THE UNIVERSITY OF CHICAGO | Genetic Services Laboratories

CHIME syndrome: mutation analysis of *PIGL*

Clinical Features:

CHIME syndrome [OMIM #280000], also known as Zunich neuroectodermal syndrome, is a rare multisystemic disorder characterized by Colobomas, 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.

Our CNV detection algorithm was developed and its performance determined for the sole purpose of identifying deletions and duplications within the coding region of the gene(s) tested. Partial exonic copy number changes and rearrangements of less than 400 bp may not be detected by this methodology. Regions of high homology and repetitive regions may not be analyzed. This methodology will not detect low level mosaicism, balanced translocations, inversions, or point mutations that may be responsible for the clinical phenotype. The sensitivity of our deletion/duplication assay may be reduced when DNA extracted by an outside laboratory is provided.

PIGL mutation analysis

Sample specifications:	3 to10 cc of blood in a purple top (EDTA) tube
Cost:	$1000
CPT codes:	81404
	81405
Turn-around time:	4 weeks

Note: The sensitivity of our assay may be reduced when DNA is extracted by an outside laboratory.

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.

For more information about our testing options, please visit our website at dnatesting.uchicago.edu or contact us at 773-834-0555.

References:

1. Ng BG, Hackmann K, Jones MA et al. Mutations in the glycosylphosphatidylinositol gene PIGL cause CHIME syndrome. Am J Hum Genet 2012: 90: 685-688.
2. Sidbury R, Paller AS. What syndrome is this? CHIME syndrome. Pediatr Dermatol 2001: 18: 252-254.

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