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.947A>G (p.Lys316Arg)

Version: 1.0

CA170406

143743 (ClinVar)

Gene: MECP2 (HGNC:4204)
Condition: Rett syndrome (MONDO:0010726)
Inheritance Mode: X-linked inheritance
UUID: 5b8d53e9-a3fe-4a31-9e52-1906e3cf17b6
Approved on: 2025/6/25
Published on: 2025/8/1

HGVS expressions

NM_001110792.2(MECP2):c.947A>G (p.Lys316Arg)
NM_001110792.2:c.947A>G
NC_000023.11:g.154030917T>C
CM000685.2:g.154030917T>C
NC_000023.10:g.153296368T>C
CM000685.1:g.153296368T>C
NC_000023.9:g.152949562T>C
NG_007107.2:g.111211A>G
NG_007107.3:g.111187A>G
ENST00000303391.11:c.911A>G
ENST00000453960.7:c.947A>G
ENST00000637917.1:c.85A>G
ENST00000303391.10:c.911A>G
ENST00000407218.5:c.*283A>G
ENST00000453960.6:c.947A>G
ENST00000619732.4:c.911A>G
ENST00000622433.4:c.897A>G
ENST00000628176.2:c.*283A>G
NM_001110792.1:c.947A>G
NM_001316337.1:c.632A>G
NM_004992.3:c.911A>G
NM_001316337.2:c.632A>G
NM_001369391.2:c.632A>G
NM_001369392.2:c.632A>G
NM_001369393.2:c.632A>G
NM_001369394.1:c.632A>G
NM_001369394.2:c.632A>G
NM_001386137.1:c.242A>G
NM_001386138.1:c.242A>G
NM_001386139.1:c.242A>G
NM_004992.4:c.911A>G

Pathogenic

Met criteria codes 4

PP3 PM5_Strong PS2 PM2_Supporting

Expert Panel

Rett and Angelman-like Disorders VCEP

Not Met criteria codes 2

PM1 BP4

Evidence Links 0

Criteria Specification Information

Criteria Specification: *ClinGen Rett and Angelman-like Disorders Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for MECP2 Version 4.1.0*

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Rett and Angelman-like Disorders VCEP

The p.Lys304Arg variant in MECP2 (NM_004992.4) is absent from gnomAD v4.1 (PM2_Supporting). The p.Lys304Arg variant in MECP2 has been reported as a de novo occurrence (biological parentage confirmed) in an individual with Rett syndrome (internal database - GeneDx) (PS2). Multiple pathogenic missense variants have been previously identified within this codon which indicates that this residue is critical to the function of the protein (ClinVar, internal database - GeneDx, internal database - Labcorp Genetics) (PM5_Strong). Computational prediction analysis tools suggests a deleterious impact; however, this information does not predict clinical significance on its own (PP3). In summary, the p.Lys304Arg variant in MECP2 (NM_004992.4) is classified as pathogenic for Rett Syndrome based on the ACMG/AMP criteria (PM2_Supporting, PS2, PM5_Strong, PP3). (MECP2 Specifications v.4.1; curation approved on 06/25/2025)

Met criteria codes

PP3	✔	Computational prediction analysis tools suggests a deleterious impact; however, this information does not predict clinical significance on its own (PP3).
PM5_Strong	✔	Multiple pathogenic missense variants have been previously identified within this codon which indicates that this residue is critical to the function of the protein (ClinVar, internal database - GeneDx; internal database - Labcorp Genetics) (PM5_Strong).
PS2	✔	The p.Lys304Arg variant in MECP2 (NM_004992.4) has been reported as a de novo occurrence (biological parentage confirmed) in an individual with Rett syndrome (internal database - GeneDx) (PS2).
PM2_Supporting	✔	The p.Lys304Arg variant in MECP2 is absent from gnomAD v4.1 (PM2_Supporting).

Not Met criteria codes

PM1	✖	The p.Lys304Arg variant occurs in the well-characterized transcriptional repression domain (TRD) of MECP2, however this criteria was not applied given PM5_strong is met (PM1_not met).
BP4	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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