Variant: NM_130839.5(UBE3A):c.1310G>A (p.Arg437Gln)

Version: 1.0

CA7435542

1399221 (ClinVar)

Gene: UBE3A (HGNC:7337)
Condition: Angelman syndrome (MONDO:0007113)
Inheritance Mode: Autosomal dominant inheritance
UUID: c8c3c298-e55d-42a1-81fc-03fb395d44fb
Approved on: 2025-02-28
Published on: 2025-03-27

HGVS expressions

NM_130839.5:c.1310G>A
NM_130839.5(UBE3A):c.1310G>A (p.Arg437Gln)
NC_000015.10:g.25370864C>T
CM000677.2:g.25370864C>T
NC_000015.9:g.25616011C>T
CM000677.1:g.25616011C>T
NC_000015.8:g.23167104C>T
NG_009268.1:g.73118G>A
ENST00000438097.6:c.1250G>A
ENST00000625778.3:c.1250G>A
ENST00000635914.1:c.1250G>A
ENST00000637886.1:c.1310G>A
ENST00000638011.1:c.1250G>A
ENST00000638155.1:c.1250G>A
ENST00000648336.2:c.1310G>A
ENST00000649550.1:c.1250G>A
ENST00000650110.1:c.1319G>A
ENST00000675000.1:n.1985G>A
ENST00000675177.1:c.1133G>A
ENST00000675593.1:n.4006G>A
ENST00000232165.7:c.1250G>A
ENST00000397954.6:c.1319G>A
ENST00000428984.6:c.1250G>A
ENST00000438097.5:c.1250G>A
ENST00000566215.5:c.1250G>A
ENST00000614096.4:c.1310G>A
ENST00000625778.2:c.1250G>A
ENST00000630424.2:c.1250G>A
NM_000462.3:c.1319G>A
NM_130838.1:c.1250G>A
NM_130839.2:c.1310G>A
NM_000462.5:c.1319G>A
NM_001354505.1:c.1310G>A
NM_001354506.1:c.1250G>A
NM_001354507.1:c.1250G>A
NM_001354508.1:c.1250G>A
NM_001354509.1:c.1250G>A

NM_001354511.1:c.1250G>A
NM_001354512.1:c.1250G>A
NM_001354513.1:c.1250G>A
NM_001354523.1:c.1250G>A
NM_001354526.1:c.1250G>A
NM_001354538.1:c.1310G>A
NM_001354539.1:c.1250G>A
NM_001354540.1:c.1250G>A
NM_001354541.1:c.1250G>A
NM_001354542.1:c.1250G>A
NM_001354543.1:c.1250G>A
NM_001354544.1:c.1250G>A
NM_001354545.1:c.1310G>A
NM_001354546.1:c.1133G>A
NM_001354547.1:c.1250G>A
NM_001354548.1:c.1250G>A
NM_001354549.1:c.1250G>A
NM_001354550.1:c.361+4601G>A
NM_001354551.1:c.301+4601G>A
NM_130838.3:c.1250G>A
NM_130839.4:c.1310G>A
NR_146177.1:n.18393-20732C>T
NR_148916.1:n.1858G>A
NM_001354506.2:c.1250G>A
NM_001354507.2:c.1250G>A
NM_001354508.2:c.1250G>A
NM_001354509.2:c.1250G>A
NM_001354511.2:c.1250G>A
NM_001354512.2:c.1250G>A
NM_001354513.2:c.1250G>A
NM_001354523.2:c.1250G>A
NM_001354538.2:c.1310G>A
NM_001354539.2:c.1250G>A
NM_001354540.2:c.1250G>A
NM_001354541.2:c.1250G>A
NM_001354542.2:c.1250G>A
NM_001354543.2:c.1250G>A
NM_001354544.2:c.1250G>A
NM_001354545.2:c.1310G>A
NM_001354546.2:c.1133G>A
NM_001354547.2:c.1250G>A
NM_001354548.2:c.1250G>A
NM_001354549.2:c.1250G>A
NM_001354550.2:c.361+4601G>A
NM_001354551.2:c.301+4601G>A
NM_001374461.1:c.1250G>A
NM_130838.4:c.1250G>A
NR_148916.2:n.1826G>A

Met criteria codes 2

Expert Panel

Uncertain Significance

PS2 PP4

Not Met criteria codes 5

PS4 BA1 PP3 PM2 BS1

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 UBE3A Version 4.0.0*

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Rett and Angelman-like Disorders VCEP

The c.1310G>A (p.Arg437Gln) variant in the UBE3A gene has been identified as a de novo occurrence with confirmed parental relationships in 1 individual with clinical features of Angelman syndrome and the described phenotype meets PP4 criteria (PS2, PP4; GeneDx: internal database). The p.Arg437Gln variant has been reported in 1 additional proband with a neurodevelopmental phenotype consistent with Angelman syndrome. However, PS4 cannot be applied because PM2 does not apply (PS4_not met). The highest population minor allele frequency of the p.Arg437Gln variant in UBE3A in gnomAD v4.1 is 0.00003 in "Remaining" populations (not sufficient to meet BS1 criteria). Computational prediction analysis tools are inconclusive for this variant (REVEL gives a score of 0.329). In summary, this variant meets the criteria to be classified as a Variant of Uncertain Significance for Angelman syndrome based on the ACMG/AMP criteria applied, as specified by the ClinGen Rett and Angelman-like Disorders VCEP (PS2, PP4). (UBE3A specifications version 4.0; 02/28/2025).

Met criteria codes

PS2	✔	This variant has been identified as a de novo occurrence with confirmed parental relationships in 1 individual with clinical features of Angelman syndrome (PS2; GeneDx: internal database).
PP4	✔	The p.Arg437Gln variant in UBE3A has been reported in an individual with a clinical phenotype suggestive of Angelman syndrome (GeneDx, internal data) (PP4).

Not Met criteria codes

PS4	✖	The p.Arg437Gln variant has been reported in 2 probands with a neurodevelopmental phenotype consistent with Angelman syndrome. However, PS4 cannot be applied because PM2 does not apply (PS4_not met).
BA1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3	✖	Computational prediction analysis tools are inconclusive for this variant (REVEL gives a score of 0.329).
PM2	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1	✖	The highest population minor allele frequency of the p.Arg437Gln variant in UBE3A in gnomAD v4.1 is 0.00003 in "Remaining" subpopulation (not sufficient to meet BS1 criteria).

Curation History

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