Clinical Features:
Sotos syndrome is characterized by characteristic facial features, developmental delay, and increased height and head circumference. Other features may include: neonatal jaundice, scoliosis, seizures, strabismus, conductive hearing loss, congenital heart defects, renal anomalies, and behavioral problems (1).

Inheritance:
Sotos syndrome is an autosomal dominant condition that occurs in 1 in 14,000 live births (1). More than 95% of cases appear to be de novo. Recurrence risk for unaffected parents of an isolated case is <1%. However, due to the variability in expression, parents of affected individuals may be carriers. Recurrence risk for affected individuals and carrier parents is 50%.

Molecular Genetics:
Microdeletions and mutations of the NSD1 gene have been identified in approximately 80% of patients with a clinical diagnosis of Sotos syndrome (2, 3). Recently, intragenic deletions of one or more exons of NSD1 have been reported in approximately 5% of patients with a clinical diagnosis of Sotos syndrome (4). These intragenic deletions/duplications will not be detected by FISH or CGH analysis.

Additional Resources:
Sotos Syndrome Support Association
P.O. Box 4626
Wheaton IL 60187
Phone: 888-246-7772
Email: sssa@well.com
www.well.com/sssa/

Test methods:
We offer full gene sequencing of the entire coding region for the NSD1 gene. We also offer deletion/duplication analysis of the NSD1 gene by MLPA or oligonucleotide array-CGH to identify deletions/duplications of one or more exons. Partial exonic copy number changes and rearrangements of less than 400 bp may not be detected by array-CGH. Array-CGH will not detect low-level mosaicism, balanced translocations, inversions, or point mutations that may be responsible for the clinical phenotype. The sensitivity of this assay may be reduced when DNA is extracted by an outside laboratory. For best results, please provide a fresh blood sample for this testing.

NSD1 sequencing
Sample specifications: 3 to 10 cc of blood in a purple top (EDTA) tube
Cost: $1,990
CPT codes: 81406
Turn-around time: 4 - 6 weeks

NSD1 intragenic deletion/duplication analysis
Sample specifications: 3 to 10 cc of blood in a purple top (EDTA) tube
Cost: $1,000
CPT codes: 81405
Turn-around time: 4 weeks

Testing for a known mutation in additional family members by sequence analysis
Sample specifications: 3 to 10 cc of blood in a purple top (EDTA) tube
Cost: $390
CPT codes: 81403
Turn-around time: 3-4 weeks
Prenatal testing for a known mutation by sequence analysis
Sample specifications: 2 T25 flasks of cultured cells from amniocentesis or CVS or 10 mL of amniotic fluid
Cost: $540
CPT codes: 81403
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:
2. Douglas J, Hanks S, Temple IK et al. NSD1 mutations are the major cause of Sotos syndrome and occur in some cases of Weaver syndrome but are rare in other overgrowth phenotypes. Am J Hum Genet 2003: 72: 132-143.