The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000152.5(GAA):c.2055C>A (p.Tyr685Ter)

Version: 1.0

CA401370359

1322965 (ClinVar)

Gene: GAA (HGNC:2548)
Condition: glycogen storage disease II (MONDO:0009290)
Inheritance Mode: Autosomal recessive inheritance
UUID: 4d408bb8-09f8-4db6-a0da-b6d66ba3cece
Approved on: 2025/8/31
Published on: 2025/9/16

HGVS expressions

NM_000152.5(GAA):c.2055C>A (p.Tyr685Ter)
NM_000152.5:c.2055C>A
NC_000017.11:g.80113232C>A
CM000679.2:g.80113232C>A
NC_000017.10:g.78087031C>A
CM000679.1:g.78087031C>A
NC_000017.9:g.75701626C>A
NG_009822.1:g.16677C>A
ENST00000570803.6:c.2055C>A
ENST00000572080.2:c.*193C>A
ENST00000577106.6:c.2055C>A
ENST00000302262.8:c.2055C>A
ENST00000302262.7:c.2055C>A
ENST00000390015.7:c.2055C>A
ENST00000570716.1:n.495C>A
ENST00000572080.1:c.474C>A
NM_000152.3:c.2055C>A
NM_001079803.1:c.2055C>A
NM_001079804.1:c.2055C>A
NM_000152.4:c.2055C>A
NM_001079803.2:c.2055C>A
NM_001079804.2:c.2055C>A
NM_001079803.3:c.2055C>A
NM_001079804.3:c.2055C>A

Pathogenic

Met criteria codes 4

PVS1 PM3 PP4 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

Evidence submitted by expert panel

Lysosomal Diseases VCEP

The NM_000152.5:c.2055C>A (p.Tyr685Ter) variant in GAA is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 15 out of 20 total exons, leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). This variant has been detected in at least 2 individuals with late-onset Pompe disease who were both compound heterozygous for the variant and another variant that has been classified as pathogenic by the ClinGen LD VCEP, c.-32-13T>G (ClinVar Variation ID: 4027) (PMIDs 39879733, 17643989) (PM3, PP4). This variant is absent in gnomAD v4.1.0. (PM2_Supporting). There is a ClinVar entry for this variant (Variation ID: 1322965). In summary, this variant meets the criteria to be classified as Pathogenic 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): PVS1, PM3, PP4, PM2_Supporting. (Classification approved by the ClinGen Lysosomal Diseases Variant Curation Expert Panel, August 31, 2025)

Met criteria codes

PVS1	✔	The NM_000152.5:c.2055C>A (p.Tyr685Ter) variant in GAA is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 15/20, leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).
PM3	✔	This variant has been detected in at least 2 individuals with Pompe disease who were both compound heterozygous for the variant and a pathogenic variant, c.-32-13T>G (1 pt, PMIDs 39879733, 17643989) (PM3).
PP4	✔	At least 2 patient(s) with this variant had documented GAA deficiency with activity in the affected range in muscle, cultured skin fibroblasts, leukocytes, lymphocytes, whole blood or dried blood spot (1 pt, PMIDs 39879733, 17643989) (PP4).
PM2_Supporting	✔	This variant is absent in gnomAD v4.0. (PM2_Supporting).

Curation History

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