

Variant: *NM\_000152.5(GAA):c.236\_246del (p.Pro79fs)*

Version: 1.0

CA16041880 [↗](#)

371302 (ClinVar) [↗](#)

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

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

**Inheritance Mode:** Autosomal recessive inheritance

**UUID:** dc90ac1d-ebd6-428f-bb4a-d24b6f97f6a9

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### *HGVS expressions*

**NM\_000152.5(GAA):c.236\_246del (p.Pro79fs)**

**NM\_000152.5:c.236\_246del**

NC\_000017.11:g.80104822\_80104832del

CM000679.2:g.80104822\_80104832del

NC\_000017.10:g.78078621\_78078631del

CM000679.1:g.78078621\_78078631del

NC\_000017.9:g.75693216\_75693226del

NG\_009822.1:g.8267\_8277del

ENST00000570803.6:c.236\_246del

ENST00000572080.2:c.236\_246del

ENST00000577106.6:c.236\_246del

ENST00000302262.8:c.236\_246del

ENST00000302262.7:c.236\_246del

ENST00000390015.7:c.236\_246del

ENST00000570803.5:c.236\_246del

ENST00000577106.5:c.236\_246del

NM\_000152.3:c.236\_246del

NM\_001079803.1:c.236\_246del

NM\_001079804.1:c.236\_246del

NM\_000152.4:c.236\_246del

NM\_001079803.2:c.236\_246del

NM\_001079804.2:c.236\_246del

NM\_001079803.3:c.236\_246del

NM\_001079804.3:c.236\_246del

**Pathogenic**

**Met criteria codes** **4**

**PM2**

**PM3**

**PVS1**

**PP4**

**Evidence Links** **12**

Expert Panel

[Lysosomal Diseases VCEP](#) [↗](#)

Criteria Specification Information **!**

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

Evidence submitted by expert panel

***Lysosomal Diseases VCEP***

This variant, c.236\_246del (p.Pro79ArgfsTer13), has been reported in multiple patients with Pompe disease. For two of these patients, residual GAA activity is reported and meets the ClinGen LSD VCEP's specifications for PP4 (PMID 17056254, 30778879). Both of these patients are compound heterozygous for the variant and a unique pathogenic variant; one with c.377G>A (p.Trp126Ter), in trans (PMID 17056254), and the other with c.1655T>C (p.Leu552Pro), phase unknown (PMID 30778879). This data meets PM3. Additional cases, both homozygous and compound heterozygous, have been reported but were not included because the residual GAA activity was not provided, and therefore PP4 cannot be assessed (PMIDs, 19588081, 22194990, 22980766, 23825616, 25998610, 26913919, 29143201, 30022036, 32125626). There is a ClinVar entry for this variant (Variation ID: 371302, 1 star review status) with 1 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, PM2, PM3, PP4.

**Met criteria codes**

|      |                                                                                     |                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
|------|-------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| PM2  |    |    | This variant is absent in gnomAD v2.1.1, meeting PM2.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| PM3  |    |    | <p>This variant was found in compound heterozygosity with a unique pathogenic variant in GAA in 2 patients with Pompe disease who also meet the ClinGen LSD VCEP's PP4 specifications, with either c.377G&gt;A (p.Trp126Ter), in trans (PMID 17056254), or c.1655T&gt;C (p.Leu552Pro), phase unknown (PMID 30778879). Based on the ClinGen LSD VCEP's specifications, this data was given a total of 1.5 points which meets PM3. Additional cases, both homozygous and compound heterozygous, have been reported but were not included because the residual GAA activity was not provided, and therefore PP4 cannot be assessed (PMIDs, 19588081, 22194990, 22980766, 23825616, 25998610, 26913919, 29143201, 30022036, 32125626).</p> <div><div>PubMed:22194990</div><div>PubMed:26913919</div><div>PubMed:30371346</div><div>PubMed:22980766</div><div>PubMed:17056254</div><div>PubMed:19588081</div><div>PubMed:30778879</div><div>PubMed:23825616</div><div>PubMed:29143201</div><div>PubMed:25998610</div></div> |
| PVS1 |  |  | This is a frameshift variant which is predicted to result in a premature termination codon, nonsense mediated decay, and lack of gene product. Therefore, PVS1 can be applied.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| PP4  |  |  | <p>Two individuals have been reported with this variant and GAA activity in the affected range when compared to the laboratory's control range (PMIDs 17056254, 30778879) . This meets the criteria for PP4.</p> <div><div>PubMed:32125626</div><div>PubMed:30022036</div></div>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |



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