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Variant: NM_003159.2(CDKL5):c.1247_1248delAG (p.Glu416Valfs)

Version: 1.0

CA235608

189554 (ClinVar)

Gene: CDKL5 (HGNC:6792)
Condition: CDKL5 disorder (MONDO:0100039)
Inheritance Mode: X-linked inheritance (dominant (HP:0001423))
UUID: 933d9c7c-3865-4a89-9a0a-565d7134d1a8
Approved on: 2021/3/26
Published on: 2021/5/17

HGVS expressions

NM_003159.2:c.1247_1248delAG
NM_003159.2:c.1247_1248del
NM_003159.2(CDKL5):c.1247_1248delAG (p.Glu416Valfs)
NC_000023.11:g.18604171_18604172del
CM000685.2:g.18604171_18604172del
NC_000023.10:g.18622291_18622292del
CM000685.1:g.18622291_18622292del
NC_000023.9:g.18532212_18532213del
NG_008475.1:g.183567_183568del
ENST00000623535.2:c.1247_1248del
ENST00000635828.1:c.1247_1248del
ENST00000637881.1:c.1247_1248del
ENST00000674046.1:c.1247_1248del
ENST00000379989.6:c.1247_1248del
ENST00000379996.7:c.1247_1248del
ENST00000463994.4:c.1247_1248del
ENST00000623535.1:c.1247_1248del
NM_001037343.1:c.1247_1248del
NM_001323289.1:c.1247_1248del
NM_001323289.2:c.1247_1248del
NM_001037343.2:c.1247_1248del
NM_003159.3:c.1247_1248del

Pathogenic

Met criteria codes 4

PM6_Strong PS4 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.Glu416Valfs variant in CDKL5 is predicted to cause a premature stop codon that leads to a truncated or absent protein in a gene in which loss-of-function is an established mechanism. There is significant evidence that loss of this region of the gene is pathogenic (PVS1). The p.Glu416Valfs variant has been observed in at least 5 individuals with CDKL5 disease (PMID: 27779742, 27864847, 23064044, ClinVar Variation ID 189554) (PS4). The p.XX variant in GENE has been reported in at least 2 de novo occurrences (biological parentage unconfirmed) in individuals with CDKL5 disorder (PMID XX) (PMID 27779742, 27864847) (PM6_strong). This variant is absent from gnomAD (PM2_supporting). In summary, this variant meets criteria to be classified as pathogenic for CDKL5-associated disorder based on the ACMG/AMP criteria applied (PVS1, PS4, PM6_strong, PM2_supporting).

Met criteria codes

PM6_Strong	✔	The p.(Glu416Valfs*2) variant in CDKL5 has been reported in at least 2 unconfirmed de novo occurrences in individuals with early onset epileptic encephalopathy (PMID 27779742, PMID 27864847).
PS4	✔	The p.(Glu416Valfs*2) variant has been observed in at least 5 other individuals with CDKL5 disease (PMID: 27779742, PMID: 27864847, PMID: 23064044, ClinVar Variation ID 189554).
PVS1	✔	The p.(Glu416Valfs*2) 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.(Glu416Valfs*2) variant in CDKL5 is absent from gnomAD

Curation History

Showing 1 to 1 of 1 rows

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