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Variant: NM_001142805.2:c.1426C>T

Version: 1.0

CA415087684

2583093 (ClinVar)

Gene: SLC6A8 (HGNC:6535)
Condition: creatine transporter deficiency (MONDO:0010305)
Inheritance Mode: X-linked inheritance
UUID: ffff00ed-7b84-47f8-b970-fb01172a5121
Approved on: 2023/8/7
Published on: 2023/8/24

HGVS expressions

NM_001142805.2:c.1426C>T
NC_000023.11:g.153694407C>T
CM000685.2:g.153694407C>T
NC_000023.10:g.152959862C>T
CM000685.1:g.152959862C>T
NC_000023.9:g.152613056C>T
NG_012016.1:g.11111C>T
NG_012016.2:g.11111C>T
ENST00000253122.10:c.1456C>T
ENST00000253122.9:c.1456C>T
ENST00000413787.1:c.385C>T
ENST00000430077.6:c.1111C>T
ENST00000442457.1:c.510C>T
ENST00000485324.1:n.1677C>T
NM_001142805.1:c.1426C>T
NM_001142806.1:c.1111C>T
NM_005629.3:c.1456C>T
NM_005629.4:c.1456C>T

Pathogenic

Met criteria codes 3

PVS1 PP4_Strong PM2_Supporting

Not Met criteria codes 2

PS4 PP1

Evidence Links 0

Expert Panel

Cerebral Creatine Deficiency Syndromes VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Cerebral Creatine Deficiency Syndromes VCEP

The NM_005629.4:c.1456C>T (p.Gln486Ter) variant in SLC6A8 is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 10/13 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). This variant has been reported in two monozygotic male twins with developmental delay, elevated urine

creatine/creatinine, and absent creatine peak on brain MRS (PMID: 22196490) and was inherited from their mother, who had intellectual disability (PP4_Strong). The variant is absent in gnomAD v2.1.1. (PM2_Supporting). There is no ClinVar entry for this variant. In summary, this variant meets criteria to be classified as pathogenic for creatine transporter deficiency. SLC6A8-specific criteria applied, as specified by the ClinGen CCDS VCEP (Specifications Version 1.1.0): PVS1, PP4_Strong, PM2_Supporting. (Classification approved by the ClinGen CCDS VCEP, August 7, 2023)

Met criteria codes

PVS1	✔	The NM_005629.4:c.1456C>T (p.Gln486Ter) variant in SLC6A8 is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 10/13 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).
PP4_Strong	✔	PMID: 22196490: male twins had 'urinary creatine/creatinine ratio was increased (2.24 and 1.84, respectively; normal range, 0.04-0.56), with a normal level of guanidinoacetic acid (42 and 40 µmol/mmol creatinine, respectively; normal range, 18-130 µmol/mmol creatinine) and a low level of creatinine plasma (2.2 and 1.84 mmol/L, respectively; normal range, 5-19.5 mmol/L)' and absent creatine peak on brain MRS
PM2_Supporting	✔	The variant is absent in gnomAD v2.1.1. (PM2_Supporting).

Not Met criteria codes

PS4	✖	PMID: 22196490: 2 affected male monozygotic twins, inherited from het mom who had ID (1 aff seg); not counted for PS4 b/c counted for PP4
PP1	✖	PMID: 22196490: 2 affected male monozygotic twins, inherited from het mom who had ID (1 aff seg)

Curation History

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