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_001323289.2(CDKL5):c.469G>C (p.Ala157Pro)

Version: 1.0

CA412352120

1387019 (ClinVar)

Gene: CDKL5 (HGNC:6792)
Condition: CDKL5 disorder (MONDO:0100039)
Inheritance Mode: X-linked inheritance
UUID: 66d37eeb-e461-41c1-b2d6-4c2179e29b0a
Approved on: 2023/10/13
Published on: 2023/12/11

HGVS expressions

NM_001323289.2:c.469G>C
NM_001323289.2(CDKL5):c.469G>C (p.Ala157Pro)
NC_000023.11:g.18584268G>C
CM000685.2:g.18584268G>C
NC_000023.10:g.18602388G>C
CM000685.1:g.18602388G>C
NC_000023.9:g.18512309G>C
NG_008475.1:g.163664G>C
ENST00000623535.2:c.469G>C
ENST00000635828.1:c.469G>C
ENST00000637881.1:c.469G>C
ENST00000674046.1:c.469G>C
ENST00000379989.6:c.469G>C
ENST00000379996.7:c.469G>C
ENST00000463994.4:c.469G>C
ENST00000623535.1:c.469G>C
NM_001037343.1:c.469G>C
NM_003159.2:c.469G>C
NM_001323289.1:c.469G>C
NM_001037343.2:c.469G>C
NM_003159.3:c.469G>C

Likely Pathogenic

Met criteria codes 4

PM2_Supporting PP3 PM5 PS2

Not Met criteria codes 1

PM1

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.Ala157Pro variant in CDKL5 has been reported as a de novo occurrence (biological parentage confirmed) in an individual with clinical features of CDKL5 disorder (internal database - Invitae) (PS2). A pathogenic missense variant (p.Ala157Val) has been previously identified within this codon which indicates that this residue is critical to the function of the protein (ClinVar - ClinGen Rett and Angelman-like Disorders Variant Curation Expert Panel) (PM5). The p.Ala157Pro 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). In summary, the p.Ala157Pro variant in CDKL5 is classified as Likely Pathogenic for CDKL5 disorder based on the ACMG/AMP criteria (PS2, PM5, PM2_Supporting, PP3).

Met criteria codes

PM2_Supporting	✔	The p.Ala157Pro variant in CDKL5 is absent from gnomAD (PM2_Supporting).
PP3	✔	Computational prediction analysis tools suggests a deleterious impact; however, this information does not predict clinical significance on its own (PP3).
PM5	✔	A pathogenic missense variant (p.Ala157Val) has been previously identified within this codon which indicates that this residue is critical to the function of the protein (ClinVar - ClinGen Rett and Angelman-like Disorders Variant Curation Expert Panel) (PM5).
PS2	✔	The p.Ala157Pro variant in CDKL5 has been reported as a de novo occurrence (biological parentage confirmed) in an individual with clinical features of CDKL5 disorder (internal database - Invitae) (PS2_moderate).

Not Met criteria codes

PM1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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