The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_001079804.3:c.763C>T

Version: 1.0

CA401363371

984801 (ClinVar)

Gene: GAA (HGNC:2548)
Condition: glycogen storage disease II (MONDO:0009290)
Inheritance Mode: Autosomal recessive inheritance
UUID: 24039e0f-56fe-4560-913a-4fc9c4967106
Approved on: 2020/6/16
Published on: 2020/11/11

HGVS expressions

NM_001079804.3:c.763C>T
NC_000017.11:g.80107627C>T
CM000679.2:g.80107627C>T
NC_000017.10:g.78081426C>T
CM000679.1:g.78081426C>T
NC_000017.9:g.75696021C>T
NG_009822.1:g.11072C>T
ENST00000570803.6:c.763C>T
ENST00000572080.2:c.763C>T
ENST00000577106.6:c.763C>T
ENST00000302262.8:c.763C>T
ENST00000302262.7:c.763C>T
ENST00000390015.7:c.763C>T
ENST00000570803.5:c.763C>T
NM_000152.3:c.763C>T
NM_001079803.1:c.763C>T
NM_001079804.1:c.763C>T
NM_000152.4:c.763C>T
NM_001079803.2:c.763C>T
NM_001079804.2:c.763C>T
NM_000152.5:c.763C>T
NM_001079803.3:c.763C>T

Pathogenic

Met criteria codes 3
PVS1 PM2 PP4

Not Met criteria codes 1
PM3

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.763C>T (p.Gln255Ter), is a nonsense variant that is predicted to result in nonsense medicated decay and lack of gene product, meeting PVS1. The variant is absent in gnomAD v2.1.1, meeting PM2. It has been reported in trans with c.670C>T (p.Arg224Trp) in an individual with infantile-onset Pompe disease who meets the ClinGen LSD VCEP's specifications for PP4 (PMID 25026126). The in trans data from this patient was used in the assessment of p.Arg224Trp, and was not included here in order to avoid circular logic. It was also found in a heterozygote, identified by newborn screening (PMID 23430949). 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 criteria applied, as specified by the ClinGen LSD VCEP: PVS1, PM2, PP4.

Met criteria codes

PVS1	✔	This is a nonsense variant which is predicted to result in nonsense mediated decay and lack of gene product, meeting PVS1.
PM2	✔	This variant is absent in gnomAD v2.1.1, meeting PM2.
PP4	✔	One individual with this variant has been reported with <1% residual GAA activity (PMID 25026126), meeting PP4.

Not Met criteria codes

PM3	✖	This variant has been reported in trans with c.670C>T (p.Arg224Trp) in an individual with infantile-onset Pompe disease who meets the ClinGen LSD VCEP's specifications for PP4 (PMID 25026126). The in trans data from this patient was used in the assessment of p.Arg224Trp, and was not included here in order to avoid circular logic. Therefore, PM3 is not met based on currently available evidence.

PubMed:23430949
PubMed:25026126

Curation History

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