



## The University of Chicago Genetic Services Laboratories

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### Genetic Testing for Polymicrogyria

#### Information for Non-genetics Professionals

##### 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.*

##### Etiology and Inheritance:

*GPR56*-related BFPP is caused by mutations of the *GPR56* (G-protein coupled receptor 56) gene. Approximately 100% of patients with BFPP are homozygous for *GPR56* mutations. Less severe or incomplete phenotypes due to *GPR56* mutations are possible, but have not yet been reported. *GPR56*-related BFPP is inherited in an autosomal recessive pattern. Parents of an affected child are most likely non-symptomatic obligate carriers. Recurrence risk for carrier parents is 25%.

##### Genetic Testing:

The first person to be tested in any family should be the individual thought to have *GPR56*-related BFPP. Testing is done by direct sequencing of the 13 coding exons of the *GPR56* gene. When two changes in *GPR56* are found in the person with BFPP, testing other family members, even during a pregnancy, is easy and fast because we know where to look. Testing is now available at The University of Chicago Genetics Services Laboratory.

##### Reasons for genetic testing for a *GPR56* defect:

- confirm the diagnosis
- check if other family members are carriers
- provide accurate information and counseling resources for future pregnancies
- provide information during a pregnancy regarding possible *GPR56*-related BFPP in the baby

##### Test ordering and Billing:

A test requisition form and consent form are required for testing. You will also be asked to fill out a clinical data form about each patient and submit it with the blood sample. This information will be used to aid in test interpretation. The clinical data form, along with the test result, will be shared with Dr. Dobyns and stored anonymously in a *GPR56* database. These forms can be found on the lab website or by calling the lab.

All insurance companies are different, but most of them should cover at least part of the cost of testing. We recommend that a parent or physician’s office contact the patient’s insurance company with the specific CPT codes (below) to learn more about the specific coverage prior to testing. The University of Chicago will bill the patient’s insurance company, hospital or referring laboratory. The patient may receive a bill for any amount not covered by the insurance company. If the patient does not have medical insurance and we cannot bill their institution, we will require payment by check or credit card before beginning testing.

#### 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

### **Possible Results of Genetic Testing:**

- **2 mutations detected:** finding two mutations will confirm a diagnosis of *GPR56*-related BFPP. When two changes have been identified in an affected individual then it allows for easy testing of other family members, who may choose to be tested.
- **1 mutation detected:** finding one mutation does not confirm or rule out the possibility of *GPR56*-related BFPP. It is likely that this patient has another, unidentified mutation, in the *GPR56* gene that was not detected by our sequence analysis assay. Dr. Dobyns is conducting research to look for other causes of BFPP or similar conditions. Please contact Mary King at 773-702-8247 for more information about these studies.
- **No mutation detected:** not finding a mutation rules out the diagnosis of *GPR56*-related BFPP. Dr. Dobyns is conducting research to look for other causes of BFPP or similar conditions. Please contact Mary King at 773-702-8247 for more information about these studies.
- **Variant of unknown significance:** A small number of patients will have a change in the gene, but we are not sure whether that change causes *GPR56*-related BFPP or not. Testing parents for this change may give us more information.

### **Reporting of Results:**

Results, along with an interpretive report, will be faxed and mailed to the referring physician as soon as they are complete. All abnormal results will be reported by telephone.

### **Research studies:**

Patients with or without *GPR56* gene mutations can enroll in Dr. Dobyns' research study for further studies. Please contact Mary King at 773-702-8247 for more information about these studies.

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

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

Stuart Schwartz, Ph.D.  
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