Russell-Silver Syndrome: UPD7

Test Code: NM  
Turnaround time: 3 weeks  
CPT Codes: 81402 x1

Condition Description

Russell-Silver syndrome (RSS) is a disorder of growth characterized by intrauterine growth retardation with postnatal growth deficiency. Many patients have diminished subcutaneous fat and may experience hypoglycemia during infancy. Short stature typically presents between 2 and 10 years and is proportional. Bone age may be delayed. Serum growth hormone levels are typically normal and patients generally have normal growth velocity. Limb length asymmetry is common, and isolated relative hemi-symmetry, due to underdevelopment of the affected side, is reported. Children may be at risk for motor delays and learning disabilities, however typically do not have mental retardation. Other symptoms include gastrointestinal and genitourinary dysfunction. Gastroesophageal reflux is most common; however, esophagitis and food aversions are also reported. Many patients are considered failure to thrive. Congenital genitourinary disorders have been reported. Additional features include fifth finger clinodactyly, brachydactyly, and multiple cafe au lait spots. Suggested criteria for diagnosis include the following:

- IUGR with a birth weight >2 SD below the mean.
- Postnatal growth >2 SD below the mean for length.
- Proportional short stature with preservation of occipitofrontal head circumference.
- Facial features include prominent forehead, small triangular face & narrow chin.
- Limb, body, or facial asymmetry.
- Additional features that can be diagnostically helpful include fifth finger clinodactyly, brachydactyly, cafe au lait spots, and arm span less than height.

RSS is a heterogeneous disorder that may present a clinical spectrum rather than a discrete clinical entity. The occurrence of RSS is thought to be sporadic in most cases, and is seen in all racial and ethnic groups. Defects in gene expression are associated with RSS. It is estimated that between 20-35% of RSS are due to hypomethylation of the differentially methylated region (DMR1) at the H19 gene (located on chromosome 11p15). The recurrence risk of RSS due to hypomethylation of H19 is estimated to be very low. Approximately 10% of RSS is due to maternal uniparental disomy (UPD) for chromosome 7. Some forms of RSS are inherited in autosomal dominant or autosomal recessive patterns, for which genes have not been identified. No single explanation can account for the phenotypic heterogeneity seen in patients with RSS.

References:


Indications

This test is indicated for:

- Individuals with a clinical diagnosis of RSS.
- Individuals with limb asymmetry combined with prenatal and postnatal growth delay.

Methodology

A DNA methylation specific PCR assay targeting the GRB10 and PEG1/MEST genes on the short and long arms of chromosome 7, respectively, is used to test for maternal uniparental disomy of chromosome 7 (matUPD7). Parental samples are NOT required for matUPD7 analysis, but may be requested to confirm a diagnosis.

Detection

Hypomethylation of H19 is expected to detect up to 35% of individuals with a clinical diagnosis of RSS. Maternal uniparental disomy (UPD) for chromosome 7 will be detected in an additional 10% of patients with a clinical diagnosis, for a total detection of up to 45%.

Specimen Requirements

Submit only 1 of the following specimen types

Type: DNA, Isolated

Specimen Requirements:

- Microtainer
- 3µg
- Isolation using the Perkin Elmer™Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping:

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Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

**Type: Whole Blood (EDTA)**

**Specimen Requirements:**
EDTA (Purple Top)
Infants and Young Children (2 years of age to 10 years old): 3-5 ml
Older Children & Adults: 5-10 ml
Autopsy: 2-3 ml unclotted cord or cardiac blood

**Specimen Collection and Shipping:**
Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

**Related Tests**

- Standard Blood Chromosome Analysis (CA, CB) and the Chromosomal Microarray, EmArray 60K (VA) are available for children with growth and developmental delay.