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

Physician: Doctor, Example

Patient: Patient, Example

DOB	10/10/2021
Gender:	Male
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Beckwith-Wiedemann Syndrome (BWS) and Russell-Silver Syndrome (RSS) by Methylation-Specific MLPA

ARUP test code 3001635

BWS-RSS Specimen	Whole Blood
Imprinting Center 1 Methylation	Normal
Imprinting Center 2 Methylation	Normal
Copy Number Analysis	Normal
BWS-RSS Interpretation	See Note

Negative for Beckwith-Wiedemann and Russell-Silver Syndrome
Imprinting Center 1 Methylation: Normal methylation
Imprinting Center 2 Methylation: Normal methylation
Copy Number Analysis: Normal

This sample demonstrates normal methylation of imprinting center 1 and 2 of the Beckwith-Wiedemann syndrome (BWS)/Russell-Silver syndrome (RSS) critical region. Copy number analysis of this region was also normal. This result reduces, but does not exclude, a diagnosis of BWS or RSS. Please see the background information included in this report for limitations of this assay.

Recommendations: Medical screening and management should rely on clinical findings 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: Beckwith-Wiedmann Syndrome (BWS) and Russell-Silver Syndrome (RSS) by Methylation-Specific MLPA
CHARACTERISTICS: Beckwith-Wiedemann syndrome (BWS) and Russell-Silver syndrome (RSS) is a phenotypically variable overgrowth syndrome associated with an increased risk for embryonal tumor development, neonatal hypoglycemia, macroglossia, macrosomia, hemihyperplasia, omphalocele, renal abnormalities, and ear creases or pits. RSS is characterized by pre- and postnatal growth deficiency, proportionate short stature, developmental delay, learning disabilities, limb-length asymmetry and distinctive faces.
PREVALENCE: BWS occurs 1 in 10,000-13,700 newborns; RSS 1 in 100,000 newborns.
INHERITANCE: BWS - 85 percent of cases are sporadic and 15 percent autosomal dominant; RSS - 60 percent of cases are sporadic, 40 percent unknown, rarely autosomal dominant or recessive.
PENETRANCE: RSS - complete; BWS - incomplete; individuals with a pathogenic CDKN1C variant will be asymptomatic if the variant is on the allele normally silenced due to imprinting.
CAUSE: BWS - 50 percent by loss of maternal methylation at imprinting center (IC)2, 20 percent by paternal uniparental disomy (UPD) of chromosome 11p15; 5 to 10 percent by pathogenic CDKN1C sequence variants, 5 percent by maternal methylation of IC1, 1 percent by chromosome rearrangements or duplications. RSS - 35 to 50 percent by paternal hypomethylation of IC1, 10 percent by maternal UPD of chromosome 7.
CLINICAL SENSITIVITY: 75 percent for BWS; 35-50 percent for RSS.
METHODOLOGY: Methylation-specific multiplex ligation probe amplification (MLPA).
ANALYTICAL SENSITIVITY AND SPECIFICITY: 99 percent.
LIMITATIONS: This assay determines methylation patterns of IC1 and IC2 for chromosome 11p15. Disease mechanisms causing BWS and RSS that do not alter methylation patterns, such as sequence variants in CDKN1C, maternal UPD of chromosome 7 or chromosomal translocations, and
inversions or duplications, will not be assessed. Diagnostic errors can occur due to rare sequence variations.

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

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.

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

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
BWS-RSS Specimen	24-116-401379	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Imprinting Center 1 Methylation	24-116-401379	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Imprinting Center 2 Methylation	24-116-401379	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Copy Number Analysis	24-116-401379	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
BWS-RSS Interpretation	24-116-401379	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

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