# The University of Chicago Genetic Services Laboratories

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# Genetic Testing for Autosomal Recessive Primary Microcephaly

***Information for Patients and Families***

## What do I need to know about genetic testing for autosomal recessive primary microcephaly for my child?

Some forms of microcephaly (small head size) are caused by a change in someone's DNA. People with autosomal recessive primary microcephaly (MCPH) have microcephaly at birth and throughout life. They have learning problems and possibly seizures, but no other neurological findings. Parents of a child with autosomal recessive primary microcephaly have a 25% chance of having another child with autosomal recessive primary microcephaly with each pregnancy. *ASPM* is one gene that causes MCPH. There are a number of other genes, including *ARFGEF2, CASC5, CDK5RAP2, CDK6, CENPJ, CEP63, CEP135, CEP152, MCPH1, MED17, NDE1, PHC1, PNKP, SLC25A19, STAMBP, STIL, WDR62* and *ZNF335.* This blood test may prove that your child has autosomal recessive primary microcephaly. There is also a chance that the test will find something that we do not understand. This information sheet will provide more details about autosomal recessive primary microcephaly and this testing. Please talk to a genetic counselor, if you have more questions about testing.

## What is autosomal recessive primary microcephaly?

People with autosomal recessive primary microcephaly have microcephaly at birth and throughout life. They have learning problems and possibly seizures, but no other neurological findings. They may be shorter than other individuals, but usually have normal weight and appearance.

## What causes autosomal recessive primary microcephaly?

Some forms of microcephaly are caused by a change in someone's DNA. Autosomal recessive primary microcephaly can be caused by two changes (mutations) in the *ASPM* (abnormal spindle-like, microcephaly-associated) gene. We each have two copies of the *ASPM* gene. Some children with autosomal recessive primary microcephaly have a change in each copy of the *ASPM* gene that we can find by sequencing (reading the gene). Genes are written instructions to make proteins. When there is a change in the instructions, the protein may not be made or may not work properly. Thus, both copies of the ASPM protein are not working properly in these kids. Autosomal recessive primary microcephaly can also be caused by changes in other genes, including *ARFGEF2, CASC5, CDK5RAP2, CDK6, CENPJ, CEP63, CEP135, CEP152, MCPH1, MED17, NDE1, PHC1, PNKP, SLC25A19, STAMBP, STIL, WDR62* and *ZNF335.* These genes are included in the Autosomal Recessive Primary Microcephaly Tier 2 Sequencing Panel.

## Will we have another child with autosomal recessive primary microcephaly?

If a child is found to have two changes in the *ASPM* gene or one of the other genes in the Autosomal Recessive Primary Microcephaly Tier 2 Sequencing Panel, that child's parents are most likely carriers. This means that they have one normal copy of the gene and one copy with a change. They do not have any problems because one normal copy of the gene is enough. However, they can pass the changed copy down in each pregnancy. If both parents pass their changed copy to their child, the child will have autosomal recessive primary microcephaly. This is a process that we cannot control. Parents of a child with autosomal recessive primary microcephaly have a 25% chance of having another child with autosomal recessive primary microcephaly with each pregnancy.

## Can my child be tested? Can I be tested? Can my family members be tested?

The first person to be tested in any family is the individual with autosomal recessive primary microcephaly. Testing for mutations in a gene is complex. It is like reading a very long book and looking for two spelling mistakes. You may read the whole book and miss one or both "typos," however when you do find them, then it is easy to test other family members (i.e. you know that a change is on page 875 in the second paragraph). Once the changes are found in the person with autosomal recessive primary microcephaly, testing other family members, even during a pregnancy, is easier because we know where to look. Testing is now available at The University of Chicago Genetics Services Laboratory.

## Why should I consider genetic testing for autosomal recessive primary microcephaly?

Genetic testing may confirm the diagnosis of autosomal recessive primary microcephaly in your child. Genetic testing may provide information and resources for future pregnancies. Testing may also be done during a pregnancy to predict autosomal recessive primary microcephaly in the baby.

## What are the chances that this test will find something on my child?

A genetics doctor or neurologist should decide if your child meets all of the findings for autosomal recessive primary microcephaly. If so, there is about a 40% chance that your child will have at least one change in *ASPM*. If the *ASPM* test is negative, you and your doctor may discuss ordering the Autosomal Recessive Primary Microcephaly Tier 2 Sequencing and Deletion/Duplication Panels. The chance that your child has a change found by this second test is extremely low, but possible.

## What does it mean for my child if they find two changes? What does it mean for our family?

Finding two changes in one of these genes means that the cause of your child's autosomal recessive primary microcephaly has been identified. You have a 25% chance of having another child with autosomal recessive primary microcephaly with each pregnancy. Other family members may be tested, if they choose to.

## What does it mean if they find one change?

Finding only one change in a patient with microcephaly means that that particular gene is the likely cause of your child's autosomal recessive primary microcephaly. It is likely that your child has a second change in this gene that we cannot find with our test. You probably have a 25% chance of having another child with autosomal recessive primary microcephaly with each pregnancy, however future testing is difficult because we don't know both changes.

## What does it mean for my child if they don't find a change?

Not finding a change means that these genes are not causing your child's autosomal recessive primary microcephaly. Another gene or other factors may be the cause. Without finding the exact cause, we cannot estimate the risk to future pregnancies.

## What does it mean for my child if they find a variant of unknown significance?

Some patients will be found to have a change in the gene, but we are not sure what that change means.

## How do I get my child tested?

We recommend that a genetic doctor or genetic counselor help you order the test for your child. If you think your child may have autosomal recessive primary microcephaly, you should make an appointment with someone that works in genetics. This can be made through your local physician or hospital. They can order the testing. If there are any questions about ordering the testing, please ask them to contact The University of Chicago Genetics Services Laboratory. A blood sample is required for testing.

## How much does the testing cost and will my child's health insurance cover it?

Please see the table below for a list of prices and CPT (Current Procedural Terminology) codes for each available test. All insurance companies are different, but most of them should cover at least part of the cost of testing. You can contact your insurance company to learn more about your coverage prior to testing. You will want to ask your insurance company what your coverage is for the appropriate CPT (Current Procedural Terminology) codes:

| Test | CPT code | Price |
|---|---|---|
| Autosomal Recessive Primary Microcephaly Series Tier 1 (ASPM sequencing and deletion/duplication analysis) | 81479 | $1500 |
| Autosomal Recessive Primary Microcephaly Series Tier 2 (sequencing of 18 genes and deletion/duplication analysis of 16 genes) | 81479 | $3500 |
| ASPM sequencing | 81407 | $2100 |
| *ASPM* deletion/duplication testing | 81406 | $1000 |
| Autosomal Recessive Primary Microcephaly Tier 2 Sequencing Panel | 81407 | $3400 |
| Autosomal Recessive Primary Microcephaly Tier 2 Deletion/Duplication Panel | 81407 | $1545 |

Insurance companies use the CPT code for each test to define the method of testing. In most cases, The University of Chicago will bill your hospital or lab, which will then bill your insurance company. You may receive a

bill for any amount not covered by your insurance company, i.e. co-payment, deductible, etc. In some cases, The University of Chicago cannot bill your hospital or lab. In this case, we will need payment from you by check or credit card before testing. You will need to get repaid from your insurance company. The University of Chicago is not responsible for this.

## When/how will I get the results?

Testing takes approximately 4 weeks for *ASPM* testing, 8 weeks for the Autosomal Recessive Primary Microcephaly Tier 2 Sequencing Panel and 6 weeks for the Autosomal Recessive Primary Microcephaly Tier 2 Deletion/Duplication Panel. Your physician will be informed of the results as soon as it is complete. Results will be faxed to your physician.

## Additional Resources:

**Foundation for Children with Microcephaly**
Phone: 602-487-6445
email: jenni@childrenwithmicro.org
www.childrenwithmicro.org

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