The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_003159.2(CDKL5):c.513C>A (p.Tyr171Ter)

Version: 1.0

CA171644

143822 (ClinVar)

Gene: CDKL5 (HGNC:6792)
Condition: CDKL5 disorder (MONDO:0100039)
Inheritance Mode: X-linked inheritance (dominant (HP:0001423))
UUID: 97f599c7-1e02-4611-ad6e-421907114ae2
Approved on: 2021/3/9
Published on: 2021/5/7

HGVS expressions

NM_003159.2(CDKL5):c.513C>A (p.Tyr171Ter)
NM_003159.2:c.513C>A
NC_000023.11:g.18584312C>A
CM000685.2:g.18584312C>A
NC_000023.10:g.18602432C>A
CM000685.1:g.18602432C>A
NC_000023.9:g.18512353C>A
NG_008475.1:g.163708C>A
ENST00000623535.2:c.513C>A
ENST00000635828.1:c.513C>A
ENST00000637881.1:c.513C>A
ENST00000674046.1:c.513C>A
ENST00000379989.6:c.513C>A
ENST00000379996.7:c.513C>A
ENST00000463994.4:c.513C>A
ENST00000623535.1:c.513C>A
NM_001037343.1:c.513C>A
NM_001323289.1:c.513C>A
NM_001323289.2:c.513C>A
NM_001037343.2:c.513C>A
NM_003159.3:c.513C>A

Pathogenic

Met criteria codes 4

PM6 PVS1 PM2_Supporting PS4_Supporting

Evidence Links 1

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.Tyr171* 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. There is significant evidence that loss of this region of the gene is pathogenic (PVS1). The p.Tyr171* variant in CDKL5 has been reported as a de novo occurrence (biological parentage unconfirmed) in an individual with CDKL5 disorder (PMID 23583054) (PM6. This variant has been observed in at least 1 other individual with CDKL5 disorder (ClinVar) (PS4_Supporting). This variant was absent from gnomAD (PM2_ Supporting). In summary, p.Tyr171* variant in CDKL5 is classified as Pathogenic for CDKL5 disorder based on the ACMG/AMP criteria (PVS1, PM6, PM2_Supporting, PS4_Supporting).

Met criteria codes

PM6	The p.Tyr171* variant in CDKL5 occurs in the unconfirmed de novo state in the patient reported in PMID 23583054. The p.Tyr171* variant in CDKL5 occurs in the unconfirmed de novo state in this individual. PubMed:23583054
PVS1	The p.Tyr171* 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.
PM2_Supporting	The p.Tyr171* variant in CDKL5 is absent from gnomAD.
PS4_Supporting	The p.Tyr171* variant has been observed in at least 1 other individual with CDKL5 disorder (PMID 23583054, ClinVar Variation ID 143822). The p.Tyr171* variant was observed in a male individual with CDKL5-related disease (intractable epilepsy, cerebral/cerebellar atrophy, global developmental delay) in the de novo state. PubMed:23583054

Curation History

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