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.1848dup

Version: 1.0

CA658795267

1710193 (ClinVar)

Gene: GAA (HGNC:2548)
Condition: glycogen storage disease II (MONDO:0009290)
Inheritance Mode: Autosomal recessive inheritance
UUID: 7e1ef8dd-eb14-4dab-87ce-7bbcdff6c6bf
Approved on: 2022/9/6
Published on: 2022/9/19

HGVS expressions

NM_001079804.3:c.1848dup
NC_000017.11:g.80112671dup
CM000679.2:g.80112671dup
NC_000017.10:g.78086470dup
CM000679.1:g.78086470dup
NC_000017.9:g.75701065dup
NG_009822.1:g.16116dup
ENST00000570803.6:c.1848dup
ENST00000572080.2:c.1848dup
ENST00000577106.6:c.1848dup
ENST00000302262.8:c.1848dup
ENST00000302262.7:c.1848dup
ENST00000390015.7:c.1848dup
ENST00000570716.1:n.288dup
ENST00000572080.1:c.236dup
ENST00000572803.1:n.462dup
NM_000152.3:c.1848dup
NM_001079803.1:c.1848dup
NM_001079804.1:c.1848dup
NM_000152.4:c.1848dup
NM_001079803.2:c.1848dup
NM_001079804.2:c.1848dup
NM_000152.5:c.1848dup
NM_001079803.3:c.1848dup

Pathogenic

Met criteria codes 3

PM2_Supporting PVS1 PP4_Moderate

Not Met criteria codes 1

PM3

Evidence Links 0

Expert Panel

Lysosomal Diseases VCEP

Criteria Specification Information

Criteria Specification: *ClinGen Lysosomal Storage Disorders Variant Curation Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 2*
PDF
Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Lysosomal Diseases VCEP

The NM_000152.5c.1848dup in GAA is a frameshift variant predicted to cause a premature stop codon (p.Val617ArgfsTer19), leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). One patient with the variant has been reported who has infantile onset Pompe disease, <1% GAA activity in skin fibroblasts, and is on enzyme replacement therapy (PMID: 22252923, personal communication with first author) (PP4_Moderate). This patient is compound heterozygous, phase unknown, for c.1832G>A (p.Gly611Asp) (PMID: 22252923, personal communication with first author). The allelic data from this patient was used in the evaluation of c.1832G>A (p.Gly611Asp) and is not included here to avoid circular logic. The variant is absent in gnomAD v2.1.1 (PM2_Supporting). 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 met, as specified by the ClinGen LSD VCEP (Specifications Version 2.0): PVS1, PP4_Moderate, PM2_Supporting.

Met criteria codes

PM2_Supporting	✔	The variant is absent in gnomAD v2.1.1 (PM2_Supporting).
PVS1	✔	The NM_000152.5c.1848dup in GAA is a frameshift variant predicted to cause a premature stop codon (p.Val617ArgfsTer19), leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).
PP4_Moderate	✔	One patient with the variant has been reported who has infantile onset Pompe disease, <1% GAA activity in skin fibroblasts and is on enzyme replacement therapy (PMID: 22252923, personal communication with first author) (PP4_Moderate).

Not Met criteria codes

PM3	✖	The variant has been identified in one patient in compound heterozygosity, phase unknown, with c.1832G>A (p.Gly611Asp) (PMID: 22252923, personal communication with first author). The allelic data from this patient was used in the evaluation of c.1832G>A (p.Gly611Asp) and is not included here to avoid circular logic.

Curation History

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