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Variant: NM_130838.1(UBE3A):c.2T>C (p.Met1Thr)

Version: 1.0

CA333472

136199 (ClinVar)

Gene: UBE3A (HGNC:7337)
Condition: Angelman syndrome (MONDO:0007113)
Inheritance Mode: Autosomal dominant inheritance (with paternal imprinting (HP:0012274))
UUID: ca3b17bd-94fc-4e26-a127-06213fba2385
Approved on: 2021/3/26
Published on: 2021/5/17

HGVS expressions

NM_130838.1(UBE3A):c.2T>C (p.Met1Thr)
NM_130838.1:c.2T>C
NC_000015.10:g.25405461A>G
CM000677.2:g.25405461A>G
NC_000015.9:g.25650608A>G
CM000677.1:g.25650608A>G
NC_000015.8:g.23201701A>G
NG_009268.1:g.38521T>C
ENST00000438097.6:c.2T>C
ENST00000625778.3:c.2T>C
ENST00000635914.1:c.2T>C
ENST00000637886.1:c.62T>C
ENST00000638011.1:c.-112T>C
ENST00000638155.1:c.2T>C
ENST00000648336.2:c.62T>C
ENST00000649550.1:c.2T>C
ENST00000650110.1:c.71T>C
ENST00000675000.1:n.737T>C
ENST00000675038.1:n.797T>C
ENST00000675177.1:c.-115-29698T>C
ENST00000675593.1:n.2758T>C
ENST00000232165.7:c.2T>C
ENST00000397954.6:c.71T>C
ENST00000428984.6:c.2T>C
ENST00000438097.5:c.2T>C
ENST00000566215.5:c.2T>C
ENST00000614096.4:c.62T>C
ENST00000625778.2:c.2T>C
ENST00000626068.2:c.83T>C
ENST00000626793.2:n.309T>C
ENST00000628267.2:c.2T>C
ENST00000628733.2:c.62T>C
ENST00000628890.1:c.62T>C
ENST00000629252.2:c.2T>C
ENST00000629886.2:c.62T>C
ENST00000630424.2:c.2T>C
ENST00000630607.2:c.2T>C

ENST00000630907.2:c.62T>C
NM_000462.3:c.71T>C
NM_130839.2:c.62T>C
NM_000462.5:c.71T>C
NM_001354505.1:c.62T>C
NM_001354506.1:c.2T>C
NM_001354507.1:c.2T>C
NM_001354508.1:c.2T>C
NM_001354509.1:c.2T>C
NM_001354511.1:c.2T>C
NM_001354512.1:c.2T>C
NM_001354513.1:c.2T>C
NM_001354523.1:c.-112T>C
NM_001354526.1:c.2T>C
NM_001354538.1:c.62T>C
NM_001354539.1:c.2T>C
NM_001354540.1:c.2T>C
NM_001354541.1:c.2T>C
NM_001354542.1:c.2T>C
NM_001354543.1:c.2T>C
NM_001354544.1:c.2T>C
NM_001354545.1:c.62T>C
NM_001354546.1:c.-115-29698T>C
NM_001354547.1:c.2T>C
NM_001354548.1:c.2T>C
NM_001354549.1:c.2T>C
NM_001354550.1:c.62T>C
NM_001354551.1:c.2T>C
NM_130838.3:c.2T>C
NM_130839.4:c.62T>C
NR_146177.1:n.18589-13327A>G
NR_148916.1:n.610T>C
NM_001354506.2:c.2T>C
NM_001354507.2:c.2T>C
NM_001354508.2:c.2T>C
NM_001354509.2:c.2T>C
NM_001354511.2:c.2T>C
NM_001354512.2:c.2T>C
NM_001354513.2:c.2T>C
NM_001354523.2:c.-112T>C
NM_001354538.2:c.62T>C
NM_001354539.2:c.2T>C
NM_001354540.2:c.2T>C
NM_001354541.2:c.2T>C
NM_001354542.2:c.2T>C
NM_001354543.2:c.2T>C
NM_001354544.2:c.2T>C
NM_001354545.2:c.62T>C
NM_001354546.2:c.-115-29698T>C
NM_001354547.2:c.2T>C
NM_001354548.2:c.2T>C
NM_001354549.2:c.2T>C

NM_001354550.2:c.62T>C
NM_001354551.2:c.2T>C
NM_001374461.1:c.2T>C
NM_130838.4:c.2T>C
NM_130839.5:c.62T>C
NR_148916.2:n.578T>C

Pathogenic

Met criteria codes 6

PP1 PP4 PS4_Moderate PM6 PVS1 PM2_Supporting

Evidence Links 2

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.M1? variant in UBE3A is predicted to cause a truncated or absent protein by altering the start codon of the coding sequence in a UBE3A where loss-of-function is an established disease mechanism. Pathogenic variants affecting the start site have been described in affected patients (PVS1). The p.M1? variant has been observed in 3 other individuals with Angelman syndrome (PMID 29737008, 25212744) (PS4_Moderate). The p.M1? variant in UBE3A is absent from gnomAD (PM2_Supporting). The p.M1? variant in UBE3A has been reported as a de novo occurrence (biological parentage unconfirmed) in an individual with Angelman syndrome (PMID 29737008) (PM6). The variant has been reported to segregate in two informative meioses (PP1). The p.M1? variant in UBE3A has been reported in an individual with a clinical phenotype suggestive of Angelman syndrome (PMID 29737008, 25212744) (PP4). In summary, the p.M1? variant in UBE3A is classified as pathogenic for Angelman syndrome based on the ACMG/AMP criteria (PVS1, PS4_moderate, PM2_supporting, PM6, PP1, PP4).

Met criteria codes

PP1	✔	The variant has been reported to segregate in two informative meioses
PP4	✔	The p.M1? variant in UBE3A has been reported in an individual with a clinical phenotype suggestive of Angelman syndrome (PMID 29737008, 25212744)
PS4_Moderate	✔	The p.M1? variant has been observed in 3 other individuals with Angelman syndrome (PMID 29737008, 25212744) Study of two families with Angelman syndrome. Variant was identified in two affected siblings (maternally inherited), and in an unrelated proband from another family (de novo). These cases were noted to have more advanced developmental skills than typical non-mosaic AS individuals, with spontaneous syntactic language. PubMed:29737008 Review of UBE3A variants identified in a cohort of 2515 AS patients. Variant was identified in one patient with Angelman syndrome. PubMed:25212744
PM6	✔	The p.M1? variant in UBE3A has been reported as a de novo occurrence (biological parentage unconfirmed) in an individual with Angelman syndrome (PMID 29737008)

Study of two families with Angelman syndrome. Variant was identified in two affected siblings (maternally inherited), and in an unrelated proband from another family (de novo). These cases were noted to have more advanced developmental skills than typical non-mosaic AS individuals, with spontaneous syntactic language.
PubMed:29737008

PVS1	✔	The p.M1? variant in UBE3A is predicted to cause a truncated or absent protein by altering the start codon of the coding sequence in a UBE3A where loss-of-function is an established disease mechanism. Pathogenic variants affecting the start site have been described in affected patients.
PM2_Supporting	✔	The p.M1? variant in UBE3A is absent from gnomAD

Curation History

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