Clinical Features:
Patients with Schinzel-Giedion syndrome (SGS) [OMIM #269150] have characteristic facial features, midface retraction, skull anomalies abnormal genitalia, and cardiac and renal malformations. SGS is a lethal condition, as most patients die in infancy of respiratory failure or infections. Most patients have profound developmental delay. Characteristic facial features include large fontanelles, prominent forehead, hypertelorism, shortened and retracted midface, macroglossia, and a short neck. Failure to thrive, seizures, vision and hearing problems are also very common. Patients with SGS also have an increased risk for tumors, particularly neuroepithelial neoplasia (1).

Lehman (2008) reviewed 46 reported cases of SGS and proposed the following diagnostic criteria:

- **Mandatory features:**
  - Developmental delay
  - Facial phenotype
    - prominent forehead
    - midface retraction
    - short upturned nose
  - Hydronephrosis

- **Skeletal features (at least 2 of following):**
  - Sclerotic skull base,
  - Wide occipital suture
  - Increased cortical density or thickness
  - Broad ribs (at least 2)

These diagnostic criteria yield 100% sensitivity for the 46 reviewed cases of SGS (1).

Molecular Genetics:
Mutations of the **SETBP1** [OMIM #611060] gene were identified in four patients with SGS by whole exome sequencing (2). Additional sequencing of the **SETBP1** gene in individuals with SGS identified mutations in 8/9. All 13 patients in this study met Lehman’s above diagnostic criteria (2). **SETBP1** has 6 coding exons and all mutations reported to date have been *de novo* missense mutations within a stretch of 11 base pairs in exon 4 (2, 3).

Inheritance:
**SETBP1** mutations are inherited in an autosomal dominant pattern. Most cases appear to be *de novo*. Germine mosaicism is hypothesized to explain rare sibling occurrences; recurrence risk for unaffected parents of an isolated case is approximately 1-5%. Recurrence risk for affected individuals and carrier parents is 50%.

Test methods:
We offer mutation analysis of all coding exons and intron/exon boundaries of **SETBP1** by direct sequencing of amplification products in both the forward and reverse directions. Deletion/duplication analysis is performed by oligonucleotide array-CGH. 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.

**SETBP1 sequencing analysis**
- Sample specifications: 3 to 10 cc of blood in a purple top (EDTA) tube
- Cost: $1675
- CPT codes: 81404
- Turn-around time: 4 - 6 weeks
**SETBP1 deletion/duplication analysis**

Sample specifications: 3 to 10 cc of blood in a purple top (EDTA) tube  
Cost: $1000  
CPT codes: 81403  
Turn-around time: 4 weeks  
*Note: The sensitivity of our assay may be reduced when DNA is extracted by an outside laboratory.*

**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:**


*Committed to CUSTOMIZED DIAGNOSTICS, TRANSLATIONAL RESEARCH & YOUR PATIENTS’ NEEDS*