

AUTISM FAQ



NAAR Autism Genome Project: Frequently Asked Questions

What is the NAAR Autism Genome Project?

The **NAAR Autism Genome Project** is a large-scale, collaborative genetics research project designed to map the human genome in the search for *autism susceptibility genes* – the genes responsible for the inherited risk for autism. This unprecedented endeavor is the largest research collaboration ever to focus on the genetics of autism and includes approximately 170 of the world's leading genetic researchers from 50 academic and research institutions throughout the United States, Canada and Europe. The project includes approximately 1,500 multiplex families (two children with autism spectrum disorders and their parents) from all over the world who are directly affected by autism spectrum disorders.

While autism was first identified more than 50 years ago, the disorder remains a medical mystery because the tools necessary to learn more about the genetics of autism simply did not exist. With the development of promising new technology and 6,000 genetic samples, the research "Dream Team" of the *NAAR Autism Genome Project* hopes to reveal genetic information about autism that was previously undetectable. Using the data that they find, scientists will identify those genes that demonstrate a likelihood of being linked to autism. These discoveries will ultimately allow the medical research community to develop medical treatments for those affected by the disorder on a case by case basis.

This project required unprecedented collaboration between the top autism researchers in North America and Europe. It is a credit to all the research organizations involved and also to NAAR's vision and coordination of efforts that this is now possible.

How will this study be conducted?

- In mid-July 2004, 6,000 genetic samples (four from each family) will be taken from 1,500 multiplex families that have two children with autism spectrum disorders and sent to the Translational Genomics Research Institute (TGen) for genotyping
- TGen will genotype each patient sample using Affymetrix' GeneChip® Mapping 10K Array, yielding over 10,000 genome-wide SNPs per patient
- The Affymetrix Mapping 10K Array will allow researchers to examine mutations in a person's DNA in finer detail than was previously possible
- In early fall, The SNPs will be analyzed by NAAR associated investigators
- Further studies will be conducted to identify related genes on a base by base level
- Ultimately, researchers hope to develop a diagnostic tool, followed by knowledge-based drug development

Why couldn't this be done before?

AUTISM FAQ

The technology simply didn't exist until just under a year ago. Researchers were unable to analyze DNA at a sufficiently high resolution that would enable them to see the mutations that are at least in part responsible for autism.

Everything changed with the introduction of the Affymetrix GeneChip® Mapping 10K Array. It finally gave researchers the ability to see these tiny little genetic changes that will ultimately help them figure out what happens to the DNA of those affected with autism.

How did this project get started?

The origins of the *NAAR Autism Genome Project* can be traced to 2000, with NAAR's initial support of the Autism Genetics Cooperative, a research consortium, which provided a forum for the researchers to meet and discuss unpublished data. NAAR and the Nancy Lurie Marks Family Foundation co-funded this effort through 2003. In 2002, NAAR began working to bring top autism researchers together to find the genes that cause autism. Over the past two years, additional research consortiums joined NAAR's initiative to determine the genetic underpinnings of autism. In 2003, the National Institutes of Health (NIH) committed its support to the project. Later that year, NAAR and the NIH officially unveiled the *NAAR Autism Genome Project* at the Autism Summit Conference in Washington, D.C.

Who is part of the NAAR Autism Genome Project?

The project is a partnership between NAAR and four institutes of the National Institutes of Health (NIH): the National Institute of Mental Health (NIMH), National Institute of Child Health & Human Development (NICHD), National Institute of Neurological Disorders & Stroke (NINDS), and National Institute of Deafness and Other Communication Disorders (NIDCD). At the core of the *NAAR Autism Genome Project* are the investigators bringing it to life – a “collaboration of collaborations” composed of four main research teams:

- the Autism Genetics Cooperative (AGC)
- the International Molecular Genetic Study of Autism Consortium (IMGSAC)
- the Collaborative Programs of Excellence (CPEA)
- the Autism Genetics Resource Exchange (AGRE).

About Autism

What is autism?

Autism is a complex brain disorder that affects a child's ability to communicate, respond to surroundings, or form relationships with others. Autism is a developmental disorder of the brain that occurs in people of all racial, ethnic and social backgrounds. Children with autism are not unruly kids who choose not to behave.

Generally diagnosed at age 2 or 3, few disorders are as devastating to a child and his or her family. Many children with autism will never be able to tell their parents they love them.

While some people with autism are mildly affected, most people with the condition will require lifelong supervision and care and have significant language impairments. In the most severe cases, affected children exhibit repetitive, aggressive and self-injurious behavior. This behavior may persist over time and prove very difficult to change, posing a tremendous challenge to those who must live with, treat, teach and care for these individuals. The mildest forms of autism resemble a personality disorder associated with a perceived learning disability.

AUTISM FAQ

First described over 50 years ago, the incidence of autism is rising steadily. While criteria for diagnosing autism have changed over time and the number of cases reported have increased, studies indicate that:

- An estimated one in 1,000 children have autistic disorder, or classic autism.
- Two to six children per 1,000 have an autism spectrum disorder.
- As many as 1.5 million Americans today are believed to be living with some form of autism.
- Based on statistics from the U.S. Department of Education and other governmental agencies, autism is growing at a rate of 10-17 percent per year.
- Changes in how autism is diagnosed, criteria for diagnosing autism and number of cases reported may account for some of the increases in incidence of the disorder.
- Autism is four times more prevalent in boys than girls.
- If a family has one child with autism, there is a 5 to 10 percent chance that the family will have another child with autism.
- If a family does NOT have a child with autism, there is only a 0.1 to 0.2 percent chance that the family will have a child with autism

[Source: Centers for Disease Control and Prevention (CDC), National Institutes of Health (NIH), National Alliance for Autism Research (NAAR)]

What causes autism?

While identified over 50 years ago, no one is sure what causes the disorder. Researchers believe this it is probably a combination of genetic and environmental factors. One thing is certain – autism is an extremely complex disorder. It is likely caused by multiple gene changes throughout the genome; probably 10 or more genes are involved.

Various studies have been done to identify the cause of the disorder and multiple theories have been proposed:

- Under certain conditions, a cluster of unstable genes may interfere with brain development resulting in autism.
- Problems occurring during delivery.
- Environmental factors such as viral infections, metabolic imbalances, and exposure to environmental chemicals; harmful substances ingested during pregnancy.
- In 1998, British researchers published a controversial paper suggesting a link between the growing number of autism cases and the standard childhood vaccine for measles, mumps and rubella (MMR). The possibility of a relationship between vaccines and autism is being debated to this day.
- Long since disproved, in the 1950s and 1960s, doctors believed autism was a psychological disturbance caused by detached, or uncaring “refrigerator” mothers.

Is there a cure for autism?

No. There is no cure, but if a child is provided with special education, significant improvements may be made in the child’s social development.

There is no blood test or diagnostic scan that can diagnose the disorder. Physicians rely on behavioral observations to make their diagnosis.

AUTISM FAQ

While the public has become more aware of the disorder in recent years, autism research remains one of the lowest funded areas of medical research by both public and private sources.

How long have we known about autism?

People have lived with autism throughout history – published descriptions of behavior resembling autism date back to the 18th century. A number of researchers and doctors have studied autism over more than 50 years:

- 1943 – Dr. Leo Kanner was the first person to describe a specific condition as autism.
- 1940s – Dr. Bruno Bettelheim suggested that detached, uncaring “refrigerator” mothers caused psychologically disturbed children to develop autism, a belief that most doctors held through the 50s and 60s.
- 1964 – Dr. Bernard Rimland provided evidence that proved autism was a biological condition, proving that Bettelheim was wrong, thus liberating mothers from years of shame and guilt.
- 1977 – Dr. Susan Folstein and Dr. Michael C. Rutter published the first autism twin study, revealing evidence of a genetic basis for autism.
- 1991 – Drs. Catherine Lord, Michael Rutter and Ann LeCouteur published the Autism Diagnostic Interview.
- 1992 – The American Psychiatric Association released the Diagnostic and Statistical Manual (DSM-IV), which refined diagnostic criteria for autistic disorder.
- 1993 – The World Health Organization released a similar diagnostic manual known as the International Classification of Diseases (ICD-10).
- In 1994, the National Alliance for Autism Research (NAAR) was established, becoming the first organization in the U.S. dedicated to funding and accelerating biomedical research into the autism spectrum disorders.
- 2003 – NAAR and the NIH unveil the *NAAR Autism Genome Project*, a public/private research partnership that is the largest research collaboration ever to focus on the genetics of the disorder, with the hope of finding the underlying causes of autism.
- 2004 – The first phase of the *NAAR Autism Genome Project*, the genome scan, is launched. The scan will utilize DNA Array technology and be conducted by Translational Genomics Research Institute in conjunction with Affymetrix, Inc. A second scan based on microsatellite technology is also scheduled and will be conducted by the Center for Inherited Disease Research (CIDR).

Why hasn't anything been discovered, even after so much research has been done?

Autism is an extremely complex disorder. Studies have revealed that it has a genetic component, but environmental factors are also thought to be involved.

While studies have been done for a long period of time, researchers have not had sufficiently large patient populations to provide insight into the underlying disease

Where can I get more information about autism?

<http://www.naar.org>

<http://www.nih.gov>

<http://www.cdc.gov>

NATIONAL ALLIANCE FOR AUTISM RESEARCH (NAAR)

AUTISM FAQ

What is NAAR?

The National Alliance for Autism Research (NAAR) is the first non-profit organization in the U.S. dedicated to funding, promoting and accelerating the pace of biomedical research and science-based approaches that seek to determine the causes, prevention, effective treatments and, ultimately, a cure for autism spectrum disorders.

The story of NAAR begins with Karen & Eric London and their son, Zachary, who was diagnosed with autism when he was twenty-two months old. As the Londons learned more and more about the mysterious disorder, it became evident that there was a severe lack of information available about autism. When they tried to donate money for autism research, they were shocked to learn that there wasn't even one non-profit organization dedicated to biomedical research focusing on the disorder. In 1994, the Londons founded NAAR, the first national non-profit organization dedicated to funding biomedical research of autism spectrum disorders.

What does NAAR do?

NAAR provides grants to researchers for innovative, new pilot studies; mentoring fellowships to recruit new researchers to focus on autism; and funds larger, collaborative research programs that have the potential to yield major scientific advances in autism research.

What types of research does NAAR fund?

- Genetics
- Language & Communication
- Molecular & Cellular Biology
- Immunology
- Neuroanatomy & Neuroimaging
- Epidemiology Studies
- Behavioral Sciences

How much money has NAAR committed to autism research?

To date, NAAR has committed \$21.1 million to fund more than 200 biomedical research projects and fellowships worldwide – more than any other non-governmental organization. In addition, NAAR co-funds several collaborative research partnerships with the National Institutes of Health that are focused on autism. These programs include the *Autism Tissue Program*, a parent-led, science driven brain tissue donation program dedicated to autism research; the *High Risk Baby Sibling Autism Research Program*, a behavioral sciences program focusing on the infant siblings of children diagnosed with autism; and the *NAAR Autism Genome Project*.

Where is NAAR headquartered?

Princeton, NJ

How many employees does NAAR have?

About 33 employees.

How can I get more information about NAAR?

For more information about NAAR, visit <http://www.naar.org> or call (888) 777-NAAR.

AUTISM FAQ

AFFYMETRIX

What is Affymetrix? What does Affymetrix do?

Affymetrix is a pioneering company (Nasdaq: AFFX) that creates tools that are driving the genomic revolution. In the late 1980's a team of scientists led by Stephen P.A. Fodor, Ph.D., combined semiconductor manufacturing techniques with advances in combinatorial chemistry to build vast amounts of biological data on a small glass chip. This chip, the GeneChip® brand microarray, became the industry-standard tool that researchers use to analyze genetic information.

The microarray has been described as a "molecular microscope" that allows researchers to see what is happening in a biological sample at a molecular level. Prior to the invention of microarrays, exploring the molecular features and function of the human genetic system was limited to one or a few genes at a time and the complex interaction between these genes was largely a mystery. Microarrays have revolutionized that research model and opened up a new world of possibilities for scientists.

How is Affymetrix involved in the NAAR Autism Genome Project?

Affymetrix has continued its pioneering work in the area of DNA analysis. Just under a year ago, Affymetrix launched the new GeneChip Mapping 10K array, a revolutionary tool that allows scientist to identify mutations, or changes, in a person's DNA in finer detail than was previously possible. In fact, the Mapping 10K array will allow scientists to look at mutations at a single base pair level, a change in genetic sequence that is called a SNP, or single nucleotide polymorphism.

Before the 10K array, researchers had to rely on microsatellite arrays which contained only 400 markers compared with the 10,000 SNPs on a 10K array. Microsatellites provided very limited information, not enough to do detailed studies of a complex disorder such as autism.

6,000 genetic samples will be taken from 1,500 families – one sample from each parent, one from each of two children – and will then be genotyped at TGen using the Affymetrix Mapping 10K. The results will then be sent to NAAR researchers who will analyze the scans.

Who uses Affymetrix' products?

The products are used by hundreds of pharmaceutical, biotechnology, agrichemical, diagnostics and consumer products companies as well as academic, government and other non-profit research institutes to analyze the relationship between genes and human health.

Where is Affymetrix headquartered?

Affymetrix has headquarters in Santa Clara, California with offices worldwide.

How many employees does Affymetrix have?

Around 875 employees.

How can I get more information about Affymetrix?

For more information about Affymetrix, go to <http://www.affymetrix.com>

AUTISM FAQ

TGEN

What is TGen?

On February 7, 2002 an assembly of more than fifty leaders and visionaries gathered at the Arizona state capitol to discuss genomics and the possibility of establishing Arizona as a player in the new economy of the biotechnology industry. In the midst of a national recession, scientific and medical experts, government officials and businesspeople gathered to decide if it would be possible to create a genomics institute in Arizona.

Over \$90 million was raised within five months and the Translational Genomics Research Institute (TGen) became a reality in mid-2002.

The Translational Genomics Research Institute (TGen) is a non-profit biomedical research institute. TGen's mission is to accelerate the translations of genomic discoveries to the diagnosis and treatment of disease. Using the data emerging from human genome project, TGen hopes to be able to translate it into direct benefits for patients.

How many TGen employees are there?

160 employees.

Where is TGen located?

Phoenix, AZ

How can I get more information about TGen?

For more information about TGen, go to <http://www.tgen.org>