Leu901Gln). At least one patient with this variant had documented GAA deficiency with 5.4% of normal mean control level of GAA activity in muscle and undetectable GAA activity in cultured fibroblasts (PP4_moderate). This patient presented at 8 months of age with moderate proximal muscle weakness and elevated CK with mild left ventricular hypertrophy without cardiac insufficiency. The patient was classified as having childhood onset Pompe disease (PMID: 15145338). This individual was compound heterozygous for the variant and a second pathogenic GAA variant confirmed in trans by parental testing (PM3). This variant is absent in gnomAD v4.1.0. (PM2_Supporting). When expressed in COS cells, this variant resulted in <1% GAA activity using 4-MUG and glycogen substrates. Western blot of transfected cell lysates showed impaired processing of the precursor protein to the mature form (PS3_moderate). The computational predictor REVEL gives a score of 0.923 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: 2585303). In summary, this variant meets the criteria to be classified as Likely Pathogenic for Pompe disease based on the GAA-specific ACMG/AMP criteria applied, as specified by the ClinGen Lysosomal Diseases Variant Curation Expert Panel (Specifications Version 2.0): PP4_moderate, PM3, PM2_supporting, PS3_moderate, PP3 (Classification approved by the ClinGen Lysosomal Diseases Variant Curation Expert Panel, August 4, 2026)

Met criteria codes

PS3_Moderate			When expressed in COS cells, this variant resulted in <1% GAA activity using 4-MUG and glycogen substrates. Western blot of transfected cell lysates showed impaired processing of the precursor protein to the mature form (PS3_moderate).
The mutation was introduced in GAA cDNA and expressed in COS cells. GAA activity in transfected cells was <1% using both 4-MU and glycogen as substrate. Western blot of transfected COS cells showed impaired processing from the 110kDa precursor to the mature form in cells. 110kDa precursor was absent in medium suggesting premature protein degradation. Of note these transfected cells had the same GAA activity as mock transfected cells. PubMed:15145338 			
PP3			The computational predictor REVEL gives a score of 0.923 which is above the threshold of 0.7, evidence that correlates with impact to GAA function (PP3).
PM3			One individual was compound heterozygous for the variant and a second pathogenic variant confirmed in trans by parental testing (1.0 pts for PM3). The variant is c.1933T>A (p.Asp645Asn) classified as pathogenic by the ClinGen Lysosomal Diseases VCEP (ClinVar ID: 188728).
PM2_Supporting			This variant is absent in gnomAD v4.1.0. (PM2_Supporting)
PP4_Moderate			At least one patient with this variant had documented GAA deficiency with 5.4% of normal mean control level of GAA activity in muscle and undetectable GAA activity in cultured fibroblasts (PMID: 15145338). This patient presented at 8 months of age with moderate proximal muscle weakness and elevated CK with mild left ventricular hypertrophy without cardiac insufficiency. The patient was classified as having childhood onset Pompe disease.

Not Met criteria codes

PM5



No other missense changes at this residue have been reported.

Curation History

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