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Jonathan R. Genzen, MD, PhD, Chief Medical Officer



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

Physician: Doctor, Example

**Patient: Patient, Example**

| | |
|---|---|
| **DOB** | [redacted]/2023 |
| **Gender:** | Female |
| **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: **AS Deletion** *

Methylation Pattern: Abnormal maternal methylation pattern
Copy Number Analysis: Deletion detected

Only the paternally contributed Angelman Syndrome (AS)/ Prader-Willi Syndrome (PWS) critical region is present in this sample. Copy number analysis of this region detected a deletion. This result is consistent with a diagnosis of AS due to a deletion in AS/PWS critical region.

Recommendations: Genetic consultation is indicated, including a discussion of medical screening and management.

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 | 25-335-152607 | 00/00/0000 00:00 | 00/00/0000 00:00 | 00/00/0000 00:00 |
| AS-PWS Interpretation | 25-335-152607 | 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