

Variant: *NM_000152.5:c.722_723del*

Version: 1.2

CA658795235 [↗](#)

932903 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 1b742d4e-033e-469e-b02a-e368ad095141

Approved on: 2020/1/21

Published on: 2020/5/26

HGVS expressions

NM_000152.5:c.722_723del

NC_000017.11:g.80107586_80107587del

CM000679.2:g.80107586_80107587del

NC_000017.10:g.78081385_78081386del

CM000679.1:g.78081385_78081386del

NC_000017.9:g.75695980_75695981del

NG_009822.1:g.11031_11032del

ENST00000570803.6:c.722_723del

ENST00000572080.2:c.722_723del

ENST00000577106.6:c.722_723del

ENST00000302262.8:c.722_723del

ENST00000302262.7:c.722_723del

ENST00000390015.7:c.722_723del

ENST00000570803.5:c.722_723del

NM_000152.3:c.722_723del

NM_001079803.1:c.722_723del

NM_001079804.1:c.722_723del

NM_000152.4:c.722_723del

NM_001079803.2:c.722_723del

NM_001079804.2:c.722_723del

NM_001079803.3:c.722_723del

NM_001079804.3:c.722_723del

Pathogenic

Met criteria codes **4**

PP4

PM2

PM3_Strong

PVS1

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.722_723del (p.Phe241CysfsTer), is a frameshift variant that is predicted to result in a premature termination codon, 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 found in at least two patients with Pompe disease who meet the ClinGen LSD VCEP’s specifications for PP4 (PMID 19775921). One of these patients is compound heterozygous for the variant and c.1687C>T (p.Gln563Ter), and the other is compound heterozygous for the variant and c.1754+1G>A. In both cases, the variants were confirmed to be in trans. This data meets PM3_Strong. Additional cases have been reported, but did not meet PP4 (PMID 28838325). There is no ClinVar entry for this variant. 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_Strong, PP4.

Met criteria codes

PP4			This variant has been found in at least two patients with <1% residual GAA activity in skin fibroblasts (PMID 19775921) meeting the ClinGen LSD VCEP's specifications for PP4.
PubMed:19775921 			
PM2			This variant is absent in gnomAD v2.1.1.
PM3_Strong			This variant has been found in at least two patients with Pompe disease who meet the ClinGen LSD VCEP’s specifications for PP4 (PMID 19775921). One of these patients is compound heterozygous for the variant and c.1687C>T (p.Gln563Ter), and the other is compound heterozygous for the variant and c.1754+1G>A. In both cases, the variants were confirmed to be in trans. One point was given to each case (total 2 points), meeting PM3_Strong.
PubMed:28838325 			
PVS1			This is a frameshift variant which is predicted to result in a premature termination codon and nonsense mediated decay resulting in no gene product.

Curation History



Showing 1 to 3 of 3 rows

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