

Variant: *NM_000152.5(GAA):c.2655_2656del (p.Val886fs)*

Version: 1.0

CA913191011 [↗](#)

597005 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 73dc276a-44f8-4f4e-ad99-3769378ea110

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HGVS expressions

NM_000152.5(GAA):c.2655_2656del (p.Val886fs)

NM_000152.5:c.2655_2656del

NC_000017.11:g.80118661_80118662del

CM000679.2:g.80118661_80118662del

NC_000017.10:g.78092460_78092461del

CM000679.1:g.78092460_78092461del

NC_000017.9:g.75707055_75707056del

NG_009822.1:g.22106_22107del

ENST00000570803.6:c.2655_2656del

ENST00000572080.2:c.*793_*794del

ENST00000577106.6:c.2655_2656del

ENST00000302262.8:c.2655_2656del

ENST00000302262.7:c.2655_2656del

ENST00000390015.7:c.2655_2656del

ENST00000573556.1:n.608_609del

NM_000152.3:c.2655_2656del

NM_001079803.1:c.2655_2656del

NM_001079804.1:c.2655_2656del

NM_000152.4:c.2655_2656del

NM_001079803.2:c.2655_2656del

NM_001079804.2:c.2655_2656del

NM_001079803.3:c.2655_2656del

NM_001079804.3:c.2655_2656del

Pathogenic

Met criteria codes **4**

PP4_Moderate

PM3_Supporting

PM2_Supporting

PVS1

Evidence Links **0**

Expert Panel

Lysosomal Diseases VCEP [↗](#)

Criteria Specification Information **!**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Lysosomal Diseases VCEP

The NM_000152.5:c.2655_2656del (p.Val886GlufsTer2) variant in GAA is a frameshift variant predicted to cause a premature stop codon and to lead to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). Two siblings with this variant and late-onset Pompe disease have been reported with GAA activity in dried blood spots below the normal range, and both are on enzyme replacement therapy (PMID 31392188, personal communication)(PP4_Moderate). These individuals are compound heterozygous for the variant and a pathogenic variant in GAA, c.-32-13T>G, phase unknown (PM3_Supporting). The variant is absent in gnomAD v2.1.1 (PM2_Supporting). There is a ClinVar entry for this variant (Variation ID: 597005; 1 star review status) with one submitter classifying the variant as pathogenic. In summary, this variant meets the criteria to be classified as pathogenic for Pompe disease. GAA-specific ACMG/AMP criteria met, based on the specifications of the ClinGen LSD VCEP (Specifications Version 2.0): PVS1, PP4_Moderate, PM2_Supporting, PM3_Supporting.

Met criteria codes

PP4_Moderate			Two siblings with Pompe disease who are compound heterozygous have documented GAA activity in dried blood spot below the normal range, and both are on enzyme replacement therapy (PMID 31392188, personal communication)meeting the ClinGen LSD VCEP's specifications for PP4_Moderate.
PM3_Supporting			Two siblings with late-onset Pompe disease are compound heterozygous for the variant and c.-32-13T>G, a known pathogenic variant in GAA (PMID 31392188). The phase is unknown. Total 0.5 points (PM3_Supporting).
PM2_Supporting			This variant is absent in gnomAD v2.1.1 (PM2_Supporting).
PVS1			The NM_000152.5:c.2655_2656del (p.Val886GlufsTer2) variant in GAA is a frameshift variant predicted to cause a premature stop codon and to lead to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).

Curation History

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