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	**Positive**	*

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

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

RESULT
One pathogenic variant was detected in the UBE3A gene.

DNA VARIANT
Classification: Pathogenic
Gene: UBE3A
Nucleic Acid Change: c.2343_2344delCT; Heterozygous
Amino Acid Alteration: p.Phe782LeufsTer40

INTERPRETATION
One pathogenic variant, c.2343_2344delCT; p.Phe782LeufsTer40, was detected in the UBE3A gene by sequencing. This result is consistent with a diagnosis of Angelman syndrome (AS). If the identified variant was inherited from the patient's mother, this individual's siblings are at 50 percent risk for AS.

Evidence for variant classification: The UBE2A c.2343_2344delCT; p.Phe782LeufsTer40, to our knowledge, is not reported in the medical literature or gene specific databases. However, nearby deletions including c.2344_2345delTT, has been described in individuals affected with Angelman syndrome (Sadikovic 2014). The c.2343_2344delCT variant causes a frameshift and is predicted to result in a truncated protein or absent transcript. Based on available information, this variant is considered to be pathogenic.

RECOMMENDATIONS
A genetics consultation, including a discussion of medical screening and management, is indicated. This individual's mother, and other maternal family members who might be at-risk for having offspring with AS, should be offered targeted sequencing for the identified UBE3A variant (Familial Mutation, Targeted Sequencing, ARUP test code 2001961). As molecular testing cannot exclude maternal germline mosaicism, prenatal testing for the familial UBE3A variant should be offered in subsequent pregnancies to all females who have a child with AS.

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

REFERENCES
Sadikovic B et al. Mutation Update for UBE3A variants in Angelman syndrome. Hum Mutat. 2014;35(12):1407-17.

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	20-329-111630	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Angelman Syndrome (UBE3A) Seq Interp	20-329-111630	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