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Variant: NM_004992.3(MECP2):c.301C>T (p.Pro101Ser)

Version: 1.0

CA270328

143524 (ClinVar)

Gene: MECP2 (HGNC:4204)
Condition: Rett syndrome (MONDO:0010726)
Inheritance Mode: X-linked inheritance
UUID: 2b8ace0a-d687-49ca-a70c-e5ca323bc4b3
Approved on: 2021/3/26
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HGVS expressions

NM_004992.3:c.301C>T
NM_004992.3(MECP2):c.301C>T (p.Pro101Ser)
NC_000023.11:g.154032283G>A
CM000685.2:g.154032283G>A
NC_000023.10:g.153297734G>A
CM000685.1:g.153297734G>A
NC_000023.9:g.152950928G>A
NG_007107.2:g.109845C>T
NG_007107.3:g.109821C>T
ENST00000303391.11:c.301C>T
ENST00000453960.7:c.337C>T
ENST00000303391.10:c.301C>T
ENST00000369957.5:c.*355C>T
ENST00000407218.5:c.337C>T
ENST00000453960.6:c.337C>T
ENST00000486506.5:n.2649C>T
ENST00000611468.1:c.289C>T
ENST00000619732.4:c.301C>T
ENST00000622433.4:c.289C>T
ENST00000628176.2:c.301C>T
NM_001110792.1:c.337C>T
NM_001316337.1:c.22C>T
NM_001110792.2:c.337C>T
NM_001316337.2:c.22C>T
NM_001369391.2:c.22C>T
NM_001369392.2:c.22C>T
NM_001369393.2:c.22C>T
NM_001369394.1:c.22C>T
NM_001369394.2:c.22C>T
NM_001386137.1:c.-260C>T
NM_001386138.1:c.-260C>T
NM_001386139.1:c.-260C>T
NM_004992.4:c.301C>T

Met criteria codes 6

Expert Panel

Pathogenic

PS4 PP3 PP4 PM1 PM5_Strong PM2_Supporting

Evidence Links 0

Rett and Angelman-like Disorders VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Rett and Angelman-like Disorders VCEP

The p.Pro101Ser variant has been observed in at least 4 other individuals with Rett syndrome (RettBASE, internal database) (PS4). 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 10767337, 31439979) (PM5_Strong). The p.Pro101Ser variant in MECP2 is absent from gnomAD (PM2_Supporting). Computational prediction analysis tools suggests a deleterious impact; however, this information does not predict clinical significance on its own (PP3). The p.Pro101Ser variant in MECP2 has been reported in an individual with a clinical phenotype suggestive of Rett syndrome (PMID 11269512) (PP4). In summary, the p.Pro101Ser variant in MECP2 is classified as pathogenic for Rett syndrome based on the ACMG/AMP criteria (PS4, PM5_strong, PM2_supporting, PP3, PP4).

Met criteria codes

PS4	✔	The p.Pro101Ser variant has been observed in at least 4 other individuals with Rett syndrome (RettBASE, internal database)
PP3	✔	Computational prediction analysis tools suggests a deleterious impact; however, this information does not predict clinical significance on its own
PP4	✔	The p.Pro101Ser variant in MECP2 has been reported in an individual with a clinical phenotype suggestive of Rett syndrome (PMID 11269512)
PM1	✔	The variant p.Pro101Ser in MECP2 is affecting a mutational hotspot (Methyl-DNA binding (MDB) domain: between aa 90-162; PM1
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 10767337, 31439979)
PM2_Supporting	✔	The p.Pro101Ser variant in MECP2 is absent from gnomAD

Curation History

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