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# *Variant: NM_001079804.3:c.2411G>A*

Version: 2.0

*CA401325125*

*1693552 (ClinVar)*

**Gene**: GAA (HGNC:2548)
**Condition**: glycogen storage disease II (MONDO:0009290)
**Inheritance Mode**: Autosomal recessive inheritance
**UUID:** 58b01f86-672c-430b-8d06-a40e3609d568
**Approved on**: 2024/3/6
**Published on**: 2024/3/26

## *HGVS expressions*

**NM_001079804.3:c.2411G>A**
NC_000017.11:g.80117679G>A
CM000679.2:g.80117679G>A
NC_000017.10:g.78091478G>A
CM000679.1:g.78091478G>A
NC_000017.9:g.75706073G>A
NG_009822.1:g.21124G>A
ENST00000570803.6:c.2411G>A
ENST00000572080.2:c.*549G>A
ENST00000577106.6:c.2411G>A
ENST00000302262.8:c.2411G>A
ENST00000302262.7:c.2411G>A
ENST00000390015.7:c.2411G>A
ENST00000573556.1:n.364G>A
NM_000152.3:c.2411G>A
NM_001079803.1:c.2411G>A
NM_001079804.1:c.2411G>A
NM_000152.4:c.2411G>A
NM_001079803.2:c.2411G>A
NM_001079804.2:c.2411G>A
NM_000152.5:c.2411G>A
NM_001079803.3:c.2411G>A

**Pathogenic**

**Met criteria codes** 3

PM3_Supporting PVS1 PM2_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**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

***Lysosomal Diseases VCEP***

**The NM_000152.5:c.2411G>A (p.Trp804Ter) variant in GAA is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 17 )out of 20, leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). One patient reported to have infantile-onset Pompe disease is compound heterozygous for the variant and a variant that has been classified as pathogenic by the ClinGen Lysosomal Diseases VCEP, c.1802C>T (p.Ser601Leu) (ClinVar Variation ID: 194154, SCV002032130.1); the phase is unconfirmed (PMID: 28394184) (PM3_Supporting). There is insufficient data to apply PP4. The variant is absent in gnomAD v2.1.1. (PM2_Supporting). In summary, this variant meets the criteria to be classified as pathogenic for Pompe disease. Initially, the variant was classified a likely pathogenic by the ClinGen Lysosomal Diseases VCEP on August 17, 2021, but it was reclassified as pathogenic on Jan 15, 2024, due to the application of PM3_Supporting. GAA-specific ACMG/AMP criteria met, as specified by the ClinGen Lysosomal Diseases Variant Curation Expert Panel (Specifications Version 2.0): PVS1, PM2_Supporting, PM3_Supporting. (Classification approved by the ClinGen Lysosomal Diseases Variant Curation Panel on Feb 6, 2024).**

**Met criteria codes**

| | | |
|---|---|---|
| **PM3_Supporting** | ✔ | One patient reported to have infantile-onset Pompe disease is compound heterozygous for the variant and a variant that has been classified as pathogenic by the ClinGen Lysosomal Diseases VCEP, c.1802C>T (p.Ser601Leu) (ClinVar Variation ID: 194154, SCV002032130.1); the phase is unconfirmed (PMID: 28394184) (0.5 points) (PM3_Supporting). Note that the pathogenic classification of p.Ser601Leu does not require the allelic data from this patient. |
| **PVS1** | ✔ | The NM_000152.5: c.2411G>A (p.Trp804Ter) variant in GAA is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 17 out of 20, leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). |
| **PM2_Supporting** | ✔ | This variant is absent in gnomAD v2.1.1. and v4.0. (PM2_Supporting). |

**Not Met criteria codes**

| | | |
|---|---|---|
| **PP4** | ✖ | Insufficient details provided to apply PP4. |

Curation History

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