THE UNIVERSITY OF CHICAGO | Genetic Services Laboratories

FOXG1 Analysis for the Congenital Variant of Rett Syndrome

Clinical Features:

Rett syndrome [OMIM #312750] is a progressive neurodevelopmental disorder, primarily affecting females. Classic Rett syndrome is characterized by acquired microcephaly, loss of purposeful hand movements, and autistic behaviors, following a period of normal growth and development. There are several variants of Rett syndrome including preserved speech variant, early-onset seizures, and congenital. Patients with the congenital variant of Rett syndrome have features similar to classic Rett syndrome, but hypotonia and severe developmental delay starts in the first months of life.

Molecular Genetics:

Abnormalities of the *FOXG1* [OMIM #164874] gene, or forkhead box G1, have been identified in patients with the congenital variant of Rett syndrome (1-3). *FOXG1* has one coding exon and is located at 14q12. It encodes a brain-specific transcriptional repressor. Ariani F, et al [2008] studied 53 patients with classic Rett syndrome and the variant forms of Rett syndrome. In their study, 2/2 patients with the congenital variant of Rett syndrome had truncating mutations in *FOXG1*. None of the other patients were found to have mutations or deletions in *FOXG1 (2)*. Two additional patients with a chromosomal translocation involving *FOXG1 (3)* and a 3 Mb deletion of 14q12 including *FOXG1 (3)* have also been described.

Inheritance:

FOXG1 mutations are inherited in an autosomal dominant pattern. All reported cases were *de novo*. Recurrence risk for unaffected parents of an isolated case is low (<1%), but germline mosaicism is possible.

Additional Resources:

International Rett Syndrome Association
9121 Piscataway Road, #2B
Clinton, MD 20735
Phone: 1-800-818-RETT
Fax: 301-856-3336
Email: admin@rettsyndrome.org
www.rettsyndrome.org

Test methods:

We offer mutation analysis of the single coding exon and intron/exon boundaries of *FOXG1* by direct sequencing of amplification products in both the forward and reverse directions. We also offer deletion/duplication analysis of the *FOXG1* 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.

FOXG1 sequencing analysis

Sample specifications:	3 to 10cc of blood in a purple top (EDTA) tube
Cost:	$550
CPT codes:	81404
Turn-around time:	4 weeks

FOXG1 deletion/duplication analysis

Sample specifications:	3 to 10cc of blood in a purple top (EDTA) tube
Cost:	$1000
CPT codes:	81402
Turn-around time:	4 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.

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

References:

1. Shoichet SA, Kunde SA, Viertel P et al. Haploinsufficiency of novel FOXG1B variants in a patient with severe mental retardation, brain malformations and microcephaly. Hum Genet 2005: 117: 536-544.
2. Ariani F, Hayek G, Rondinella D et al. FOXG1 is responsible for the congenital variant of Rett syndrome. Am J Hum Genet 2008: 83: 89-93.
3. Papa FT, Mencarelli MA, Caselli R et al. A 3 Mb deletion in 14q12 causes severe mental retardation, mild facial dysmorphisms and Rett-like features. Am J Med Genet A 2008: 146A: 1994-1998.

Committed to CUSTOMIZED DIAGNOSTICS, TRANSLATIONAL RESEARCH & YOUR PATIENTS' NEEDS