**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.retsyndrome.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
**FOGX1 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:**


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