

Variant: NM_001323289.2(CDKL5):c.176G>A (p.Arg59Gln)

Version: 1.0

CA412348584 [↗](#)

496681 (ClinVar) [↗](#)

Gene: CDKL5 ([HGNC:6792](#))

Condition: CDKL5 disorder ([MONDO:0100039](#))

Inheritance Mode: X-linked inheritance

UUID: 8d74cb24-aa24-4e8e-a22d-3a88b2c4fc39

Approved on: 2025/8/27

Published on: 2025/9/30

HGVS expressions

NM_001323289.2:c.176G>A

NM_001323289.2(CDKL5):c.176G>A (p.Arg59Gln)

NC_000023.11:g.18575384G>A

CM000685.2:g.18575384G>A

NC_000023.10:g.18593504G>A

CM000685.1:g.18593504G>A

NC_000023.9:g.18503425G>A

NG_008475.1:g.154780G>A

ENST00000623535.2:c.176G>A

ENST00000635828.1:c.176G>A

ENST00000637881.1:c.176G>A

ENST00000674046.1:c.176G>A

ENST00000379989.6:c.176G>A

ENST00000379996.7:c.176G>A

ENST00000463994.4:c.176G>A

ENST00000623364.3:c.176G>A

ENST00000623535.1:c.176G>A

ENST00000624700.3:c.176G>A

NM_001037343.1:c.176G>A

NM_003159.2:c.176G>A

NM_001323289.1:c.176G>A

NM_001037343.2:c.176G>A

NM_003159.3:c.176G>A

Uncertain Significance

Met criteria codes **2**

BS2_Supporting PM6

Not Met criteria codes **7**

BA1 BS1 BP4 PP3 PM2
PM1 PM5

Evidence Links **0**

Expert Panel

[Rett and Angelman-like Disorders VCEP](#) [↗](#)

Criteria Specification Information

[↗](#) **Criteria Specification:** ClinGen Rett and Angelman-like Disorders Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for CDKL5 Version 5.0.0

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

Rett and Angelman-like Disorders VCEP

The highest population minor allele frequency of the p.Arg59Gln variant in CDKL5 in gnomAD v4.1 is 0.00000112 in Non-Finnish European population (not sufficient to meet BS1 criteria). The p.Arg59Gln variant is observed in at least 1 unaffected individual (internal database - GeneDx) (BS2-supporting). Computational prediction analysis tools are inconclusive for this variant. The p.Arg59Gln variant in CDKL5 has been reported as a de novo occurrence (biological parentage unconfirmed) in an individual with epileptic encephalopathy (internal database - Équipe Génétique des Anomalies du Développement (GAD)) (PM6). In summary, the p.Arg59Gln variant in CDKL5 is classified as uncertain significance based on the ACMG/AMP criteria (BS2_Supporting, PM6). (CDKL5 Specifications v.5.0.0; curation approved on 8/27/2025)

Met criteria codes

BS2_Supporting			The p.Arg59Gln variant is observed in at least 1 unaffected individual (internal database - GeneDx).
PM6			The p.Arg59Gln variant in CDKL5 has been reported as a de novo occurrence (biological parentage unconfirmed) in an individual with epileptic encephalopathy (internal database - Équipe Génétique des Anomalies du Développement (GAD)).

Not Met criteria codes

BA1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1			The highest population minor allele frequency of the p.Arg59Gln variant in CDKL5 in gnomAD v4.1 is 0.00000112 in Non-Finnish European population (not sufficient to meet BS1 criteria).
BP4			Computational prediction analysis tools are inconclusive for this variant.
PP3			Computational prediction analysis tools are inconclusive for this variant.
PM2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM5			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline



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