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Variant: NM_001110792.2(MECP2):c.380G>A (p.Arg127His)

Version: 1.0

CA10558640

2505626 (ClinVar)

Gene: MECP2 (HGNC:4204)
Condition: Rett syndrome (MONDO:0010726)
Inheritance Mode: X-linked inheritance
UUID: 05ef9c22-bf70-4244-9624-e0a6ffa5a371
Approved on: 2024/8/30
Published on: 2024/12/23

HGVS expressions

NM_001110792.2(MECP2):c.380G>A (p.Arg127His)
NM_001110792.2:c.380G>A
NC_000023.11:g.154032240C>T
CM000685.2:g.154032240C>T
NC_000023.10:g.153297691C>T
CM000685.1:g.153297691C>T
NC_000023.9:g.152950885C>T
NG_007107.2:g.109888G>A
NG_007107.3:g.109864G>A
ENST00000303391.11:c.344G>A
ENST00000453960.7:c.380G>A
ENST00000303391.10:c.344G>A
ENST00000369957.5:c.*398G>A
ENST00000407218.5:c.380G>A
ENST00000453960.6:c.380G>A
ENST00000486506.5:n.2692G>A
ENST00000611468.1:c.332G>A
ENST00000619732.4:c.344G>A
ENST00000622433.4:c.332G>A
ENST00000628176.2:c.344G>A
NM_001110792.1:c.380G>A
NM_001316337.1:c.65G>A
NM_004992.3:c.344G>A
NM_001316337.2:c.65G>A
NM_001369391.2:c.65G>A
NM_001369392.2:c.65G>A
NM_001369393.2:c.65G>A
NM_001369394.1:c.65G>A
NM_001369394.2:c.65G>A
NM_001386137.1:c.-217G>A
NM_001386138.1:c.-217G>A
NM_001386139.1:c.-217G>A
NM_004992.4:c.344G>A

Met criteria codes 4

Expert Panel

Pathogenic

PS2_Very Strong | PP3 | PM1 | PS4_Moderate

Not Met criteria codes 1

PM2

Evidence Links 0

Rett and Angelman-like Disorders VCEP

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.Arg115His variant in MECP2 (NM_004992.4) has been reported as a de novo occurrence (biological parentage confirmed) in at least 2 male individuals with neurodevelopmental disorders (internal database - GeneDx) (PS2_Very Strong). The p.Arg115His variant has been observed in 3 male individuals with neurodevelopmental disorders (internal database) (PS4_Moderate). The p.Arg115His variant occurs in the well-characterized Methyl-DNA binding (MDB) functional domain of the MECP2 gene (PM1). Computational prediction analysis tools suggests a deleterious impact; however, this information does not predict clinical significance on its own (PP3). The p.Arg115His variant in MECP2 is absent from gnomAD v4.1; however, this variant is present in 1 XX individual in gnomAD v2.1.1. In summary, the p.Arg115His variant in MECP2 (NM_004992.4) is classified as pathogenic for Rett syndrome based on the ACMG/AMP criteria (PS2_Very Strong, PS4_Moderate, PM1, PP3). (MECP2 Specification v.3.0.0, curation approved on 8/30/2024)

Met criteria codes

PS2_Very Strong	✓	The p.Arg115His variant in MECP2 (NM_004992.4) has been reported as a de novo occurrence (biological parentage confirmed) in at least 2 male individuals with neurodevelopmental disorders (internal database - GeneDx) (PS2_Very Strong).
PP3	✓	Computational prediction analysis tools suggests a deleterious impact; however, this information does not predict clinical significance on its own (PP3).
PM1	✓	The p.Arg115His variant (NM_004992.4) occurs in the well-characterized Methyl-DNA binding (MDB) functional domain of the MECP2 gene (PM1).
PS4_Moderate	✓	The p.Arg115His variant (NM_004992.4) has been observed in 3 male individuals with neurodevelopmental disorders (internal database) (PS4_Moderate).

Not Met criteria codes

PM2	✗	The p.Arg115His variant in MECP2 (NM_004992.4) is absent from gnomAD v4.1; however, this variant is present in 1 XX individual in gnomAD v2.1.1.

Curation History

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