

Variant: *NM_001142805.2:c.1391A>G*

Version: 1.0

CA415087450 [↗](#)

2583103 (ClinVar) [↗](#)

Gene: SLC6A8 ([HGNC:6535](#))

Condition: creatine transporter deficiency ([MONDO:0010305](#))

Inheritance Mode: X-linked inheritance

UUID: 152785aa-baf5-4eb0-8811-155c7ee159f5

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Published on: 2023/8/24

HGVS expressions

NM_001142805.2:c.1391A>G

NC_000023.11:g.153694372A>G

CM000685.2:g.153694372A>G

NC_000023.10:g.152959827A>G

CM000685.1:g.152959827A>G

NC_000023.9:g.152613021A>G

NG_012016.1:g.11076A>G

NG_012016.2:g.11076A>G

ENST00000253122.10:c.1421A>G

ENST00000253122.9:c.1421A>G

ENST00000413787.1:c.350A>G

ENST00000430077.6:c.1076A>G

ENST00000442457.1:c.475A>G

ENST00000485324.1:n.1642A>G

NM_001142805.1:c.1391A>G

NM_001142806.1:c.1076A>G

NM_005629.3:c.1421A>G

NM_005629.4:c.1421A>G

Likely Pathogenic

Met criteria codes **3**

PM2_Supporting

PP4_Strong

PP3

Not Met criteria codes **1**

PS4

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.1421A>G variant in SLC6A8 is a missense variant that is predicted to result in the substitution of aspartate by glycine at amino acid 474 (p.Asp474Gly). This variant has been reported in one (hemizygous) male proband with mild intellectual disability, elevated urine creatine/creatinine, and absent creatine peak on brain MRS (PMID: 29435807) (PP4_Strong). The variant is absent in

gnomAD v2.1.1.1. (PM2_Supporting). The computational predictor REVEL gives a score of 0.971 which is above the threshold of 0.75, evidence that correlates with impact to SLC6A8 function (PP3). There is no ClinVar entry for this variant. In summary, this variant meets criteria to be classified as likely pathogenic for creatine transporter deficiency. SLC6A8-specific criteria applied, as specified by the ClinGen CCDS VCEP (Specifications Version 1.1.0): PP4_Strong, PP3, PM2_Supporting. (Classification approved by the ClinGen CCDS VCEP, August 7, 2023)

Met criteria codes

PM2_Supporting			The variant is absent in gnomAD v2.1.1. (PM2_Supporting).
PP4_Strong			PMID: 29435807: 1 hemizygous male proband with elevated urine creatine/creatinine; absent creatine peak on brain MRS w/full SLC6A8 gene sequencing (PP4_Strong)
PP3			The computational predictor REVEL gives a score of 0.971 which is above the threshold of 0.75, evidence that correlates with impact to SLC6A8 function (PP3).

Not Met criteria codes

PS4			Patient 3: 4y M w/Mild ID, occasional febrile seizures; not counted for PS4 as proband counted for PP4 (PMID: 29435807)
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Curation History

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