Client: Example Client ABC123
123 Test Drive
Salt Lake City, UT 84108
UNITED STATES

Physician: Doctor, Example

Patient: Patient, Example

DOB	Unknown
Gender:	Unknown
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Angelman Syndrome (UBE3A) Sequencing

ARUP test code 2005564

Angelman Syndrome (UBE3A) Seq Specimen	Whole Blood

Angelman Syndrome (UBE3A) Seq Interp

Negative

TEST PERFORMED - 2005564
TEST DESCRIPTION - Angelman Syndrome (UBE3A) Sequencing
INDICATION FOR TEST - Confirm Diagnosis

RESULT
No pathogenic variants were detected in the UBE3A gene.

INTERPRETATION
No pathogenic variants were detected in the UBE3A gene by sequencing. This result decreases, but does not exclude, a diagnosis of Angelman syndrome as only 11 percent of causative variants are identifiable by sequencing. Other genetic mechanisms which may result in Angelman syndrome (eg, deletions of the maternally imprinted 15q11.2-q13 AS/PWS critical region, paternal uniparental disomy of chromosome 15 and imprinting center defects) are not detectable by this assay. In addition, this assay will not detect UBE3A regulatory region variants, deep intronic variants, or partial/whole gene deletions.

RECOMMENDATIONS
Medical screening and management should rely on clinical findings and family history. DNA methylation analysis for Angelman syndrome (ARUP test code 2005077) should be considered as approximately 78 percent of individuals with Angelman syndrome demonstrate abnormal maternal methylation patterns due to one of the following mechanisms: deletions of the AS/PWS critical region, paternal uniparental disomy of chromosome 15, or imprinting center defects. A genetics consultation is recommended.

COMMENTS
Reference Sequence: GenBank # NM_130839.4 (UBE3A exons 6 & 7) and NM_130838.1 (UBE3A exons 7-16)
Nucleotide numbering begins at the "A" of the ATG initiation codon.
Likely benign and benign variants are not included in this report.

This result has been reviewed and approved by [redacted]

H=High, L=Low, *=Abnormal, C=Critical

BACKGROUND INFORMATION: Angelman Syndrome (UBE3A) Sequencing

CHARACTERISTICS: Developmental delays by 6-12 months of age, seizures, microcephaly, movement or balance disorder, minimal or absent speech, and a unique behavioral phenotype which includes a happy demeanor with frequent laughter, hand flapping, and excitability.
PREVALENCE: 1 in 15,000.
INHERITANCE: Varies, depending upon the molecular genetic mechanism. UBE3A mutations identified by sequencing may be maternally inherited or de novo. Offspring of a female carrier of a UBE3A sequence mutation are at 50 percent risk for AS.
PENETRANCE: Paternally inherited UBE3A sequence mutations are asymptomatic.
CAUSE: Absence of maternal expression of the UBE3A gene.
MOLECULAR GENETIC MECHANISMS: Microdeletions of the AS/PWS critical region (68 percent), UBE3A mutations (11 percent), paternal uniparental disomy of chromosome 15 (7 percent), imprinting center defects (3 percent), unbalanced chromosome translocation (less than 1 percent), and unknown (11 percent).
CLINICAL SENSITIVITY: 11 percent.
METHODOLODY: Bidirectional sequencing of the UBE3A coding region and intron-exon boundaries.
ANALYTICAL SENSITIVITY AND SPECIFICITY: 99 percent.
LIMITATIONS: Diagnostic errors can occur due to rare sequence variations. Regulatory region mutations, deep intronic mutations, and large deletion/duplications will not be detected. Other molecular mechanisms resulting in Angelman syndrome will not be assessed.

Counseling and informed consent are recommended for genetic testing. Consent forms are available online at www.aruplab.com.

Test developed and characteristics determined by ARUP Laboratories. See Compliance Statement C: aruplab.com/CS

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Angelman Syndrome (UBE3A) Seq Specimen	20-329-111753	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Angelman Syndrome (UBE3A) Seq Interp	20-329-111753	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

END OF CHART

H=High, L=Low, *=Abnormal, C=Critical