

Variant: *NM_001110792.2(MECP2):c.1240_1241insT*
(*p.Pro414fs*)

Version: 1.0

CA2580101896 [↗](#)

1700183 (ClinVar) [↗](#)

Gene: MECP2 ([HGNC:4204](#))

Condition: Rett syndrome ([MONDO:0010726](#))

Inheritance Mode: X-linked inheritance

UUID: 3d4f4a0a-f039-45cd-b359-6a1680c7d2c3

Approved on: 2025/10/28

Published on: 2025/12/23

HGVS expressions

NM_001110792.2(MECP2):c.1240_1241insT (p.Pro414fs)

NM_001110792.2:c.1240_1241insT

NC_000023.11:g.154030623_154030624insA

CM000685.2:g.154030623_154030624insA

NC_000023.10:g.153296074_153296075insA

CM000685.1:g.153296074_153296075insA

NC_000023.9:g.152949268_152949269insA

NG_007107.2:g.111504_111505insT

NG_007107.3:g.111480_111481insT

ENST00000303391.11:c.1204_1205insT

ENST00000453960.7:c.1240_1241insT

ENST00000303391.10:c.1204_1205insT

ENST00000407218.5:c.*576_*577insT

ENST00000453960.6:c.1240_1241insT

ENST00000619732.4:c.1204_1205insT

ENST00000628176.2:c.*576_*577insT

NM_001110792.1:c.1240_1241insT

NM_001316337.1:c.925_926insT

NM_004992.3:c.1204_1205insT

NM_001316337.2:c.925_926insT

NM_001369391.2:c.925_926insT

NM_001369392.2:c.925_926insT

NM_001369393.2:c.925_926insT

NM_001369394.1:c.925_926insT

NM_001369394.2:c.925_926insT

NM_001386137.1:c.535_536insT

NM_001386138.1:c.535_536insT

NM_001386139.1:c.535_536insT

NM_004992.4:c.1204_1205insT

Met criteria codes **4**

Uncertain Significance

PVS1

BS2_Supporting

BP5

PM2_Supporting

Expert Panel

Rett and Angelman-like Disorders VCEP [↗](#)

Not Met criteria codes **1**

PS2

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 5.0.0*

[Criteria Specification Approval History](#)

[Criteria Specifications for this VCEP](#)

Evidence submitted by expert panel

Rett and Angelman-like Disorders VCEP

The p.Pro402LeufsTer3 variant in MECP2 (NM_004992.4) 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.Pro402LeufsTer3 variant in MECP2 is absent from gnomAD v4.1.0 (PM2_Supporting). The p.Pro402LeufsTer3 variant in MECP2 has been reported as a de novo occurrence (biological parentage confirmed) in an individual with non-specific neurodevelopmental symptoms and other features that are not typical of Rett syndrome (internal database - CeGaT Center for Human Genetics Tuebingen) (PS2 not applied). The p.Pro402LeufsTer3 has also been observed in an individual with Rett syndrome; however, this individual was also found to have a second truncating variant in MECP2 (p.Arg255*), phase unknown, that is upstream of the p.Pro402LeufsTer3 variant (PMID: 30081849). The p.Pro402LeufsTer3 variant has been observed in the hemizygous state in an individual with a neurodevelopmental disorder, and was found to be inherited from the unaffected mother (internal database - PreventionGenetics) (BS2_Supporting). The p.Pro402LeufsTer3 variant is found in a patient with an alternate molecular basis of disease (internal database - Centre de Biologie Pathologie Génétique) (BP5). In summary, the p.Pro402LeufsTer3 variant in MECP2 is classified as a variant of uncertain significance based on the ACMG/AMP criteria (PVS1, PM2_supporting, BS2_Supporting, BP5). (MECP2 Specifications v5.0; curation approved on 10/28/2025)

Met criteria codes

PVS1			The p.Pro402LeufsTer3 variant in MECP2 (NM_004992.4) 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).
BS2_Supporting			The p.Pro402LeufsTer3 variant is observed in at least 1 unaffected individual (internal database - PreventionGenetics) (BS2_Supporting).
BP5			The p.Pro402LeufsTer3 variant is found in a patient with an alternate molecular basis of disease (internal database - Centre de Biologie Pathologie Génétique) (BP5).
PM2_Supporting			The p.Pro402LeufsTer3 variant in MECP2 is absent from gnomAD v4.1.0 (PM2_Supporting).

Not Met criteria codes

PS2			The p.Pro402LeufsTer3 variant in MECP2 has been reported as a de novo occurrence (biological parentage confirmed) in an individual with neurodevelopmental symptoms that are not typical of Rett syndrome (internal database - CeGaT Center for Human Genetics Tuebingen) (PS2 not applied).
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Curation History

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