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Variant: NM_001323289.2(CDKL5):c.470C>T (p.Ala157Val)

Version: 1.0

CA279171

217360 (ClinVar)

Gene: CDKL5 (HGNC:6792)
Condition: CDKL5 disorder (MONDO:0100039)
Inheritance Mode: X-linked inheritance
UUID: c746091d-5bd3-4f1a-a94c-7ce585edbb14
Approved on: 2023/4/14
Published on: 2023/6/16

HGVS expressions

NM_001323289.2:c.470C>T
NM_001323289.2(CDKL5):c.470C>T (p.Ala157Val)
NC_000023.11:g.18584269C>T
CM000685.2:g.18584269C>T
NC_000023.10:g.18602389C>T
CM000685.1:g.18602389C>T
NC_000023.9:g.18512310C>T
NG_008475.1:g.163665C>T
ENST00000623535.2:c.470C>T
ENST00000635828.1:c.470C>T
ENST00000637881.1:c.470C>T
ENST00000674046.1:c.470C>T
ENST00000379989.6:c.470C>T
ENST00000379996.7:c.470C>T
ENST00000463994.4:c.470C>T
ENST00000623535.1:c.470C>T
NM_001037343.1:c.470C>T
NM_003159.2:c.470C>T
NM_001323289.1:c.470C>T
NM_001037343.2:c.470C>T
NM_003159.3:c.470C>T

Likely Pathogenic

Met criteria codes 5

PS2 PP3 PM5 PM2_Supporting PS4_Supporting

Not Met criteria codes 1

PP4

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.Ala157Val variant in CDKL5 has been reported as a de novo occurrence (biological parentage confirmed) in an individual with infantile epilepsy (GeneDx Internal Database) (PS2). The p.Ala157Val variant in CDKL5 is absent from gnomAD (PM2_supporting). Computational prediction analysis tools suggests a deleterious impact; however, this information does not predict clinical significance on its own (PP3). The p.Ala157Val variant has been observed in individuals reported to have Rett syndrome or CDKL5 Deficiency disorder, however, additional clinical and segregation information was not provided (PMID: 32472944; 31313283) (PS4_supporting_met, PP4_not met). A pathogenic missense variant (p.Ala157Pro) has been previously identified within this codon which indicates that this residue is critical to the function of the protein (Invitae internal database). In summary, the p.Ala157Val variant in CDKL5 is classified as likely pathogenic for CDKL5-related disorder based on the ACMG/AMP criteria (PS2, PP3, PM2_supporting, PS4_supporting,PM5).

Met criteria codes

PS2	✔	The p.Ala157Val variant in CDKL5 has been reported as a de novo occurrence (biological parentage confirmed) in an individual (GeneDx Internal Database)
PP3	✔	Computational prediction analysis tools suggests a deleterious impact; however, this information does not predict clinical significance on its own
PM5	✔	A pathogenic missense variant (p.Ala157Pro) has been previously identified within this codon which indicates that this residue is critical to the function of the protein (Invitae internal database)
PM2_Supporting	✔	The p.Ala157Val variant in CDKL5 is absent from gnomAD
PS4_Supporting	✔	The p.Ala157Val variant has been observed in at least 2 individuals with neurological disease (PMID 32472944; 31313283)

Not Met criteria codes

PP4	✖	Observed in individuals reported to have Rett syndrome or CDKL5 Deficiency disorder, however, additional clinical and segregation information was not provided (PMID: 32472944; 31313283)

Curation History

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