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_001110792.2(MECP2):c.1497A>G (p.Ter499Trp)

Version: 2.0

CA170257

143490 (ClinVar)

Gene: MECP2 (HGNC:4204)
Condition: Rett syndrome (MONDO:0010726)
Inheritance Mode: X-linked inheritance
UUID: 2bba9172-4eb1-4098-97c0-63efb3d2ff5b
Approved on: 2025/10/28
Published on: 2025/12/23

HGVS expressions

NM_001110792.2:c.1497A>G
NM_001110792.2(MECP2):c.1497A>G (p.Ter499Trp)
NC_000023.11:g.154030367T>C
CM000685.2:g.154030367T>C
NC_000023.10:g.153295818T>C
CM000685.1:g.153295818T>C
NC_000023.9:g.152949012T>C
NG_007107.2:g.111761A>G
NG_007107.3:g.111737A>G
ENST00000303391.11:c.1461A>G
ENST00000453960.7:c.1497A>G
ENST00000303391.10:c.1461A>G
ENST00000453960.6:c.1497A>G
ENST00000619732.4:c.1457A>G
ENST00000628176.2:c.*833A>G
NM_001110792.1:c.1497A>G
NM_001316337.1:c.1182A>G
NM_004992.3:c.1461A>G
NM_001316337.2:c.1182A>G
NM_001369391.2:c.1182A>G
NM_001369392.2:c.1182A>G
NM_001369393.2:c.1182A>G
NM_001369394.1:c.1182A>G
NM_001369394.2:c.1182A>G
NM_001386137.1:c.792A>G
NM_001386138.1:c.792A>G
NM_001386139.1:c.792A>G
NM_004992.4:c.1461A>G

Pathogenic

Met criteria codes 4

PS4_Moderate PS2 PM2_Supporting PM4_Strong

Not Met criteria codes 1

PP4

Expert Panel

Rett and Angelman-like Disorders VCEP

Criteria Specification Information

Evidence Links 0

Criteria Specification: *ClinGen Rett and Angelman-like Disorders Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for MECP2 Version 5.0.0*

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Rett and Angelman-like Disorders VCEP

The p.Ter487TrpextTer27 variant in MECP2 (NM_004992.4) occurs at the stop codon and causes a change in the length of the protein and an elongated mRNA transcript of MECP2 (PM4_strong). The p.Ter487TrpextTer27 variant in MECP2 has been reported as a de novo occurrence (biological parentage confirmed) in an individual with features of Rett syndrome (internal database - GeneDx) (PS2). The p.Ter487TrpextTer27 variant has been observed in 3 individuals with features of Rett syndrome (PMID 21807996; internal database - LabCorp (formerly Invitae); internal database - GeneDx) (PS4_moderate). The p.Ter487TrpextTer27 variant in MECP2 is absent from gnomAD v4.1.0 (PM2_supporting). In summary, the p.Ter487TrpextTer27 variant in MECP2 is classified as Pathogenic for Rett syndrome based on the ACMG/AMP criteria (PM4_strong, PS2, PS4_moderate, PM2_supporting). (MECP2 Specifications v5.0.0; curation approved on 10/28/2025).

Met criteria codes

PS4_Moderate	✔	The p.Ter487TrpextTer27 variant has been observed in 3 individuals with features of Rett syndrome (PMID 21807996; internal database - LabCorp (formerly Invitae); internal database - GeneDx) (PS4_moderate).
PS2	✔	The p.Ter487TrpextTer27 variant in MECP2 (NM_004992.4) has been reported as a de novo occurrence (biological parentage confirmed) in an individual with a neurodevelopmental disorder (internal database - GeneDx) (PS2).
PM2_Supporting	✔	The p.Ter487TrpextTer27 variant in MECP2 is absent from gnomAD (PM2_supporting).
PM4_Strong	✔	The p.Ter487TrpextTer27 variant in MECP2 (NM_004992.4) occurs at the stop codon and causes a change in the length of the protein and an elongated mRNA transcript of MECP2 (PM4_strong).

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

Showing 1 to 2 of 2 rows

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.