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# *Variant: NM_000152.5(GAA):c.2704C>T (p.Gln902Ter)*

Version: 1.1

*CA16041908*

*370241 (ClinVar)*

**Gene**: GAA (HGNC:2548)
**Condition**: glycogen storage disease II (MONDO:0009290)
**Inheritance Mode**: Autosomal recessive inheritance
**UUID:** 758c50e3-1f35-4df3-8818-b0d9703e7699
**Approved on**: 2023/3/8
**Published on**: 2023/3/8

## *HGVS expressions*

**NM_000152.5:c.2704C>T**
**NM_000152.5(GAA):c.2704C>T (p.Gln902Ter)**
NC_000017.11:g.80118710C>T
CM000679.2:g.80118710C>T
NC_000017.10:g.78092509C>T
CM000679.1:g.78092509C>T
NC_000017.9:g.75707104C>T
NG_009822.1:g.22155C>T
ENST00000570803.6:c.2704C>T
ENST00000572080.2:c.*842C>T
ENST00000577106.6:c.2704C>T
ENST00000302262.8:c.2704C>T
ENST00000302262.7:c.2704C>T
ENST00000390015.7:c.2704C>T
ENST00000573556.1:n.657C>T
NM_000152.3:c.2704C>T
NM_001079803.1:c.2704C>T
NM_001079804.1:c.2704C>T
NM_000152.4:c.2704C>T
NM_001079803.2:c.2704C>T
NM_001079804.2:c.2704C>T
NM_001079803.3:c.2704C>T
NM_001079804.3:c.2704C>T

**Likely Pathogenic**

**Met criteria codes** 2

PM2 PVS1

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.2704C>T (p.Gln902Ter) variant in GAA is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 19/20. Although exon 19 is the penultimate exon of GAA, the variant occurs in the region where nonsense-mediated decay is predicted to occur, in a gene in which loss-of-function is an established disease mechanism (PVS1). The variant is absent in gnomAD v.2.1.1, meeting PM2. To our knowledge, this variant has not been reported in the literature in individuals with Pompe disease, and results of experimental studies are not available. There is a ClinVar entry for this variant (Variation ID: 370241). The classification of this variant has been upgraded from Variant of Uncertain Significance to Likely Pathogenic based on the recommendations of the ClinGen Sequence Variant Interpretation Working Group, that a variant meeting PVS1 and PM2_Supporting is classified as Likely Pathogenic (https://clinicalgenome.org/site/assets/files/5182/pm2_-_svi_recommendation_-_approved_sept2020.pdf ). In summary, this variant meets the criteria to be classified as a likely pathogenic for Pompe disease. GAA-specific ACMG/AMP criteria applied, as specified by the ClinGen LSD VCEP (Specifications version 2.0): PVS1, PM2_Supporting.**

**Met criteria codes**

| | | |
|---|---|---|
| **PM2** | ✔ | This variant is absent in gnomAD v2.1.1, meeting PM2. |
| **PVS1** | ✔ | The NM_000152.5:c.2704C>T (p.Gln902Ter) variant in GAA is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 19/20. Although exon 19 is the penultimate exon of GAA, the variant occurs in the region where nonsense-mediated decay is predicted to occur, in a gene in which loss-of-function is an established disease mechanism (PVS1). |

Curation History

Showing 1 to 2 of 2 rows

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