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_000152.5(GAA):c.934del (p.Leu312fs)

Version: 2.0

CA10604123

282254 (ClinVar)

Gene: GAA (HGNC:2548)
Condition: glycogen storage disease II (MONDO:0009290)
Inheritance Mode: Autosomal recessive inheritance
UUID: a8280db4-ba7e-4d75-80c0-a8279ea96720
Approved on: 2023/6/27
Published on: 2023/9/5

HGVS expressions

NM_000152.5:c.934del
NM_000152.5(GAA):c.934del (p.Leu312fs)
NC_000017.11:g.80107875del
CM000679.2:g.80107875del
NC_000017.10:g.78081674del
CM000679.1:g.78081674del
NC_000017.9:g.75696269del
NG_009822.1:g.11320del
ENST00000570803.6:c.934del
ENST00000572080.2:c.934del
ENST00000577106.6:c.934del
ENST00000302262.8:c.934del
ENST00000302262.7:c.934del
ENST00000390015.7:c.934del
NM_000152.3:c.934del
NM_001079803.1:c.934del
NM_001079804.1:c.934del
NM_000152.4:c.934del
NM_001079803.2:c.934del
NM_001079804.2:c.934del
NM_001079803.3:c.934del
NM_001079804.3:c.934del

Pathogenic

Met criteria codes 3

PVS1 PP4_Moderate PM2_Supporting

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_000152.5:c.934del (p.Leu312CysfsTer2) variant in GAA is a frameshift variant that is predicted to cause a premature stop codon in exon 5, leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). One patient with this variant and deficient GAA activity in dried blood spots has been reported (clinical laboratory data) (PP4_Moderate). This individual is compound heterozygous for the variant and c.1219T>C (p.Tyr407His). The allelic data from this patient will be used in the assessment of p.Tyr407His and is not included here to avoid circular logic. The variant is not in gnomAD v2.1.1 (PM2_Supporting). There is a ClinVar entry for this variant (Variation ID: 282254). In summary, this variant meets the criteria to be classified as pathogenic for Pompe disease. ACMG/AMP GAA-specific criteria applied, as specified by the ClinGen Lysosomal Diseases VCEP (Specifications Version 2.0): PVS1, PP4_Moderate, PM2_Supporting. (Classification approved by the ClinGen Lysosomal Diseases VCEP, June 27, 2023)

Met criteria codes

PVS1	✔	The NM_000152.5:c.934del (p.Leu312CysfsTer2) variant in GAA is a frameshift variant that is predicted to cause a premature stop codon in biologically-relevant-exon 5/20, leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).
PP4_Moderate	✔	One patient with this variant and deficient GAA activity in dried blood spots has been reported (clinical laboratory data) (PP4_Moderate).
PM2_Supporting	✔	This variant is not in gnomAD v2.1.1.

Not Met criteria codes

PM3	✖	One patient is compound heterozygous or the variant and c.1219T>C (p.Tyr407His); phase unknown. The allelic data from this patient will be used in the assessment of p.Tyr407His and is not included here to avoid circular logic. Therefore, PM3 is not met at the current time.

Curation History

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