ARUP LABORATORIES
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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	[redacted]/2017
Gender:	Male
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Angelman Syndrome and Prader-Willi Syndrome by Methylation-Specific MLPA

ARUP test code 3006247

AS-PWS Specimen	Whole Blood
AS-PWS Interpretation	Negative

Methylation Pattern: Normal
Copy Number Analysis: Normal

Both the maternally and paternally contributed Angelman Syndrome (AS)/Prader-Willi Syndrome (PWS) critical regions are present in this sample. Copy number analysis of this region was also normal. This result reduces, but does not exclude, a diagnosis of AS. Approximately 20 percent of individuals with AS will have normal methylation patterns. Within that group, approximately half will have pathogenic UBE3A variants, 1 percent will have a cytogenetically visible chromosomal rearrangement, and the remainder (approximately 10 percent) will have an unidentified genetic mechanism. This result greatly reduces the chance for PWS because 99 percent of individuals with PWS have abnormal methylation patterns.

Recommendations: Medical screening and management should rely on clinical finding and family history. Genetic consultation is recommended.

This result has been reviewed and approved by [redacted]

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

BACKGROUND INFORMATION: Angleman Syndrome and Prader-Willi Syndrome by Methylation-Specific MLPA

Characteristics of Angelman Syndrome (AS): Developmental delays by 6-12 months of age, seizures, microcephaly, movement or balance disorder, minimal or absent speech, and a distinctive behavioral phenotype, which includes a happy demeanor with frequent laughter, hand flapping, and excitability.

Characteristics of Prader-Willi Syndrome (PWS): Neonatal hypotonia, hyperphagia, obesity, global developmental delay, mild intellectual disability, hypogonadism, and a distinctive behavioral phenotype, which includes temper tantrums, stubbornness, manipulative behavior, and obsessive-compulsive behavior.

Prevalence: 1 in 15,000 for AS; 1 in 15,000 for PWS.

Inheritance: Varies, depending on the molecular genetic mechanism.

Cause: AS: Absence of maternal expression of the UBE3A gene. PWS: Absence of the paternally contributed PWS/AS critical region of chromosome 15q11.2-q13.

Molecular Genetic Mechanisms: AS: Microdeletions in 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 (10 percent). PWS: Microdeletions in the PWS/AS critical region (70-75 percent), maternal uniparental disomy of chromosome 15 (25-29 percent), imprinting center defect or balanced chromosome translocation (less than 1 percent).

Clinical Sensitivity: PWS: Over 99 percent. AS: 80 percent. Methodology: Methylation-specific multiplex ligation probe amplification (MLPA) of the AS/PWS critical region of chromosome 15q11.2-q13.

Analytical Sensitivity and Specificity: 99 percent for AS and PWS.

Limitations: Disease mechanisms causing AS that do not alter methylation patterns will not be detected. Diagnostic errors can occur due to rare sequence variations. This assay is not validated to detect increased copy number of 15q11.2-q13 nor determine parent of origin for duplications. This assay cannot distinguish between UPD or an imprinting defect for PWS or AS. AS and PWS mosaicism will not be assessed by this assay. Interpretation of this test result may be impacted if this patient has had an allogeneic stem cell transplantation. Methylation patterns may not be fully established in early gestation; thus, diagnostic testing on chorionic villus samples is not recommended.

This test was developed and its performance characteristics determined by ARUP Laboratories. It has not been cleared or approved by the US Food and Drug Administration. This test was performed in a CLIA certified laboratory and is intended for clinical purposes.

Counseling and informed consent are recommended for genetic testing. Consent forms are available online.

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
AS-PWS Specimen	25-356-119853	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
AS-PWS Interpretation	25-356-119853	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