Clinical Features:
CHIME syndrome [OMIM #280000], also known as Zunich neuroectodermal syndrome, is a rare multisystemic disorder characterized by Coloboma, Heart defects, Ichthyosiform dermatosis, Mental retardation and Ear anomalies (1). Affected individuals typically have distinctive facial features, which include hypertelorism, brachycephaly, epicanthal folds and a broad nasal root (2). Other clinical findings include abnormal growth, genitourinary abnormalities, seizures, and feeding difficulties (1).

Inheritance:
CHIME syndrome is inherited in an autosomal recessive manner. The recurrence risk for parents of an affected child is 25%.

Molecular Genetics:
Ng et al. (2012) identified compound heterozygous mutations in the PIGL gene (phosphatidylinositol glycan, class L) [OMIM #605947] in 6/6 (100%) patients with a clinical diagnosis of CHIME syndrome. To date, mutations identified by sequencing have included frameshift, nonsense, splice site and missense mutations (1). PIGL has 7 coding exons and is located at 17p11.2. The PIGL gene codes for an enzyme which localizes to the endoplasmic reticulum and is involved in the glycosylphosphatidylinositol (GPI) biosynthesis pathway (1).

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

**PIGL 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

**PIGL 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.*

**Targeted analysis for a known sequence change in additional family members**
- 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**
- Sample specifications: 2 T25 flasks of cultured cells from amnio or CVS or 10ml 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: