

Variant: NM_000152.5(GAA):c.615G>A (p.Pro205=)

Version: 1.1

CA243111 [↗](#)

196223 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 4066d189-e5a2-4f99-82a1-3913da100053

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HGVS expressions

NM_000152.5:c.615G>A

NM_000152.5(GAA):c.615G>A (p.Pro205=)

NC_000017.11:g.80105817G>A

CM000679.2:g.80105817G>A

NC_000017.10:g.78079616G>A

CM000679.1:g.78079616G>A

NC_000017.9:g.75694211G>A

NG_009822.1:g.9262G>A

ENST00000570803.6:c.615G>A

ENST00000572080.2:c.615G>A

ENST00000577106.6:c.615G>A

ENST00000302262.8:c.615G>A

ENST00000302262.7:c.615G>A

ENST00000390015.7:c.615G>A

ENST00000570803.5:c.615G>A

ENST00000577106.5:c.615G>A

NM_000152.3:c.615G>A

NM_001079803.1:c.615G>A

NM_001079804.1:c.615G>A

NM_000152.4:c.615G>A

NM_001079803.2:c.615G>A

NM_001079804.2:c.615G>A

NM_001079803.3:c.615G>A

NM_001079804.3:c.615G>A

Uncertain Significance

Met criteria codes **3**

PM2_Supporting

BP4

BP7

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.615G>A variant in GAA is a synonymous (silent) variant (p.Pro205=) that is not predicted to impact splicing based on the computational splice predictor SpliceAI (BP4). Further, it is not in a position that is highly conserved (BP7). This variant has not been reported in a patient with Pompe disease to our knowledge. The highest population minor allele frequency in gnomAD v4.0. is 0.0004172 (38/91082 alleles) in the South Asian population. This is lower than the ClinGen Lysosomal Diseases VCEP’s threshold for PM2_Supporting (<0.001), meeting this criterion (PM2_Supporting). There is a ClinVar entry for this variant (ClinVar Variation ID: 196223). Due to conflicting evidence, this variant is classified as a variant of uncertain significance 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): BP4, BP7, PM2_supporting. (Classification approved by the ClinGen Lysosomal Diseases Variant Curation Expert Panel on July 7, 2026)

Met criteria codes

PM2_Supporting		The highest population minor allele frequency in gnomAD v4.1.0. is 0.0004172 (38/91082 alleles) in the South Asian population. This is lower than the ClinGen Lysosomal Diseases VCEP’s threshold for PM2_Supporting (<0.001), meeting this criterion (PM2_Supporting).
BP4		The computational splicing predictor SpliceAI gives a score of 0.01 for acceptor gain suggesting that the variant has no impact on splicing (BP4).
BP7		The computational splicing predictor SpliceAI gives a score of 0.01 for acceptor gain suggesting that the variant has no impact on splicing (BP4). Additionally, this variant is at a nucleotide position that is not predicted to be highly conserved (PhyloP100 score: -2.893). Thus, BP7 can be applied.

Not Met criteria codes

PP4		This variant has been reported in one individual in the Duke Molecular Genetics Laboratory with a second silent change (phase unknown) that is classified as a VUS. GAA enzyme is in the normal range. No clinical information available.
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Curation History [↗](#)



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