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.1082C>G (p.Pro361Arg)

Version: 2.0

CA10606426

289367 (ClinVar)

Gene: GAA (HGNC:2548)
Condition: glycogen storage disease II (MONDO:0009290)
Inheritance Mode: Autosomal recessive inheritance
UUID: 47ad62d9-cb93-4314-abed-a72383fae6e2
Approved on: 2026/7/10
Published on: 2026/7/21

HGVS expressions

NM_000152.5:c.1082C>G
NM_000152.5(GAA):c.1082C>G (p.Pro361Arg)
NC_000017.11:g.80108495C>G
CM000679.2:g.80108495C>G
NC_000017.10:g.78082294C>G
CM000679.1:g.78082294C>G
NC_000017.9:g.75696889C>G
NG_009822.1:g.11940C>G
ENST00000570803.6:c.1082C>G
ENST00000572080.2:c.1082C>G
ENST00000577106.6:c.1082C>G
ENST00000302262.8:c.1082C>G
ENST00000302262.7:c.1082C>G
ENST00000390015.7:c.1082C>G
NM_000152.3:c.1082C>G
NM_001079803.1:c.1082C>G
NM_001079804.1:c.1082C>G
NM_000152.4:c.1082C>G
NM_001079803.2:c.1082C>G
NM_001079804.2:c.1082C>G
NM_001079803.3:c.1082C>G
NM_001079804.3:c.1082C>G

Pathogenic

Met criteria codes 5

PM5 PP4_Moderate PP3 PM3_Strong PM2_Supporting

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 2.0*
PDF
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Lysosomal Diseases VCEP

The NM_000152.5:c.1082C>G variant in GAA is a missense variant predicted to cause substitution of proline by arginine at amino acid 361 (p.Pro361Arg). At least four individuals with this variant have been reported to have a diagnosis of late-onset Pompe disease (LOPD), with at least two with documented GAA deficiency (PMID: 30312517, 32012848, 42131243) (PP4_Moderate). Of those individuals, three were compound heterozygous for this variant and a pathogenic variant, c.-32-13T>G (PMIDs: 30312517, 32012848) or c.2238C>G (p.Trp746Cys) (PMID: 42131243), phase unknown in all cases. One individual was homozygous for this variant (PMID: 42131243) (PM3_Strong). The highest population minor allele frequency in gnomAD v4.1.1 is 8.475e-7 (1/1179974 alleles) in the European (non-Finnish) population, which is lower than the ClinGen Lysosomal Diseases VCEP's threshold for PM2_Supporting (<0.001), meeting this criterion (PM2_Supporting). The computational predictor REVEL gives a score of 0.945 which is above the threshold of 0.7, evidence that correlates with impact to GAA function (PP3). Another missense variant (c.1082C>T (p.Pro361Leu)) (ClinVar Variation ID: 403712) in the same codon has been classified as pathogenic for Pompe disease by the ClinGen Lysosomal Diseases VCEP (PM5). There is a ClinVar entry for this variant (Variation ID: 289367). In summary, this variant meets the criteria to be classified as pathogenic for Pompe disease based on the GAA-specific ACMG/AMP criteria applied, as specified by the ClinGen Lysosomal Diseases Variant Curation Expert Panel (Specifications Version 2.0): PM2_Supporting, PM3_Strong, PM5, PP3, PP4_Moderate. (Classification approved by the ClinGen Lysosomal Diseases Variant Curation Expert Panel on July 10, 2026)

Met criteria codes

PM5	✓	Another missense variant (c.1082C>T (p.Pro361Leu)) (ClinVar Variation ID: 403712) in the same codon has been classified as pathogenic for Pompe disease by the ClinGen Lysosomal Diseases VCEP (PM5).
PP4_Moderate	✓	At least four individuals with this variant have been reported to have a diagnosis of late-onset Pompe disease (LOPD), with at least two with documented GAA deficiency (PMID: 30312517, 32012848, 42131243) (PP4_Moderate).
PP3	✓	The computational predictor REVEL gives a score of 0.945 which is above the threshold of 0.7, evidence that correlates with impact to GAA function (PP3).
PM3_Strong	✓	This variant has been detected in at least four individuals with late-onset Pompe disease. Of those individuals, three were compound heterozygous for this variant and a pathogenic variant, c.-32-13T>G (PMIDs: 30312517, 32012848) or c.2238C>G (p.Trp746Cys) (PMID: 42131243), phase unknown in all cases (1.5 points). One individual was homozygous for this variant (PMID: 42131243) (0.5 points) (total of 2.0 points) (PM3_Strong).
PM2_Supporting	✓	The highest population minor allele frequency in gnomAD v4.1.1 is 8.475e-7 (1/1179974 alleles) in the European (non-Finnish) population, which is lower than the ClinGen Lysosomal Diseases VCEP's threshold for PM2_Supporting (<0.001), meeting this criterion (PM2_Supporting).

Curation History

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