

# The University of Chicago Genetic Services Laboratories



5841 S. Maryland Ave., Rm. L035, MC 0077, Chicago, Illinois 60637  
Toll Free: (888) UC GENES (888) 824 3637  
Local: (773) 834 0555 FAX: (773) 834 0556  
ucgslabs@genetics.uchicago.edu www.genes.uchicago.edu  
CLIA #: 14D0917593 CAP #: 18827-49

## GPR56 Sequencing for Bilateral Frontoparietal Polymicrogyria

### Clinical Features:

Bilateral frontoparietal polymicrogyria (BFPP) [OMIM #606854] is characterized by moderate-severe mental retardation, seizures, dysconjugate gaze, and characteristic radiological findings. Piao X, et al [2005] suggest the following diagnostic criteria: (1) moderate-severe mental retardation; (2) delay of motor development; (3) seizures; (4) cerebellar signs, primarily ataxia; (5) dysconjugate gaze; (6) bilateral polymicrogyria (more accurately “cobblestone malformation”) with anterior to posterior gradient; (7) bilateral patchy white matter signal changes; and (8) brainstem and cerebellar hypoplasia [1]. The “polymicrogyria” is actually atypical and more closely resembles the brain malformation seen in muscle-eye-brain disease, known as a “cobblestone malformation”. Developmental delay and gaze issues present in early childhood, whereas seizures may not begin until after 5 years of age. Patients with *GPR56*-associated BFPP do not have findings outside of the central nervous system.

*Dr. William Dobyns at the University of Chicago is available to review MRI scans and give recommendations regarding genetic testing. Please contact Mary King at 773-702-8247 to arrange this, if desired.*

### Molecular and Biochemical Genetics:

Mutations of the *GPR56* [OMIM #604110] gene, or G-protein coupled receptor 56, have been identified in patients with BFPP [2]. *GPR56* has 13 coding exons. It appears to be necessary for human cerebral cortical development and patterning. All reported patients, to date, have homozygous mutations. Piao X, et al [2005] studied patients with BFPP along with some patients with other polymicrogyria syndromes. All 29 patients with BFPP were found to be homozygous for *GPR56* mutations. However, no patients without the BFPP cortical distribution or without both white matter and posterior fossa changes were found to mutations in *GPR56* [1].

### Inheritance:

*GPR56*-related BFPP is inherited in an autosomal recessive pattern. Parents of an affected child are most likely obligate carriers. Recurrence risk for carrier parents is 25%.

### Additional Resources:

**The Lissencephaly Network** [www.lissencephaly.org](http://www.lissencephaly.org)  
Phone: 260-432-4310 Email: [lissnet@lissencephaly.org](mailto:lissnet@lissencephaly.org)

### The Brain Malformation Research Project at The University of Chicago

William B. Dobyns, Principal Investigator  
Contact Mary King at 773-702-8247

### Test methods:

The University of Chicago Laboratory offers mutation analysis of all 13 coding exons and intron/exon boundaries of *GPR56* by direct sequencing of amplification products in both the forward and reverse directions.

*Please, send a completed GPR56 Clinical Checklist and patient consent form with each sample.*

This information will be used to aid in interpretation of the test result. The clinical data form, along with the test result, will be shared with Dr. Dobyns and stored anonymously in a *GPR56* database. Patients with BFPP, with or without *GPR56* gene mutations, can enroll in Dr. Dobyns' research study.

#### GPR56 sequencing:

Sample specifications:	3 to 10cc of blood in a purple top (EDTA) tube
Cost:	\$1500
CPT codes:	83891, 83898 x 4, 83904 x 6, 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.

### **Laboratory Faculty and Staff:**

Soma Das, Ph.D.  
Director, Molecular Genetics Laboratory  
ABMG Certified Molecular Geneticist

Stuart Schwartz, Ph.D.  
Director, Cytogenetics Laboratory  
ABMG Certified Cytogeneticist

Eden Haverfield, Ph.D.  
Assistant Director, Molecular Genetics Laboratory

Melissa Dempsey, M.S.  
Certified Genetic Counselor

Darrel J. Waggoner, M.D.  
Clinical Advisor  
ABMG Certified Clinical Geneticist

William B. Dobyns, M.D.  
Clinical Advisor  
ABMG Certified Clinical Geneticist

### **References:**

1. Piao X, et al. Genotype-phenotype analysis of human frontoparietal polymicrogyria syndromes (2005) *Ann Neurol* 58:680-7.
2. Piao X, et al. G protein-coupled receptor-dependent development of human frontal cortex (2004) *Science* 303: 2033-36.

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