Clinical Features:
Goldberg-Shprintzen megacolon syndrome (GOSHS, OMIM #609460) is a multiple malformation disorder characterized by Hirschsprung megacolon, microcephaly, hypertelorism, submucous cleft palate, short stature, and learning problems (1). Some reported patients also have iris coloboma, and bilateral generalized polymicrogyria malformation of the cerebral cortex (2, 3). The distinctive facial features include sparse scalp hair, synophrys, arched eyebrows, hypertelorism, ptosis, large ears and prominent nose (4).

Differential Diagnosis:
- Mowat-Wilson syndrome (OMIM # 235730), has phenotypic overlap with GOSHS but is a genetically distinct disorder caused by mutations in the ZEB2 gene (5). Distinctive features of Mowat-Wilson syndrome include epilepsy, cortical malformations and agenesis of the corpus callosum which have not been well characterized in patients with GOSHS.
- Despite some resemblance to GOSHS, Shprintzen-Goldberg craniosynostosis syndrome (SGS, OMIM #182212) tends to associate with craniofacial or skeletal abnormalities, and at least in some cases, mutations in the FBN1 gene have been reported in affected individuals (6).
- Velocardiofacial syndrome (VCFS, OMIM #192430) (VCFS) is caused by a 1.5- to 3.0-Mb deletion of chromosome 22q11.2. It is associated with a highly variable phenotype, including frequent features such as cleft palate, cardiac anomalies, typical facies, learning disabilities, and lack of or underdeveloped thymus and parathyroid glands (7).

Molecular Genetics:
Mutations in the KIAA1279 gene (OMIM #609367) have been identified in patients with GOSHS and homozygous nonsense mutations have been reported in 10 affected individuals in two families [3]. The KIAA1279 gene maps to 10q22.1 and is likely important in both enteric and central nervous system development as it is highly expressed in heart, brain, reproductive, spinal cord regions. It has 7 exons, spanning 28 kb, with 2 tetratricopeptide repeats (TPR).

Inheritance:
GOSHS is inherited in an autosomal recessive condition. Parents of an affected child are likely carriers. Recurrence risk for carrier parents is 25%.

Test methods:
We offer full gene sequencing of all 7 coding exons and intron/exon boundaries 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.

KIAA1279 sequencing analysis
Sample specifications: 3 to 10 cc of blood in a purple top (EDTA) tube
Cost: $1000
CPT codes: 81405
Turn-around time: 4 - 6 weeks
**KIAA1279 deletion/duplication analysis**

Sample specifications: 3 to 10 cc of blood in a purple top (EDTA) tube  
Cost: $1000  
CPT codes: 81404  
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**