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.437C>T (p.Ser146Phe)

Version: 1.0

CA270398

143563 (ClinVar)

Gene: MECP2 (HGNC:4204)
Condition: Rett syndrome (MONDO:0010726)
Inheritance Mode: X-linked inheritance
UUID: cdabb0b8-00e6-4545-a4b7-f8005af1d548
Approved on: 2021/10/26
Published on: 2021/12/27

HGVS expressions

NM_001110792.2(MECP2):c.437C>T (p.Ser146Phe)
NM_001110792.2:c.437C>T
NC_000023.11:g.154031427G>A
CM000685.2:g.154031427G>A
NC_000023.10:g.153296878G>A
CM000685.1:g.153296878G>A
NC_000023.9:g.152950072G>A
NG_007107.2:g.110701C>T
NG_007107.3:g.110677C>T
ENST00000303391.11:c.401C>T
ENST00000453960.7:c.437C>T
ENST00000637917.1:c.34C>T
ENST00000303391.10:c.401C>T
ENST00000369957.5:c.*455C>T
ENST00000407218.5:c.437C>T
ENST00000453960.6:c.437C>T
ENST00000486506.5:n.2749C>T
ENST00000611468.1:c.389C>T
ENST00000619732.4:c.401C>T
ENST00000622433.4:c.389C>T
ENST00000628176.2:c.401C>T
NM_001110792.1:c.437C>T
NM_001316337.1:c.122C>T
NM_004992.3:c.401C>T
NM_001316337.2:c.122C>T
NM_001369391.2:c.122C>T
NM_001369392.2:c.122C>T
NM_001369393.2:c.122C>T
NM_001369394.1:c.122C>T
NM_001369394.2:c.122C>T
NM_001386137.1:c.-160C>T
NM_001386138.1:c.-160C>T
NM_001386139.1:c.-160C>T
NM_004992.4:c.401C>T

Pathogenic

Met criteria codes 7

PM2_Supporting | PS2 | PS4_Moderate | PM1 | PM5 | PP3 | PP4

Evidence Links 0

Expert Panel

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.Ser134Phe variant in MECP2 (NM_004992.3) has been reported as a de novo occurrence (biological parentage both confirmed and unconfirmed) in at least 2 individuals with Rett syndrome (PMID 15737703, internal database - GeneDx) (PS2, PP4). The p.Ser134Phe variant has been observed in at least 1 other individual with Rett syndrome (PMID 21160487) (PS4_moderate). A pathogenic missense variant (p.Ser134Cys) has been previously identified within this codon which indicates that this residue is critical to the function of the protein (PMID 10814718, 11738864, 17089071, 12655490, 21160487, 11738883, 18337588, 10767337, 23696494, 22182064) (PM5). The p.Ser134Phe variant occurs in the well-characterized methyl-binding domain (MBD) functional domain of MECP2 (PMID 1326358, 23770565) (PM1). The p.Ser134Phe 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). In summary, the p.Ser134Phe variant in MECP2 is classified as Pathogenic for Rett syndrome based on the ACMG/AMP criteria (PS2, PS4_moderate, PM1, PM5, PM2_supporting, PP3, PP4).

Met criteria codes

PM2_Supporting	✔	The p.Ser134Phe variant in MECP2 is absent from gnomAD (PM2_supporting).
PS2	✔	The p.Ser134Phe variant in MECP2 has been reported as a de novo occurrence (biological parentage both confirmed and unconfirmed) in at least 2 individuals with Rett syndrome (PMID 15737703, internal database - GeneDx) (PS2).
PS4_Moderate	✔	The p.Ser134Phe variant has been observed in at least 1 other individual with Rett syndrome (PMID 21160487) (PS4_moderate). [The variant has been seen in 3 affected individuals total, 2 de novo and documented under PM6_strong]
PM1	✔	The p.Ser134Phe variant occurs in the well-characterized methyl-binding domain (MBD) functional domain of MECP2 (PMID 1326358, 23770565) (PM1).
PM5	✔	A pathogenic missense variant (p.Ser134Cys) has been previously identified within this codon which indicates that this residue is critical to the function of the protein (PMID 10814718, 11738864, 17089071, 12655490, 21160487, 11738883, 18337588, 10767337, 23696494, 22182064) (PM5).
PP3	✔	Computational prediction analysis tools suggests a deleterious impact; however, this information does not predict clinical significance on its own (PP3).
PP4	✔	The p.Ser134Phe variant in MECP2 has been reported in an individual with a clinical phenotype suggestive of Rett syndrome (PMID 15737703) (PP4).

Curation History

Showing 1 to 1 of 1 rows

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.