

Variant: *NM_000152.4(GAA):c.1687C>T (p.Gln563Ter)*

Version: 1.2

CA16041895 [↗](#)

370357 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 779d712a-8d04-4013-8f4b-68f5464ecb1b

Approved on: 2020/2/14

Published on: 2020/5/26

HGVS expressions

NM_000152.4(GAA):c.1687C>T (p.Gln563Ter)

NM_000152.4:c.1687C>T

NC_000017.11:g.80112033C>T

CM000679.2:g.80112033C>T

NC_000017.10:g.78085832C>T

CM000679.1:g.78085832C>T

NC_000017.9:g.75700427C>T

NG_009822.1:g.15478C>T

ENST00000570803.6:c.1687C>T

ENST00000572080.2:c.1687C>T

ENST00000577106.6:c.1687C>T

ENST00000302262.8:c.1687C>T

ENST00000302262.7:c.1687C>T

ENST00000390015.7:c.1687C>T

ENST00000572080.1:c.75C>T

ENST00000572803.1:n.301C>T

NM_000152.3:c.1687C>T

NM_001079803.1:c.1687C>T

NM_001079804.1:c.1687C>T

NM_001079803.2:c.1687C>T

NM_001079804.2:c.1687C>T

NM_000152.5:c.1687C>T

NM_001079803.3:c.1687C>T

NM_001079804.3:c.1687C>T

Pathogenic

Met criteria codes **4**

PM2

PM3

PVS1

PP4

Evidence Links **2**

Expert Panel

Lysosomal Diseases VCEP [↗](#)

Criteria Specification Information **!**

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

Evidence submitted by expert panel

Lysosomal Diseases VCEP

This variant, c.1687C>T (p.Gln563Ter), is a nonsense variant that is predicted to result in nonsense-mediated decay and lack of gene product. Therefore, PVS1 can be applied. This variant is absent in gnomAD v2.1.1, meeting PM2. It has been reported in trans with a frameshift variant in GAA, c.722_723delTT, in an individual who meets the ClinGen LSD VCEP’s specifications for PP4 (PMID 19775921). This data meets PP4 and PM3. Additional patients with this variant have been reported but were not included because the residual GAA activity was not reported and therefore PP4 cannot be assessed (PMID 25741864). There is a ClinVar entry for this variant (Variation ID: 370357, one star review status) with one submitter classifying the variant as likely 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, PM2, PM3, PP4.

Met criteria codes

PM2	 	This variant is absent in gnomAD v2.1.1.
PM3	 	<p>This variant was found in compound heterozygosity with a unique pathogenic variant in GAA, c.722_723delTT, in one patient with Pompe disease who also meets the ClinGen LSD VCEP's PP4 specifications. The phase was confirmed as in trans. Based on the ClinGen LSD VCEP's guidelines, this data was given a total of 1 point, which meets PM3.</p> <div><div>PubMed:25741864 </div><div>PubMed:19775921 </div></div>
PVS1	 	This is a nonsense variant which is predicted to cause nonsense mediated decay resulting in no gene product.
PP4	 	<p>1 individual has been reported with this variant and GAA activity <10% normal in lymphocytes, leukocytes or muscle samples. This meets the criteria for PP4.</p> <div><p>Patient has <1% of normal GAA activity (in skin fibroblasts and/or muscle biopsy). <div>PubMed:19775921 </div></p></div>

**Curation History **

▼

▼

Showing 1 to 3 of 3 rows

--

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.

[ClinGen Terms of Use.](#)

[✕ Powered by BCM's Genboree.](#)