The University of Chicago Genetic Services Laboratories

5841 S. Maryland Ave., Rm. G701, MC 0077, Chicago, Illinois 60637
Toll Free: (888) UC GENES (888) 824 3637
Local: (773) 834 0555 FAX: (773) 702 9130
ucgslabs@genetics.uchicago.edu dnatesting.uchicago.edu
CLIA #: 14D0917593 CAP #: 18827-49

UPD7 Testing for Russell-Silver Syndrome

Clinical Features:

A clinical diagnosis of Russell-Silver syndrome (RSS) is based upon the following features:

- Intrauterine growth retardation (IUGR)
- Postnatal growth delay (<3%)
- Short stature accompanied by normal skeletal survey and frequently delayed bone age
- Normal head circumference
- Typical appearance includes a triangular face with small chin and prominent forehead
- Limb assymetry

The presence of café-au-lait spots, fifth finger clinodactly and/or brachydactyly can assist in diagnosing RSS. Gastrointestinal prolems are common in RSS, including gastroesophageal reflux disease, esophagitis, food aversion, and failure to thrive. Other features associated with RSS are hypotonia and hypogenitalism or cryptorchidism in males. Although some individuals have reportedly normal intelligence, cognitive development can vary with individuals and include developmental delay and learning disabilities. Due to the short stature of individuals with RSS, the administration of growth hormone has been suggested. Treatment with GH remains controversial as RSS individuals are not GH deficient and studies have shown little increase in expected adult height (1).

Molecular Genetics:

Most cases of RSS are of unknown cause. Approximately 7-10% of cases of RSS are caused by maternal uniparental disomy (UPD) for chromosome 7 (1). Whereas maternal UPD of chromosome 7 gives rise to RSS, normal growth and development has been seen in individuals with paternal UPD 7 (2). Multiple imprinted genes (*PEG1/MEST*, *γ2-COP* and *GRB10*) have been identified on chromosome 7 although their role in RSS is unknown (3). Mutations in *GRB10* have been reported in two patients with RSS (4). Recently, researchers discovered a maternal duplication or an epigenetic mutation of the imprinting center region in 11p15 in approximately 35% of individuals with RSS (5). In addition, RSS has been reported in individuals with various chromosomal abnormalities. No genotype-phenotype correlations have been observed in RSS (1).

Inheritance:

Because it is difficult to confirm the diagnosis of RSS, the incidence remains unknown. Multiple inheritance patterns have been seen including maternal uniparental disomy (UPD) of chromosome 7, autosomal recessive, autosomal dominant or X-linked inheritance. UPD is sporadic, thus, the recurrence risk is not above general population risk.

Indications for Testing:

Prenatal testing for RSS may be indicated in the following situations:

- Mosaic trisomy 7 or a marker chromosome is detected in a prenatal sample
- Trisomy 7 is detected in chorionic villi, followed by a normal karyotype on amniocytes.
- Pregnancies in which one parent carries a balanced translocation involving chromosome 7 and the fetus is found to have a normal karyotype
- Pregnancies affected with a balanced translocation involving chromosome 7.

Clinical features suggestive of Russell-Silver syndrome

Additional Resources:

Russell-Silver Syndrome Support
Website: www.russell-silversupport.com
Email: support@russell-silversupport.com

Test methods:

We offer UPD testing for chromosome 7 by microsatellite analysis comparing both parents and the child or fetus. In order for UPD to be determined, a significant number of informative microsatellite markers must be obtained. Although testing is possible if only one parent is available, the chance of obtaining a significant number of informative markers is decreased. Sample submission paperwork and instructions are included with this packet.

UPD 7 testing

Sample specifications:	3-10 cc of blood from the patient and parents in purple top (EDTA) tubes
Cost:	$540 (total for a patient's and both parents' blood samples)
CPT codes:	81402
Turn-around time:	2-4 weeks

Prenatal Testing

Sample specifications:	2 T-25 flasks of cultured chorionic villi or amniocytes
Cost:	$690 (total for a prenatal sample and both parents' blood samples)
CPT codes:	81402
Turn-around time:	1-2 weeks

Results:

Results, along with an interpretive report, will be faxed to the referring physician. Additional reports will be provided as requested. All abnormal results will be reported by telephone.

References:

1. Saal H. Russell-Silver Syndrome. In: Pagon R, Bird T, Dolan C, eds. GeneReviews [Internet]. Seattle: University of Washington, 2002.
2. Höglund P, Holmberg C, de la Chapelle A et al. Paternal isodisomy for chromosome 7 is compatible with normal growth and development in a patient with congenital chloride diarrhea. Am J Hum Genet 1994: 55: 747-752.
3. Hannula K, Lipsanen-Nyman M, Kontiokari T et al. A narrow segment of maternal uniparental disomy of chromosome 7q31-qter in Silver-Russell syndrome delimits a candidate gene region. Am J Hum Genet 2001: 68: 247-253.
4. Yoshihashi H, Maeyama K, Kosaki R et al. Imprinting of human GRB10 and its mutations in two patients with Russell-Silver syndrome. Am J Hum Genet 2000: 67: 476-482.
5. Eggermann T, Schönherr N, Meyer E et al. Epigenetic mutations in 11p15 in Silver-Russell syndrome are restricted to the telomeric imprinting domain. J Med Genet 2006: 43: 615-616.

Committed to CUSTOMIZED DIAGNOSTICS, TRANSLATIONAL RESEARCH & YOUR PATIENTS' NEEDS