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Variant: NM_001110792.1(MECP2):c.916C>T (p.Arg306Ter)

Version: 1.0

CA121700

11819 (ClinVar)

Gene: MECP2 (HGNC:4204)
Condition: Rett syndrome (MONDO:0010726)
Inheritance Mode: X-linked inheritance
UUID: ede88874-946c-4213-9897-197e908f3c6d
Approved on: 2021/3/26
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HGVS expressions

NM_001110792.1(MECP2):c.916C>T (p.Arg306Ter)
NM_001110792.1:c.916C>T
NC_000023.11:g.154030948G>A
CM000685.2:g.154030948G>A
NC_000023.10:g.153296399G>A
CM000685.1:g.153296399G>A
NC_000023.9:g.152949593G>A
NG_007107.2:g.111180C>T
NG_007107.3:g.111156C>T
ENST00000303391.11:c.880C>T
ENST00000453960.7:c.916C>T
ENST00000637917.1:c.66-12C>T
ENST00000303391.10:c.880C>T
ENST00000407218.5:c.*252C>T
ENST00000453960.6:c.916C>T
ENST00000619732.4:c.880C>T
ENST00000622433.4:c.866C>T
ENST00000628176.2:c.*252C>T
NM_001316337.1:c.601C>T
NM_004992.3:c.880C>T
NM_001110792.2:c.916C>T
NM_001316337.2:c.601C>T
NM_001369391.2:c.601C>T
NM_001369392.2:c.601C>T
NM_001369393.2:c.601C>T
NM_001369394.1:c.601C>T
NM_001369394.2:c.601C>T
NM_001386137.1:c.211C>T
NM_001386138.1:c.211C>T
NM_001386139.1:c.211C>T
NM_004992.4:c.880C>T

Pathogenic

Met criteria codes 5

PVS1 PS4 PS2_Very Strong PM2_Supporting PS3_Supporting

Expert Panel

Rett and Angelman-like Disorders VCEP

Evidence Links 0

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Rett and Angelman-like Disorders VCEP

The p.Arg294* variant in MECP2 is predicted to cause a premature stop codon that leads to a truncated or absent protein in a gene where loss-of-function is an established mechanism. There is significant evidence that loss of this region of the gene is pathogenic (PVS1). The p.Arg294* variant in MECP2 has been reported as a de novo occurrence (biological parentage confirmed) in at least 2 individuals with Rett syndrome (internal database, GeneDx) (PS2_very strong). The p.Arg294* variant in MECP2 has been observed in at least 5 other individuals with Rett syndrome (PMID: 15737703, 11960578, 19722030, 21982064, RettBASE) (PS4). A transcription assay performed in Xenopus oocytes has shown that this variant impacts protein function (PMID 11058114) (PS3_supporting). The p.Arg294* variant in MECP2 is absent from gnomAD (PM2_supporting). In summary, the p.Arg294* variant in MECP2 is classified as Pathogenic for Rett syndrome based on the ACMG/AMP criteria (PVS1, PS2_very strong, PS4, PS3_supporting, PM2_supporting).

Met criteria codes

PVS1	✔	The variant p.Arg294* variant in MECP2 is predicted to cause a premature stop codon that leads to a truncated or absent protein in a gene where loss-of-function is an established mechanism.
PS4	✔	The p.Arg294* variant in MECP2 has been observed in at least 5 other individuals with RettSyndrome (15737703, 11960578, 19722030, 21982064, RettBASE)
PS2_Very Strong	✔	This variant has been observed confirmed de novo in over 2 affected individuals at GeneDx and in the literature.
PM2_Supporting	✔	The p.Arg306Ter variant in MECP2 is absent from gnomAD.
PS3_Supporting	✔	The p.Arg294* variant in MECP2 failed to repress transcription in oocytes in the transcription assay and decreased levels of protein stability.

Curation History

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