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.656A>G (p.Gln219Arg)

Version: 1.0

CA412353461

2572403 (ClinVar)

Gene: CDKL5 (HGNC:6792)
Condition: CDKL5 disorder (MONDO:0100039)
Inheritance Mode: X-linked inheritance
UUID: 6db16dfc-f96f-46c9-b3c1-6205b63f926d
Approved on: Tue, 25 Aug 2026 00:00:00 +0000
Published on: Thu, 24 Sep 2026 00:00:00 +0000

HGVS expressions

NM_001323289.2(CDKL5):c.656A>G (p.Gln219Arg)
NM_001323289.2:c.656A>G
NC_000023.11:g.18588055A>G
CM000685.2:g.18588055A>G
NC_000023.10:g.18606175A>G
CM000685.1:g.18606175A>G
NC_000023.9:g.18516096A>G
NG_008475.1:g.167451A>G
ENST00000623535.2:c.656A>G
ENST00000635828.1:c.656A>G
ENST00000637881.1:c.656A>G
ENST00000674046.1:c.656A>G
ENST00000379989.6:c.656A>G
ENST00000379996.7:c.656A>G
ENST00000463994.4:c.656A>G
ENST00000623535.1:c.656A>G
ENST00000623610.1:n.370A>G
NM_001037343.1:c.656A>G
NM_003159.2:c.656A>G
NM_001323289.1:c.656A>G
NM_001037343.2:c.656A>G
NM_003159.3:c.656A>G

Likely Pathogenic

Met criteria codes 5

PM5 PS4_Supporting PS2 PM2_Supporting PP3

Not Met criteria codes 1

PP4

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 6.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Rett and Angelman-like Disorders VCEP

The p.Gln219Arg variant in CDKL5 has been reported as a de novo occurrence (biological parentage confirmed) in an individual with CDKL5 disorder (PMID: 39944418) (PS2). The p.Gln219Arg variant has been observed in at least 1 additional individual with CDKL5 disorder, in a de novo state (biological parentage unconfirmed) (PMID: 33219631) (PS4_Supporting). The variant is absent from gnomAD v4.1.1 (PM2_Supporting), and computational prediction analysis tools suggests a deleterious impact; however, this information does not predict clinical significance on its own (PP3). A pathogenic missense variant (p.Gln219Pro) 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). In summary, the p.Gln219Arg variant in CDKL5 is classified as Likely Pathogenic for CDKL5 disorder based on the ACMG/AMP criteria (PS2, PS4_Supporting, PP3, PM2_Supporting, PM5). CDKL5 Specifications v6.0; curation approved on 25-Aug-2026.

Met criteria codes

PM5	✔	A pathogenic missense variant (p.Gln219Pro) 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).
PS4_Supporting	✔	The p.(Gln219Arg) variant has been observed in at least 2 individuals with CDKL5 disorder (PMID: 33219631, 399444418) (PS4_Supporting).
PS2	✔	The p.Gln219Arg variant in CDKL5 has been reported as a de novo occurrence (biological parentage confirmed) in an individual with CDKL5 disorder (PMID:39944418) (PS2).
PM2_Supporting	✔	The p.Gln219Arg variant in CDKL5 is absent from gnomAD v4.1.1 (PM2_Supporting).
PP3	✔	Computational prediction analysis tools suggests a deleterious impact; however, this information does not predict clinical significance on its own (PP3).

Not Met criteria codes

PP4	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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