

Variant: NM_001079804.3:c.1670T>G

Version: 1.1

CA401368920 [↗](#)

1693547 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 0e64774c-b953-45ac-94bd-d0c295b0f820

Approved on: 2026/1/14

Published on: 2026/1/14

HGVS expressions

NM_001079804.3:c.1670T>G

NC_000017.11:g.80112016T>G

CM000679.2:g.80112016T>G

NC_000017.10:g.78085815T>G

CM000679.1:g.78085815T>G

NC_000017.9:g.75700410T>G

NG_009822.1:g.15461T>G

ENST00000570803.6:c.1670T>G

ENST00000572080.2:c.1670T>G

ENST00000577106.6:c.1670T>G

ENST00000302262.8:c.1670T>G

ENST00000302262.7:c.1670T>G

ENST00000390015.7:c.1670T>G

ENST00000572080.1:c.58T>G

ENST00000572803.1:n.284T>G

NM_000152.3:c.1670T>G

NM_001079803.1:c.1670T>G

NM_001079804.1:c.1670T>G

NM_000152.4:c.1670T>G

NM_001079803.2:c.1670T>G

NM_001079804.2:c.1670T>G

NM_000152.5:c.1670T>G

NM_001079803.3:c.1670T>G

Likely Pathogenic

Met criteria codes **5**

PP4_Moderate

PM3_Supporting

PP3

PM5

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

[↗](#) Criteria Specifications for this VCEP

Lysosomal Diseases VCEP

The NM_000152.5:c.1670T>G variant in GAA is a missense variant predicted to cause substitution of isoleucine by serine at amino acid 557 (p.Ile557Ser). One patient with clinically asymptomatic Pompe disease, persistent elevated creatine kinase, abnormal muscle MRI, and <10% normal mean GAA activity in muscle has been reported (PMID:26474166, presumably the same patient is reported in PMID:31342611, 40813881, Cardiogenetics 2024, 14, 38-50) (PP4_Moderate). This patient is compound heterozygous for the variant and another variant that has been classified by the ClinGen LD VCEP as pathogenic for Pompe disease, c.-32-13T>G (ClinVar Variation ID: 4027), phase unknown (PMID: 26474166, 31342611, 40813881; Cardiogenetics 2024, 14, 38-50), 0.5 points (PM3_Supporting). The variant is not in gnomAD v4.1.0. (PM2_Supporting). The computational predictor REVEL gives a score of 0.746 which is above the threshold of 0.7, evidence that correlates with impact to GAA function (PP3). Another missense variant in the same codon, c.1669A>T (p.Ile557Phe) (ClinVar Variation ID: 558634; PMID 23884227), has been classified as pathogenic for Pompe disease by the ClinGen LD VCEP (PM5). 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 2.0.0): PM5, PP4_Moderate, PM3_Supporting, PP3, PM2_Supporting. (Classification approved by the ClinGen Lysosomal Diseases Variant Curation Expert Panel on January 14, 2026)

Met criteria codes

PP4_Moderate			One patient with clinically asymptomatic Pompe disease, persistent elevated creatine kinase, abnormal muscle MRI, and <10% normal mean GAA activity in muscle has been reported (PMID 26474166)(PP4_Moderate).
PM3_Supporting			At least one patient is compound heterozygous for the variant and another variant that has been classified by the ClinGen LD VCEP as pathogenic for Pompe disease, c.-32-13T>G (ClinVar Variation ID: 4027), phase unknown (PMID: 26474166, 31342611, 40813881; Cardiogenetics 2024, 14, 38-50), 0.5 points (PM3_Supporting).
PP3			The computational predictor REVEL gives a score of 0.746 which is above the threshold of 0.7, evidence that correlates with impact to GAA function (PP3).
PM5			Another missense variant in the same codon, c.1669A>T (p.Ile557Phe) (ClinVar Variation ID: 558634; PMID 23884227), has been classified as pathogenic for Pompe disease by the ClinGen LD VCEP (PM5). An additional variant at the same codon, c.1669A>G (p.Ile557Val) (ClinVar Variation ID: 856959), is a variant of uncertain significance.
PM2_Supporting			This variant is not in gnomAD v4.1.0. (PM2_Supporting).

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