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.948G>C (p.Lys316Asn)

Version: 1.0

CA415169023

655729 (ClinVar)

Gene: MECP2 (HGNC:4204)
Condition: Rett syndrome (MONDO:0010726)
Inheritance Mode: X-linked inheritance
UUID: 24c0e8dd-b3a1-4239-9171-cff0f28ec2ab
Approved on: 2024/2/23
Published on: 2024/6/27

HGVS expressions

NM_001110792.2(MECP2):c.948G>C (p.Lys316Asn)
NM_001110792.2:c.948G>C
NC_000023.11:g.154030916C>G
CM000685.2:g.154030916C>G
NC_000023.10:g.153296367C>G
CM000685.1:g.153296367C>G
NC_000023.9:g.152949561C>G
NG_007107.2:g.111212G>C
NG_007107.3:g.111188G>C
ENST00000303391.11:c.912G>C
ENST00000453960.7:c.948G>C
ENST00000637917.1:c.86G>C
ENST00000303391.10:c.912G>C
ENST00000407218.5:c.*284G>C
ENST00000453960.6:c.948G>C
ENST00000619732.4:c.912G>C
ENST00000622433.4:c.898G>C
ENST00000628176.2:c.*284G>C
NM_001110792.1:c.948G>C
NM_001316337.1:c.633G>C
NM_004992.3:c.912G>C
NM_001316337.2:c.633G>C
NM_001369391.2:c.633G>C
NM_001369392.2:c.633G>C
NM_001369393.2:c.633G>C
NM_001369394.1:c.633G>C
NM_001369394.2:c.633G>C
NM_001386137.1:c.243G>C
NM_001386138.1:c.243G>C
NM_001386139.1:c.243G>C
NM_004992.4:c.912G>C

Pathogenic

Met criteria codes 3

PS2 PM5_Strong PM2_Supporting

Expert Panel

Rett and Angelman-like Disorders VCEP

Not Met criteria codes 2

PP3 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 3.0.0*

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Rett and Angelman-like Disorders VCEP

The p.Lys304Asn variant in MECP2 (NM_004992.3) is absent from gnomAD v2 (PM2_supporting). Multiple pathogenic missense variants have been previously identified within this codon which indicates that this residue is critical to the function of the protein (PMID: 23770565, PMID: 16077736, PMID: 16473305, RettBASE) (PM5_strong). The p.Lys304Asn variant in MECP2 has been reported as a de novo occurrence (biological parentage confirmed) in an individual with Rett syndrome (internal database - Invitae) (PS2). In summary, the p.Lys304Asn variant in MECP2 is classified as pathogenic for Rett syndrome based on the ACMG/AMP criteria (PM2_supporting, PM5_strong, PS2).

Met criteria codes

PS2	✔	The p.Lys304Asn variant in MECP2 has been reported as a de novo occurrence (biological parentage confirmed) in an individual with Rett syndrome (internal database-Invitae) (PS2).
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 (PMID: 23770565, PMID: 16077736, PMID: 16473305, RettBASE) (PM5_strong).
PM2_Supporting	✔	The p.Lys304Asn variant in MECP2 (NM_004992.3) is absent from gnomAD v2 (PM2_supporting).

Not Met criteria codes

PP3	✖	Computational prediction analysis tools are inconclusive for this variant (no criteria met).
BP4	✖	Computational prediction analysis tools are inconclusive for this variant (no criteria met).

Curation History

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