

Variant: NM\_138924.3:c.212T>G

Version: 1.0

CA402997146 [↗](#)

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

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

**Inheritance Mode:** Autosomal recessive inheritance

**UUID:** f30e3f4a-26c4-4512-b76c-65fd307746c9

**Approved on:** 2025/10/8

**Published on:** 2025/10/8

### HGVS expressions

**NM\_138924.3:c.212T>G**

NC\_000019.10:g.1399908A>C

CM000681.2:g.1399908A>C

NC\_000019.9:g.1399907A>C

CM000681.1:g.1399907A>C

NC\_000019.8:g.1350907A>C

NG\_009785.1:g.6646T>G

ENST00000252288.8:c.212T>G

ENST00000447102.8:c.212T>G

ENST00000640762.1:c.143T>G

ENST00000252288.6:c.212T>G

ENST00000447102.7:c.212T>G

NM\_000156.5:c.212T>G

NM\_138924.2:c.212T>G

NM\_000156.6:c.212T>G

**Likely Pathogenic**

**Met criteria codes** **4**

PP3\_Moderate

PM3

PP4\_Strong

PM2\_Supporting

**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.212T>G variant in GAMT is predicted to result in the substitution of methionine by arginine at amino acid 71 (p.Met71Arg). A Chinese male with clinical features consistent with GAMT deficiency has been reported who has elevated urine

guanidinoacetate, low urine creatine, and decreased creatine on brain MRS. This patient is compound heterozygous for the variant and another variant in GAMT that has been classified as pathogenic for GAMT deficiency by the ClinGen CCDS VCEP, c.418\_419del. The variants were confirmed to be in trans by parental testing (Journal of Clinical Pediatrics, 2024 Vol.42 No.12 1039-1046 (article in Chinese), link to article - <https://jcp.xinhuamed.com.cn/EN/10.12372/jcp.2024.24e0300>) (PP4\_Strong, PM3). The computational predictor REVEL gives a score of 0.931 which is in the range of 0.773-0.932, evidence that correlates with impact to GAMT function at the moderate level (PMID: 36413997) (PP3\_Moderate). The variant is absent in gnomAD v4.1.0. (PM2\_Supporting). In summary, this variant meets the criteria to be classified as likely pathogenic for GAMT deficiency. GAMT-specific ACMG/AMP criteria applied, as specified by the ClinGen Cerebral Creatine Deficiency Syndromes Variant Curation Expert Panel (Specifications Version 2.0.0): PP4\_Strong, PM3, PP4\_Moderate, PM2\_Supporting (Classification approved by the ClinGen Cerebral Creatine Deficiency Syndromes Variant Curation Expert Panel on October 8, 2025)

Met criteria codes

|                |                                                                                     |                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
|----------------|-------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| PP3_Moderate   |    |    | The computational predictor REVEL gives a score of 0.931 which is in the range of 0.773-0.932, evidence that correlates with impact to GAMT function at the moderate level (PMID: 36413997) (PP3_Moderate).                                                                                                                                                                                                                                                                                                 |
| PM3            |    |    | One patient is compound heterozygous for the variant and another variant in GAMT that has been classified as pathogenic for GAMT deficiency by the ClinGen CCDS VCEP, c.418_419del. The variants were confirmed to be in trans by parental testing (1 point) (Journal of Clinical Pediatrics, 2024 Vol.42 No.12 1039-1046 (article in Chinese), link to article - <a href="https://jcp.xinhuamed.com.cn/EN/10.12372/jcp.2024.24e0300">https://jcp.xinhuamed.com.cn/EN/10.12372/jcp.2024.24e0300</a> ) (PM3) |
| PP4_Strong     |    |    | A Chinese male with clinical features consistent with GAMT deficiency has been reported who has elevated urine guanidinoacetate, low urine creatine, and decreased creatine on brain MRS (Journal of Clinical Pediatrics, 2024 Vol.42 No.12 1039-1046 (article in Chinese), link to article - <a href="https://jcp.xinhuamed.com.cn/EN/10.12372/jcp.2024.24e0300">https://jcp.xinhuamed.com.cn/EN/10.12372/jcp.2024.24e0300</a> ) (PP4_Strong).                                                             |
| PM2_Supporting |  |  | The variant is absent in gnomAD v4.1.0. (PM2_Supporting)                                                                                                                                                                                                                                                                                                                                                                                                                                                    |

Curation History 

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