

The University of Chicago Genetic Services Laboratories



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FOXG1 Sequencing 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* [1] 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:

The University of Chicago Laboratory offer sequencing of the single coding exon and intron/exon boundaries of *FOXG1* by direct sequencing of amplification products in both the forward and reverse directions.

FOXG1 sequencing:

Sample specifications:	3 to 10cc of blood in a purple top (EDTA) tube
Cost:	\$400
CPT codes:	83891, 83898, 83904, 83912
Turn-around time:	4 - 6 weeks

Testing for a known mutation in additional family members

Sample specifications:	3 to 10 cc of blood in a purple top (EDTA) tube
Cost:	\$390
CPT codes:	83891, 83898 x 2, 83894, 83912
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:	\$590
CPT codes:	83891, 83898 x 2, 83894, 83912, 99051
Turn-around time:	1-2 weeks

Results

You will be informed of the results of your case as soon as it has been completed. Results, along with an interpretive report, will be faxed and mailed to the referring physician. Additional reports will be provided as requested. All abnormal results will be reported by telephone.

Molecular Diagnostics Laboratory Faculty and Staff:

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References:

1. Shoichet SA, et al. Haploinsufficiency of novel *FOXP1B* variants in a patient with severe mental retardation, brain malformations and microcephaly (2005) *Hum Genet* 117: 536-544.
2. Ariani F, et al. *FOXP1* is responsible for the congenital variant of Rett syndrome (2008) *Amer J Hum Genet* 83: 1-5.
3. Pape FT, et al. A 3 Mb deletion in 14q12 causes severe mental retardation, mild facial dysmorphism and Rett-like features (2008) *Am J Med Genet* 146A(15): 1994-8.

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