

Variant: NM_001079804.3:c.246C>A

Version: 1.0

CA401360532 [↗](#)

1693546 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 44a7a89c-1d1a-40c0-b9f4-d69d061cddf7

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HGVS expressions

NM_001079804.3:c.246C>A
NC_000017.11:g.80104832C>A
CM000679.2:g.80104832C>A
NC_000017.10:g.78078631C>A
CM000679.1:g.78078631C>A
NC_000017.9:g.75693226C>A
NG_009822.1:g.8277C>A
ENST00000570803.6:c.246C>A
ENST00000572080.2:c.246C>A
ENST00000577106.6:c.246C>A
ENST00000302262.8:c.246C>A
ENST00000302262.7:c.246C>A
ENST00000390015.7:c.246C>A
ENST00000570803.5:c.246C>A
ENST00000577106.5:c.246C>A
NM_000152.3:c.246C>A
NM_001079803.1:c.246C>A
NM_001079804.1:c.246C>A
NM_000152.4:c.246C>A
NM_001079803.2:c.246C>A
NM_001079804.2:c.246C>A
NM_000152.5:c.246C>A
NM_001079803.3:c.246C>A

Pathogenic

Met criteria codes **3**

PM2_Supporting

PVS1

PP4_Moderate

Not Met criteria codes **1**

PM3

Evidence Links **0**

Expert Panel

Lysosomal Diseases VCEP [↗](#)

Criteria Specification Information **!**

[↗](#) Criteria Specifications for this VCEP

Lysosomal Diseases VCEP

The NM_000152.5:c.246C>A (p.Cys82Ter) variant in GAA is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 2/20, leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). This variant is absent in gnomAD v2.1.1 (PM2_Supporting). At least 1 patient with this variant had documented GAA deficiency with <10% of normal mean control level of GAA activity in leukocytes (PMID: 33741225) (PP4_Moderate). In summary, this variant meets the criteria to be classified as pathogenic for Pompe disease based on the ACMG/AMP criteria applied, as specified by the ClinGen Lysosomal Storage Disorders Variant Curation Expert panel (specifications Version 2.0): PVS1, PM2_Supporting, PP4_Moderate.

Met criteria codes

PM2_Supporting		This variant is absent in gnomAD v2.1.1 (PM2_Supporting).
PVS1		The NM_000152.5:c.246C>A (p.Cys82Ter) variant in GAA is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 2/20, leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).
PP4_Moderate		At least 1 patient with this variant had documented GAA deficiency with <10% of normal mean control level of GAA activity in leukocytes (PMID: 33741225) (PP4_Moderate).

Not Met criteria codes

PM3		This variant has been detected in 1 individual with Pompe disease that was compound heterozygous for the variant and a likely pathogenic variant. However, this was not applied to the curation of this variant to avoid circular logic.
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Curation History

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