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Variant: NM_001323289.2(CDKL5):c.2842C>T (p.Arg948Ter)

Version: 1.0

CA412369187

489299 (ClinVar)

Gene: CDKL5 (HGNC:6792)
Condition: CDKL5 disorder (MONDO:0100039)
Inheritance Mode: X-linked inheritance
UUID: 6f4ef230-8fe8-4a41-9161-47767f6eabf7
Approved on: 2022/9/1
Published on: 2022/9/6

HGVS expressions

NM_001323289.2:c.2842C>T
NM_001323289.2(CDKL5):c.2842C>T (p.Arg948Ter)
NC_000023.11:g.18628716C>T
CM000685.2:g.18628716C>T
NC_000023.10:g.18646836C>T
CM000685.1:g.18646836C>T
NC_000023.9:g.18556757C>T
NG_008475.1:g.208112C>T
ENST00000623535.2:c.2842C>T
ENST00000674046.1:c.2965C>T
ENST00000379989.6:c.2713+129C>T
ENST00000379996.7:c.2713+129C>T
ENST00000623535.1:c.2842C>T
NM_001037343.1:c.2713+129C>T
NM_003159.2:c.2713+129C>T
NM_001323289.1:c.2842C>T
NM_001037343.2:c.2713+129C>T
NM_003159.3:c.2713+129C>T

Pathogenic

Met criteria codes 3

PS2_Very Strong | PVS1 | PM2_Supporting

Evidence Links 0

Expert Panel

Rett and Angelman-like Disorders VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Rett and Angelman-like Disorders VCEP

The p.Arg948Ter variant in CDKL5 is absent from gnomAD (PM2_Supporting). The p.Arg948Ter variant in CDKL5 has been reported as a de novo occurrence (biological parentage confirmed) in at least 2 individuals with features of CDKL5-associated disorder (PMID 32366967; internal database) (PS2_Very Strong). The p.Arg948Ter variant in CDKL5 is predicted to cause a premature stop codon that leads to a truncated or absent protein in a gene where loss-of-function is an established mechanism. While loss-of-function variants are commonly

observed in affected individuals in this gene, there is a paucity of these variants in this region of the gene to date (PVS1). In summary, the p.Arg948Ter variant in CDKL5 is classified as pathogenic for CDKL5 disorder based on the ACMG/AMP criteria (PM2_Supporting, PS2_Very Strong, PVS1).

Met criteria codes

PS2_Very Strong	✔	The p.Arg948Ter variant in CDKL5 has been reported as a de novo occurrence (biological parentage confirmed) in at least 2 individuals with features of CDKL5-associated disorder (PMID 32366967; internal database)
PVS1	✔	The p.Arg948Ter variant in CDKL5 is predicted to cause a premature stop codon that leads to a truncated or absent protein in a gene where loss-of-function is an established mechanism. While loss-of-function variants are commonly observed in affected individuals in this gene, there is a paucity of these variants in this region of the gene to date (PVS1)
PM2_Supporting	✔	The p.Arg948Ter variant in CDKL5 is absent from gnomAD

Curation History

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