

Variant: *NM_000156.6(GAMT):c.189G>C (p.Arg63=)*

Version: 2.0

CA9043767 [↗](#)

288963 (ClinVar) [↗](#)

Gene: GAMT ([HGNC:2593](#))

Condition: guanidinoacetate methyltransferase deficiency
([MONDO:0012999](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: 2422ca9a-f7d4-4b9c-b558-d9b41e25a039

Approved on: 2025/5/20

Published on: 2025/5/20

HGVS expressions

NM_000156.6(GAMT):c.189G>C (p.Arg63=)

NM_000156.6:c.189G>C

NC_000019.10:g.1399931C>G

CM000681.2:g.1399931C>G

NC_000019.9:g.1399930C>G

CM000681.1:g.1399930C>G

NC_000019.8:g.1350930C>G

NG_009785.1:g.6623G>C

ENST00000252288.8:c.189G>C

ENST00000447102.8:c.189G>C

ENST00000640762.1:c.120G>C

ENST00000252288.6:c.189G>C

ENST00000447102.7:c.189G>C

NM_000156.5:c.189G>C

NM_138924.2:c.189G>C

NM_138924.3:c.189G>C

Likely Benign

Met criteria codes **2**

BP7

BP4

Not Met criteria codes **2**

BS1

PM2

Evidence Links **0**

Expert Panel

Cerebral Creatine Deficiency Syndromes VCEP [↗](#)

Criteria Specification Information

[↗](#) **Criteria Specification:** *ClinGen Cerebral Creatine Deficiency Syndromes Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GAMT Version 2.0.0*

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Cerebral Creatine Deficiency Syndromes VCEP

The NM_000156.6:c.189G>C (p.Arg63=) variant in GAMT is a synonymous (silent) variant that is not predicted by SpliceAI to impact splicing. In addition, it occurs at a nucleotide that is not conserved as shown by phyloP (score -1.308) (BP4, BP7). To our knowledge, this variant has not been reported among individuals with GAMT deficiency and results of functional studies are unavailable. The highest population minor allele frequency in gnomAD v4.1.0 is 0.0004955 (3/6054) in the Middle Eastern population. This is higher than the ClinGen CCDS VCEP's threshold for PM2_Supporting (<0.0004), and lower than the threshold for BS1 (>0.001). Therefore, no population criteria are met. There is a ClinVar entry for this variant (Variation ID: 288963). In summary, this variant meets the criteria to be classified as likely benign for GAMT deficiency based on the ACMG/AMP criteria applied, as specified by the ClinGen Cerebral Creatine Deficiency Syndromes Variant Curation Expert Panel (Specifications Version 2.0.0): BP4, BP7. (Classification approved by the ClinGen Cerebral Creatine Deficiency Syndromes Variant Curation Expert Panel on May 20, 2025).

Met criteria codes

BP7			The NM_000156.6:c.189G>C (p.Arg63=) variant in GAMT is a synonymous (silent) variant that is not predicted by SpliceAI to impact splicing. In addition, it occurs at a nucleotide that is not conserved as shown by phyloP (score -1.308) (BP7).
BP4			No impact on splicing predicted by SpliceAI (all scores <0.1) (BP4).

Not Met criteria codes

BS1			The highest population minor allele frequency in gnomAD v4.1.0 is 0.0004955 (3/6054) in the Middle Eastern population. This is higher than the ClinGen CCDS VCEP's threshold for PM2_Supporting (<0.0004), and lower than the threshold for BS1 (>0.001). Therefore, no population criteria are met.
PM2			The highest population minor allele frequency in gnomAD v4.1.0 is 0.0004955 (3/6054) in the Middle Eastern population. This is higher than the ClinGen CCDS VCEP's threshold for PM2_Supporting (<0.0004), and lower than the threshold for BS1 (>0.001). Therefore, no population criteria are met.

Curation History



 ▾

 ▾

Showing 1 to 2 of 2 rows

--

