

Variant: *NM_000152.5(GAA):c.1802C>A (p.Ser601Ter)*

Version: 1.0

CA401369436 [↗](#)

593486 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 8f8031f9-e04c-47ce-b028-62c2efb3ddcd

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HGVS expressions

NM_000152.5(GAA):c.1802C>A (p.Ser601Ter)

NM_000152.5:c.1802C>A

NC_000017.11:g.80112625C>A

CM000679.2:g.80112625C>A

NC_000017.10:g.78086424C>A

CM000679.1:g.78086424C>A

NC_000017.9:g.75701019C>A

NG_009822.1:g.16070C>A

ENST00000570803.6:c.1802C>A

ENST00000572080.2:c.1802C>A

ENST00000577106.6:c.1802C>A

ENST00000302262.8:c.1802C>A

ENST00000302262.7:c.1802C>A

ENST00000390015.7:c.1802C>A

ENST00000570716.1:n.242C>A

ENST00000572080.1:c.190C>A

ENST00000572803.1:n.416C>A

NM_000152.3:c.1802C>A

NM_001079803.1:c.1802C>A

NM_001079804.1:c.1802C>A

NM_000152.4:c.1802C>A

NM_001079803.2:c.1802C>A

NM_001079804.2:c.1802C>A

NM_001079803.3:c.1802C>A

NM_001079804.3:c.1802C>A

Pathogenic

Met criteria codes 4

PM3_Supporting

PP4

PM2

PVS1

Evidence Links 1

Expert Panel

Lysosomal Diseases VCEP [↗](#)

Criteria Specification Information !

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

Lysosomal Diseases VCEP

This variant, c.1802C>A (p.Ser601Ter), which results in a premature termination codon, is expected to result in nonsense mediated decay and absence of gene product, meeting PVS1. This is supported by the finding that a patient with this variant has no GAA cross-reactive immunological material in protein isolated from skin fibroblast cultures i.e. CRIM-negative (PMID 21687968). The variant is absent in gnomAD v2.1.1, meeting PM2. This variant was found in compound heterozygosity with c.525del in one patient with Pompe disease meeting the specifications for PP4. The phase is unknown (PMID 26497565). This data meets PM3_Supporting. A patient with the same genotype has been reported (PMID 21687968) and might be the same patient but this could not be verified. There is a ClinVar entry for this variant (Variation ID: 593486, 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 applied, as specified by the ClinGen LSD VCEP: PVS1, PM3_Suporting, PM2, PP4.

Met criteria codes

PM3_Supporting			One individual who meets the specifications for PP4 has been reported. This individual is compound heterozygous for c.1802C>A (p.Ser601Ter) and c.525delT (a known pathogenic variant) (PMID 26497565). The phase is unknown. 0.5 points were given towards PM3. A patient with the same genotype has been reported (PMID 21687968) and might be the same patient but this could not be verified.
<div>PubMed:21687968 </div>			
PP4			A individual with infantile onset Pompe disease has been reported with this variant and <1% of normal GAA activity on blood spot, leukocyte or fibroblast assay, meeting the specifications for PP4.
PM2			This variant is absent in gnomAD v2.1.1.
PVS1			This is a nonsense variant which is predicted to cause nonsense mediated decay resulting in no gene product. One individual with this variant has no GAA cross-reactive immunological material in protein isolated from skin fibroblast cultures (PMID 21687968). Therefore, PVS1 can be applied.

Curation History

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