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Variant: NM_001482.3(GATM):c.958C>T (p.Pro320Ser)

Version: 1.0

CA392257504

917493 (ClinVar)

Gene: GATM (HGNC:2628)
Condition: AGAT deficiency (MONDO:0012996)
Inheritance Mode: Autosomal recessive inheritance
UUID: 41a797cf-2a85-42d5-89f7-0c381f132b7d
Approved on: 2023/1/24
Published on: 2023/1/25

HGVS expressions

NM_001482.3:c.958C>T
NM_001482.3(GATM):c.958C>T (p.Pro320Ser)
NC_000015.10:g.45366066G>A
CM000677.2:g.45366066G>A
NC_000015.9:g.45658264G>A
CM000677.1:g.45658264G>A
NC_000015.8:g.43445556G>A
NG_011674.1:g.17717C>T
NG_011674.2:g.41252C>T
ENST00000396659.8:c.958C>T
ENST00000674905.1:c.958C>T
ENST00000675158.1:c.958C>T
ENST00000675323.1:c.958C>T
ENST00000675701.1:c.898C>T
ENST00000675974.1:n.1049C>T
ENST00000676090.1:c.*1689C>T
ENST00000396659.7:c.958C>T
ENST00000558336.5:c.958C>T
ENST00000558362.5:n.2614C>T
ENST00000558916.1:n.856C>T
ENST00000561376.1:n.5C>T
NM_001482.2:c.958C>T
NM_001321015.1:c.571C>T
NM_001321015.2:c.571C>T

Uncertain Significance

Met criteria codes 1

PM2_Supporting

Not Met criteria codes 2

BP4 PP3

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 GATM 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_001482.3:c.958C>T variant in GATM is a missense variant that is predicted to result in the substitution of proline by serine at amino acid 320 (p.Pro320Ser). It is absent in gnomAD v2.1.1. (PM2_Supporting). The computational predictor REVEL gives a score of 0.356 which is neither above nor below the thresholds predicting a damaging (>0.75) or benign (<0.15) impact on AGAT function. To our knowledge, this variant has not been reported in an individual with phenotypic features of AGAT deficiency. It has been reported as a single heterozygous variant segregating in a family autosomal dominant renal Fanconi syndrome and kidney failure (PMID: 29654216). However, classification with respect to this alternative disorder is outside the scope of this curation. There is a ClinVar entry for this variant (Variation ID: 917493). In summary, this variant meets the criteria to be classified as a variant of uncertain significance for AGAT deficiency. GATM-specific ACMG/AMP criteria applied, as specified by the ClinGen CCDS VCEP (Specifications Version 1.1.0): PM2_Supporting. (Classification approved by the ClinGen CCDS VCEP on January 24, 2023).

Met criteria codes

PM2_Supporting	✔	Absent in gnomAD v2.1.1.

Not Met criteria codes

BP4	✖	The computational predictor REVEL gives a score of 0.356 which is neither above nor below the thresholds predicting a damaging (>0.75) or benign (<0.15) impact on AGAT function.
PP3	✖	The computational predictor REVEL gives a score of 0.356 which is neither above nor below the thresholds predicting a damaging (>0.75) or benign (<0.15) impact on AGAT function.

Curation History

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