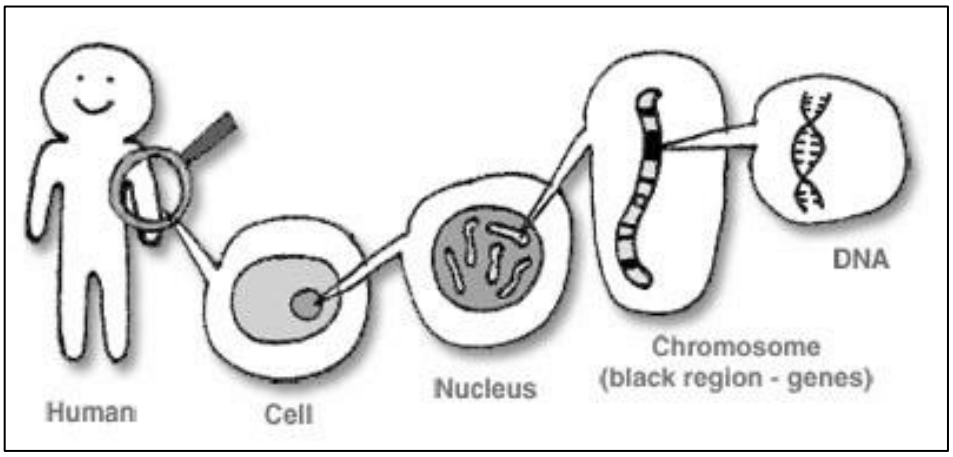
Ann & Robert H. Lurie
Children's Hospital of Chicago®

Genetic Testing for Developmental Delay and/or Autism

Disorders of childhood development – such as autism, intellectual disability, and developmental delay – often have a genetic cause. Your child's doctor has recommended genetic testing. The purpose of this fact sheet is to tell you more about genetic testing including the possible results, benefits, and limitations.

What are genes and chromosomes?

Genes are the instructions for our body to grow, develop, and function. **DNA** is the alphabet of our genetic instructions, a string of letters A, T, G, and C. Genes and DNA are packaged in **chromosomes.** In every cell in our body, we have 23 pairs of chromosomes, a total of 46. The chromosome pairs are numbered 1 – 22, and the last pair is the sex chromosomes X and Y. Females have two X's, and males have one X and one Y. Changes in the genetic instructions can result in problems or differences with development and functioning.



www.ashg.org

What is genetic testing?

In this setting, the purpose of genetic testing is to search for changes in the DNA or chromosomes that may be related to your child's developmental disorder. There are many types of genetic tests. Some tests are targeted at a specific gene or genetic condition, while others take a broader look across many genes, and yet others look at the chromosomes. The second page of this fact sheet explains two genetic tests commonly recommended for children with developmental disorders: chromosome microarray and Fragile X testing. Genetic tests can be performed on a blood sample, or for some tests, a cheek swab.

What are possible benefits of genetic testing?

These tests have the potential to identify a genetic diagnosis for your child and are recommended as first-tier diagnostic tests by the American Academy of Pediatrics, the American Academy of Neurology, and the American College of Medical Genetics. Uncovering such a diagnosis may allow us to provide more specific information about what to expect in the future (prognosis) or other medical concerns to check for (guiding management). Sometimes (rarely) there is a specific treatment for a genetic condition. We also would be able to determine whether the condition was inherited or occurred new in your child, and the chance for the condition to recur in other family members such as siblings. Some families find peace of mind knowing the cause of their child's condition and being able to connect with support groups.

What are possible risks of genetic testing?

Genetic tests can sometimes give results that are not clear, possibly leading to anxiety or uncertainty. Some types of genetic tests have the potential to find unexpected information, such as risks for health conditions not related to the reason for ordering the test. Some people have concerns about genetic discrimination; however there are laws to protect you such as the Genetic Information Nondiscrimination Act (www.GINAhelp.org), and also rules about keeping medical records confidential. If you have any concerns about undergoing genetic testing, it is important to discuss with your child's doctor. You can also request an appointment with a genetic counselor.

What are limitations of genetic testing?

Each particular genetic test has its own specific limitations. No test can diagnose or rule-out all possible genetic disorders. A "normal" or "negative" result does not mean that your child does not have a genetic condition.

Will my insurance cover genetic testing?

Many insurance plans cover genetic testing. Your child's doctor can guide you to find out your insurance coverage for a specific test and help with any requirements such as preauthorization.

There is no one else in our family with the same problem so how could it be genetic?

Sometimes genetic changes can happen new in a child, not inherited from a parent. Other times the genetic change may be inherited from a parent who is a carrier but does not show any symptoms.

Does my child have to have the genetic test?

Genetic testing is always optional. If you are unsure or have any concerns, talk to your child's doctor or request an appointment with a genetic counselor.

How will I find out about results?

Most tests take about 4-6 weeks to complete. Some tests, especially more complicated ones, may take longer. Call your doctor's office to find out the results. Ask for a copy of the genetic test report to be sent to you so you have it for your records and can share with your child's pediatrician.

What do I do after the results?

- If the results are **normal or negative**, this does not rule out the possibility that there could be a genetic cause for your child's concerns. Ask your doctor whether there is any appropriate other testing or evaluations to consider. You can request an appointment for genetic counseling or evaluation in Neurogenetics clinic.
- If the results are **positive or unclear**, your doctor will refer you to a genetic counselor, Neurogenetics clinic, or other genetics specialist.

What if I have more questions about genetic testing?

Genetic counselors are available to meet with you before or after undergoing genetic testing to answer any questions or concerns you may have. Please contact our office at 312-227-6720 so that we can hel you set this up if you are interested.

Websites for More Information

- Genetics Home Reference http://ghr.nlm.nih.gov
- Unique: Rare Chromosome Disorders Support Group http://rarechromo.org
- National Fragile X Foundation https://fragilex.org
- Simons VIP Connect (genetics and autism) https://simonsvipconnect.org

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Chromosome Microarray and Fragile X Testing

Chromosome Microarray – also called a **SNP array** – is a genetic test that looks across all the chromosomes for missing or extra pieces. Approximately 15-20% of children with autism, intellectual disability, or global developmental delay have a chromosome change as the cause.

Possible results of Chromosome Microarray testing:

- **Positive result:** a chromosome change related to developmental delays or autism. Depending in the genes that are affected by the chromosome change, there could be other symptoms or features. Your child's doctor will likely refer you to a genetic counselor or other specialist.

- **Negative result:** no chromosome changes found. This doesn't rule out the possibility that your child has a genetic condition, because this test cannot see DNA changes within individual genes. Ask your child's doctor whether there is any other appropriate testing or evaluations that should be considered.

- **Uncertain result:** a chromosome change is found but we aren't sure whether it is related to your child's symptoms, or whether it is part of normal variation. Your child's doctor will likely refer you to a genetic counselor. Sometimes it can be helpful to test parents or other family members to see if it was inherited. Knowledge about the meaning of chromosome changes can increase in the future, so it is important to follow-up periodically to ask for new information about the findings.

- **Other results:** occasionally this test will find a chromosome change that is not related to the reason for ordering the test, but that could be significant for your child's health – for example, deletion of a gene that causes high risk of cancer. This test can also show if a pair of chromosomes came from just one parent, or when a child's parents are closely related by blood.

Fragile X syndrome is one of the most common genetic disorders associated with intellectual disability and autism. It is caused by changes in a gene called FMR1 located on the X chromosome. The specific change is an increase in the number of "CGG" repeats. Too many repeats turns the gene off. This testing counts the number of repeats in the FMR1 gene. It is normal to have up to 45 repeats. Fragile X syndrome occurs when a person has more than 200 repeats (called a "full mutation"). People with an in-between number of repeats (called intermediate/gray-zone or premutation carrier) may have milder developmental or learning difficulties, or often no symptoms at all; however, they may be predisposed to an adult-onset neurologic condition called Fragile X Tremor Ataxia Syndrome (FXTAS), and/or early menopause in women. Fragile X syndrome is inherited in an X-linked pattern.

What other genetic tests or evaluations might be recommended?

Depending on your child's symptoms, your child's doctor might also recommend:

- Testing for specific conditions, such as Rett syndrome for girls or PTEN gene for children with large head size
- Blood or urine tests to screen for metabolic diseases that can cause developmental delay or autism
- Brain MRI
- Referral for evaluation in Neurogenetics clinic or other specialist