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PATIENT REPORT

Patient Age/Sex: Unknown

Specimen Collected: 04-Sep-23 16:49

Beckwith Wiedemann/Russell-Silver Synd | **Received: 05-Sep-23 16:51** **Report/Verified: 05-Sep-23 17:00**

Procedure	Result	Units	Reference Interval
BWS-RSS Specimen	Whole Blood		
Imprinting Center 1 Methylation	**Hypermethyl** *		
Imprinting Center 2 Methylation	**Hypomethyl** *		
Copy Number Analysis	Normal		
BWS-RSS Interpretation	See Note f1 i1		

Result Footnote

f1: BWS-RSS Interpretation

Positive for Beckwith-Wiedemann Syndrome
Imprinting Center 1 Methylation: Hypermethylation
Imprinting Center 2 Methylation: Hypomethylation
Copy Number Analysis: Normal

This sample demonstrates hypermethylation of imprinting center 1 and hypomethylation of imprinting center 2 of the Beckwith-Wiedemann syndrome (BWS)/Russell-Silver syndrome (RSS) critical region. Copy number analysis of this region was normal. This combination of findings is suggestive of paternal uniparental disomy of 11p15.5 and consistent with a diagnosis of BWS. If this individual has a negative family history and normal karyotype, then the recurrence risk is predicted to be very low.

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

This result has been reviewed and approved by [redacted]

Test Information

i1: BWS-RSS Interpretation

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.

Test Information

i1: BWS-RSS Interpretation

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.

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