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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

Rett Syndrome (MECP2), Full Gene Sequencing

ARUP test code 0051378

RETT FGS Specimen	Whole Blood	
Rett Syndrome, Full Gene Sequencing	Variant	*

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

TEST PERFORMED - 0051378
TEST DESCRIPTION - Rett Syndrome (MECP2), Sequencing
INDICATION FOR TEST - Not Provided

RESULT
One pathogenic variant was detected in the MECP2 gene.

DNA VARIANT
Classification: Pathogenic
Gene: MECP2
Nucleic Acid Change: c.763C>T; Heterozygous
Amino Acid Alteration: p.Arg255Ter

INTERPRETATION
One pathogenic variant, c.763C>T; p.Arg255Ter, was detected in the MECP2 gene by sequencing. Therefore, this individual is predicted to be affected with Rett syndrome.

Evidence for variant classification: The MECP2 c.763C>T, p.Arg255Ter variant (rs61749721) induces an early termination codon and is predicted to result in a truncated protein or absent transcript. This variant is one of the most common disease causing variants of Rett syndrome (RTT) (Neul 2008), and has been associated with both classical and atypical RTT (see link to RettBASE and references therein). Functional studies showed p.Arg255Ter to be less stable in vivo and lead to deficient transcriptional repression (Yusufzai 2000). Furthermore, this variant is reported as pathogenic in ClinVar (Variation ID: 11829), and is absent from population databases (Exome Variant Server, Exome Aggregation Consortium). Therefore, this variant is considered to be pathogenic.

RECOMMENDATIONS
A genetics consultation, including a discussion of screening and management, is indicated. Testing for the identified variant should be offered to the individual's mother and other relatives who may be at risk for having affected offspring (Familial Mutation, Targeted Sequencing; ARUP test 2001961).

COMMENTS
Reference Sequences: GenBank # NM_001110792.1 (MECP2 exon 1) and NM_004992.3 (MECP2 exon 2-4)
Nucleotide numbering begins at the "A" of the ATG initiation codon.
Likely benign and benign variants are not included in this report.

REFERENCES
Link to RettBASE:
http://mecp2.chw.edu.au/cgi-bin/mecp2/views/basic.cgi?form=basic

Neul JL et al. Specific mutations in methyl-CpG-binding protein 2 confer different severity in Rett syndrome. Neurology. 2008; 70(16):1313-21.

Yusufzai TM et al. Functional consequences of Rett syndrome mutations on human MeCP2. Nucleic Acids Res. 2000; 28(21):4172-9.

This result has been reviewed and approved by Rong Mao, M.D.

BACKGROUND INFORMATION: Rett Syndrome (MECP2), Full Gene Sequencing

CHARACTERISTICS: Classic Rett Syndrome is a progressive neurodevelopmental disorder characterized by normal development until 6-18 months of age followed by rapid developmental regression, deceleration of head growth, loss of speech and acquired motor skills, and seizures; purposeful use of the hands is replaced by repetitive stereotyped hand movements. MECP2-related disorders include Rett-like Syndrome, severe congenital encephalopathy, or mild to severe mental retardation.
INCIDENCE: 1 in 10,000.
INHERITANCE: X-linked dominant; most cases are sporadic.
CAUSE: Methyl-CpG-Binding Protein 2 (MECP2) gene mutations.
CLINICAL SENSITIVITY: 80 percent
METHODOLOGY: Bidirectional sequencing of the MECP2 coding regions (exons 1-4) and intron-exon boundaries.
ANALYTICAL SENSITIVITY: 99 percent
ANALYTICAL SPECIFICITY: 99 percent
LIMITATIONS: Deep intronic mutations and large deletions/duplications will not be identified. Diagnostic errors can occur due to rare sequence variations.

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

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
RETT FGS Specimen	20-056-112500	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Rett Syndrome, Full Gene Sequencing	20-056-112500	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