

Variant: *NM_000156.6(GAMT):c.225G>A (p.Ala75=)*

Version: 1.0

CA291013 [↗](#)

137433 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 6c5ec147-018b-46b8-93a3-24a7fdde31b5

Approved on: 2023/3/9

Published on: 2023/3/29

HGVS expressions

NM_000156.6(GAMT):c.225G>A (p.Ala75=)

NM_000156.6:c.225G>A

NC_000019.10:g.1399895C>T

CM000681.2:g.1399895C>T

NC_000019.9:g.1399894C>T

CM000681.1:g.1399894C>T

NC_000019.8:g.1350894C>T

NG_009785.1:g.6659G>A

ENST00000252288.8:c.225G>A

ENST00000447102.8:c.225G>A

ENST00000640762.1:c.156G>A

ENST00000252288.6:c.225G>A

ENST00000447102.7:c.225G>A

NM_000156.5:c.225G>A

NM_138924.2:c.225G>A

NM_138924.3:c.225G>A

Likely Benign

Met criteria codes **2**

BS1

BP4

Not Met criteria codes **1**

BP7

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 1.1.0*

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

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

Evidence submitted by expert panel

Cerebral Creatine Deficiency Syndromes VCEP

The NM_000156.6(GAMT):c.225G>A (p.Ala75=) variant is a synonymous variant for which splicing prediction algorithms (SpliceAI, varSEAK) predict no impact to the splice consensus sequence nor the creation of a new splice site (BP4); however, the residue altered (Ala75) is conserved through zebrafish. Thus, BP7 is not met. The highest population minor allele frequency in gnomAD v2.1.1 is 0.00117 (21/17954 alleles) in the East Asian population, which is higher than the ClinGen CCDS VCEP’s threshold for BS1 (>0.001), and therefore meets this criterion (BS1). There is a ClinVar entry for this variant (Variation ID: 137433). In summary, this variant meets the crietria to be classified as likely benign for GAMT deficiency. GAMT-specific criteria applied, as specified by the ClinGen Cerebral Creatine Deficiency Syndromes Variant Curation Expert Panel (CCDS VCEP): BS1, BP4. (Classification approved by the ClinGen CCDS VCEP on March 9, 2023).

Met criteria codes

BS1

i

✓

The highest population minor allele frequency in gnomAD v2.1.1 is 0.00117 (21/17954 alleles) in the East Asian population, which is higher than the ClinGen CCDS VCEP’s threshold for BS1 (>0.001), and therefore meets this criterion (BS1).

BP4

i

✓

No impact on splicing predicted by SpliceAI (BP4).

Not Met criteria codes

BP7

i

✗

Synonymous (silent) variant for which splicing prediction algorithms (SpliceAI, varSEAK) predict no impact to the splice consensus sequence nor the creation of a new splice site; however, the residue altered (Ala75) is conserved through zebrafish.

Curation History [↗](#)

⛶

⌵

⌵

⬇

⬇

Showing 1 to 1 of 1 rows

--

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.