



autism
CONSORTIUM

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Research Published in New England Journal of Medicine Identifies New Chromosome Abnormality Strongly Associated with Autism Spectrum Disorders

-- Autism Consortium Releases First Significant Findings from Scan of 3,000 Children and Families with Autism Spectrum Disorders --

BOSTON – JANUARY 09, 2007 – The Autism Consortium, an innovative research, clinical and family collaboration dedicated to radically accelerating research and enhancing clinical care for autism spectrum disorders (ASDs), reported strong and compelling evidence that a region on chromosome 16 appears to play an important role in susceptibility for ASDs. ASDs are diagnosed in as many as 1 in 150 children under the age of three. Symptoms can range from mild to severe and can include social, cognitive and behavioral deficits. The new findings, published online in advance of an upcoming issue of *The New England Journal of Medicine* (NEJM), are of particular significance because either a deletion or duplication of this section of chromosome 16 appears to contribute strongly to susceptibility to ASDs.

In the majority of cases the deletion was *de novo*, a newly occurring change in the DNA that the affected individual did not directly inherit from either parent. The authors verified the clinical importance of their findings through independent observations in the Genetics Diagnostics Laboratory at Children's Hospital Boston, a member of the Autism Consortium, and at deCODE Genetics Inc. in Iceland. The research team was led by Mark J. Daly, PhD, an Autism Consortium member at the Center for Human Genetic Research and the Department of Medicine at Massachusetts General Hospital; he is also a senior associate member of the Broad Institute of the Massachusetts Institute of Technology and Harvard.

Dr. James Gusella, Senior Science Advisor for the Autism Consortium and Director of the Center for Human Genetic Research at Massachusetts General Hospital said: "The power of the Autism Consortium is our ability to get rapid results by cutting across institutions and connecting families and clinicians with basic researchers. In this case, we were able to immediately verify the clinical importance of a basic research finding, and rapidly use that information to immediately help families. The translation from basic research to clinical care took a just a couple of months, rather than years."

The Autism Consortium Genome Scan, the largest, most complete, genome scan for ASDs to date, was completed in October 2007 using data made available by the Autism Genome Research Exchange (AGRE), a program of Autism Speaks. Even before its researchers had finalized their own analysis, the Consortium made the data widely available to the scientific community through AGRE. The Autism Consortium researchers scanned genetic data from more than 3,000 individuals of which 1,441 were

diagnosed with an ASD, in order to identify genes that appeared to be associated with ASDs. In addition to the genetic information, the AGRE database included information on traits and behaviors of the individuals. The Autism Consortium team took advantage of a new gene scanning technology from Affymetrix, using its new 5.0 chip, and wrote two different but complementary computer algorithms to identify the genetic variation.

Analysis by the Autism Consortium team identified five individuals who had the *de novo* deletion out of 1,441 with ASDs in the AGRE database. Independent observations at Children's Hospital Boston, which is a member of the Autism Consortium, found an additional five cases of the deletion in clinical genetic testing of 512 patients referred for developmental delay and/or suspected ASDs. An additional independent observation by deCODE genetics demonstrated three individuals out of 299 on the autism spectrum had the identical deletion, bringing the total in this three-institution study to 13 patients with the same deletion. Nobel Laureate Eric Kandel, University Professor at Columbia University and Senior Investigator, Howard Hughes Medical Institute, says: "This study adds greatly to autism research. In a highly thoughtful and systematic study, Mark Daly and his colleagues have now made a major contribution to our understanding of autism." Equally striking are the findings of gene duplications in the same region among the patients studied. Seven individuals in the AGRE database and four individuals from Children's Hospital had extra copies of genes on chromosome 16 in a region matching the area where others had missing or deleted genes.

"It is rare and rewarding to have the opportunity to take findings from a large research database such as AGRE and be able to verify the findings among, and provide diagnostic information to, families with children under clinical care at an affiliated hospital using state-of-the art technology," Daly said.

The discovery of *de novo* gene deletions and of duplications has immediate clinical implications. Chromosome microarray tests, which have recently become available for clinical use, can detect the deletion and duplication in diagnosed patients and their parents. These tests can provide clinicians with important information on the risk of recurrence for subsequent pregnancies, a concern for many parents. The tests are costly, and not always covered by insurance. The research teams are already looking for ways to reduce the cost by developing a simpler way of detecting the specific chromosome 16 deletion or duplication.

Future plans of the Autism Consortium include further analyses to identify additional genes involved in ASDs, research to understand traits that may be associated with specific genetic differences and the mechanisms at work. The ultimate goal is to better understand the efficacy of current treatments available and to develop new treatments. Eric Lander, Director of the Broad Institute of MIT and Harvard said "Our collaboration with the Autism Consortium is changing the face of research in autism spectrum disorders. We are beginning to develop a full understanding of the autism spectrum disorder genome, which in turn leads us to understanding the different types of autism, the etiology and effect of each type, and ultimately, will lead to the discovery of treatments that have the greatest promise."

About the Autism Consortium:

The Autism Consortium includes 14 leading universities and medical centers in the Boston area. The Consortium includes families, researchers and clinicians who have joined together to radically accelerate research and enhance clinical care for autism spectrum disorders. A private nonprofit, funded entirely by donors, the Consortium is ground-breaking in a number of ways. We focus on families, linking them to the resources they need and supporting them in participating in research studies to understand and treat autism spectrum disorders. The Consortium brings together the best minds across Boston, from Beth Israel Deaconess Medical Center, Boston Medical Center, Boston University, Boston

University School of Medicine, Broad Institute of MIT and Harvard, Cambridge Health Alliance, Children's Hospital Boston, Harvard University, Harvard Medical School, Massachusetts General Hospital, Massachusetts Institute of Technology, McLean Hospital and the Floating Hospital at Tufts-New England Medical Center. To learn more about the Autism Consortium, please visit www.autismconsortium.org

About Massachusetts General Hospital Center for Human Genetic Research:

Massachusetts General Hospital, established in 1811, is the original and largest teaching hospital of Harvard Medical School. The MGH conducts the largest hospital-based research program in the United States, with an annual research budget of nearly \$500 million and major research centers in AIDS, cardiovascular research, cancer, computational and integrative biology, cutaneous biology, human genetics, medical imaging, neurodegenerative disorders, regenerative medicine, transplantation biology and photomedicine. MGH and Brigham and Women's Hospital are founding members of Partners HealthCare System, a Boston-based integrated health care delivery system. The Center for Human Genetic Research (CHGR) at the MGH is a multidisciplinary cross-departmental thematic center aimed at using genetic strategies to understand and treat human disease. For further information about the CHGR, go to www.massgeneral.org/chgr

About the Broad Institute of MIT and Harvard:

The Broad Institute of MIT and Harvard were founded in 2003 to bring the power of genomics to biomedicine. It pursues this mission by empowering creative scientists to construct new and robust tools for genomic medicine, to make them accessible to the global scientific community, and to apply them to the understanding and treatment of disease. The Institute is a research collaboration that involves faculty, professional staff and students from throughout the MIT and Harvard academic and medical communities. It is jointly governed by the two universities.

Organized around Scientific Programs and Scientific Platforms, the unique structure of the Broad Institute enables scientists to collaborate on transformative projects across many scientific and medical disciplines. www.broad.mit.edu.

About Children's Hospital Boston

Children's Hospital Boston is home to the world's largest research enterprise based at a pediatric medical center. Founded as a 20-bed hospital for children, Children's Hospital Boston today is a 377-bed comprehensive center for pediatric and adolescent health care grounded in the values of excellence in patient care and sensitivity to the complex needs and diversity of children and families. Children's also is the primary pediatric teaching affiliate of Harvard Medical School. For more information about the hospital and its research visit: www.childrenshospital.org

About deCode, Inc

Headquartered in Reykjavik, Iceland, deCODE is a biopharmaceutical company applying its discoveries in human genetics to the development of drugs and diagnostics for common diseases. deCODE is a global leader in gene discovery - our population approach and resources have enabled us to isolate key genes contributing to major public health challenges from cardiovascular disease to cancer. www.decode.com

About Autism Speaks

Autism Speaks is dedicated to increasing awareness of autism spectrum disorders, to funding research into the causes, prevention, treatments and cure for autism, and to advocating for the

needs of affected families. It was founded in February 2005 by Suzanne and Bob Wright, the grandparents of a child with autism. Bob Wright is Vice Chairman, General Electric, and served as chief executive officer of NBC for more than twenty years. Autism Speaks has merged with both the National Alliance for Autism Research (NAAR) and Cure Autism Now (CAN), bringing together the nation's three leading autism advocacy organizations. To learn more about Autism Speaks, please visit www.autismspeaks.org