Variant: NM_001110792.2(MECP2):c.536G>C (p.Arg179Pro)

Version: 1.0

CA415174142

1489310 (ClinVar)

Gene: MECP2 (HGNC:4204)
Condition: Rett syndrome (MONDO:0010726)
Inheritance Mode: X-linked inheritance
UUID: 9f00974d-1929-4587-ab61-1764ab0342aa
Approved on: 2025-08-27
Published on: 2025-10-01

HGVS expressions

NM_001110792.2:c.536G>C
NM_001110792.2(MECP2):c.536G>C (p.Arg179Pro)
NC_000023.11:g.154031328C>G
CM000685.2:g.154031328C>G
NC_000023.10:g.153296779C>G
CM000685.1:g.153296779C>G
NC_000023.9:g.152949973C>G
NG_007107.2:g.110800G>C
NG_007107.3:g.110776G>C
ENST00000303391.11:c.500G>C
ENST00000453960.7:c.536G>C
ENST00000637917.1:c.65+68G>C
ENST00000303391.10:c.500G>C
ENST00000407218.5:c.469-42G>C
ENST00000453960.6:c.536G>C
ENST00000486506.5:n.2848G>C
ENST00000611468.1:c.486G>C
ENST00000619732.4:c.500G>C
ENST00000622433.4:c.488G>C
ENST00000628176.2:c.433-42G>C
NM_001110792.1:c.536G>C
NM_001316337.1:c.221G>C
NM_004992.3:c.500G>C
NM_001316337.2:c.221G>C
NM_001369391.2:c.221G>C
NM_001369392.2:c.221G>C
NM_001369393.2:c.221G>C
NM_001369394.1:c.221G>C
NM_001369394.2:c.221G>C
NM_001386137.1:c.-128-42G>C
NM_001386138.1:c.-128-42G>C
NM_001386139.1:c.-128-42G>C
NM_004992.4:c.500G>C

Met criteria codes 3

Expert Panel

Uncertain Significance

PM5 PM2_Supporting PS4_Supporting

Not Met criteria codes 4

PP3 PS1 PM1 BP4

Evidence Links 0

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 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.Arg167Pro variant in MECP2 (NM_004992.4) is absent from gnomAD v4.1 (PM2_Supporting). A pathogenic missense variant (p.Arg167Trp) has been previously identified within this codon which indicates that this residue is critical to the function of the protein (ClinVar) (PM5). The p.Arg167Pro variant has been observed in at least 2 individuals with Rett syndrome (PMID 34457282, internal database - Labcorp (formerly Invitae)) (PS4_Supporting). In summary, the p.Arg167Pro variant in MECP2 is classified as uncertain significance based on the ACMG/AMP criteria (PM2_Supporting, PM5, PS4_Supporting). (MECP2 Specifications v.5.0.0; curation approved on 8/27/2025)

Met criteria codes

PM5	✔	A pathogenic missense variant (p.Arg167Trp) has been previously identified within this codon which indicates that this residue is critical to the function of the protein (ClinVar)
PM2_Supporting	✔	The p.Arg167Pro variant in MECP2 (NM_004992.4) is absent from gnomAD v4.1 (PM2_Supporting).
PS4_Supporting	✔	The p.Arg167Pro variant has been observed in at least 2 individuals with Rett syndrome (PMID 34457282, internal database - Labcorp (formerly Invitae)) (PS4_Supporting).

Not Met criteria codes

PP3	✖	Computational prediction analysis tools are inconclusive for this variant.
PS1	✖	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
BP4	✖	Computational prediction analysis tools are inconclusive for this variant.

Curation History

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