

**The UC Davis M.I.N.D. Institute:  
Uniquely Designed to Study Gene-environmental Interactions in Autism**  
By Robert Hendren, D.O.

The University of California, Davis M.I.N.D. (Medical Investigation of Neurodevelopmental Disorders) Institute is a unique interdisciplinary biomedical center founded in 1998 to conduct research into the causes and treatment of autism, fragile X syndrome, learning disabilities and other neurodevelopmental disorders.

To accomplish this mission, the institute is bringing together parents, scientists, clinicians and educators. More than 250 faculty and staff work in the 110,000-square-foot M.I.N.D. Institute complex in Sacramento to foster creative, integrative research with the goals of finding improved interventions and, eventually, cures for these increasingly common childhood disorders.

### **Collaboration for Results**

Experts from every discipline related to the brain work together at the M.I.N.D. Institute, and the institute's multidisciplinary approach already is achieving significant outcomes. For instance, research teams are identifying:

- biological markers of autism that can lead to earlier detection and targeted interventions
- key differences in the immune systems of children with autism
- ways in which environmental toxins may contribute to autism
- interactions among genetic susceptibility, environmental exposures and neurodevelopment

The institute also recently launched the largest biomedical assessment of children with autism to date: the Autism Phenome Project. More about this study and other research projects follows.

### **Biomarkers of Autism**

Since its inception, finding a diagnostic biological marker of autism has been a major goal of the institute. In 1999, the institute funded scientists at the California Department of Developmental Services and the National Institutes of Health to conduct the "blood spot study." Robin Hansen, M.D., chief of developmental pediatrics and director of clinical services, collaborated on this project, which compared stored spots of blood taken from newborns who later received diagnoses of autism, mental retardation or cerebral palsy, with those from typically developing children.

The researchers examined eight different proteins and found that four of these proteins were elevated in the blood of children later diagnosed with autism or mental retardation, but not in the blood of children with cerebral palsy or typically developing controls. This was an exciting finding, since it raised the hope that analyzing blood from newborns might reveal markers of autism.

Recently, David Amaral, Ph.D., director of research, and Blythe Corbett, Ph.D., assistant clinical professor of psychiatry and behavioral sciences, continued the search for biomarkers using a very different approach: proteomics. They teamed up with SurroMed (now PPD Inc.), a biotech firm that uses a sophisticated form of mass spectrometry to evaluate thousands of proteins. At least 100 detected proteins were different in the group

with autism compared to the control group. The results of this study are being prepared for peer-reviewed publication.

### **The Immune System**

New research carried out by M.I.N.D. Institute scientists also suggests that problems with the immune system may be one of the causes or consequences of autism. To better define the immune status of children with autism, Judy Van de Water, Ph.D., professor of rheumatology, allergy and clinical immunology, and Paul Ashwood, Ph.D., assistant professor of medical microbiology, examined the blood levels of different types of antibodies (IgG, IgM and IgA), along with the responses of these antibodies when challenged with common vaccine antigens, in patients with autism and age-matched typically developing children. They found significant differences in the group with autism.

#### *Environmental Triggers*

M.I.N.D. Institute researchers also are studying specific toxins and their potential roles in the onset or severity of autism. A recently published study connected the mercury-based preservative thimerosal with disruptions in antigen-presenting cells known as dendritic cells obtained from mice. The study provides the first evidence that dendritic cells show unprecedented sensitivity to thimerosal, resulting in fundamental changes in the immune system's ability to respond to external factors. Isaac Pessah, Ph.D., professor of molecular biosciences and director of the Children's Center for Environmental Health and Disease Prevention (CCEH), was senior author of this study.

#### *Gene-environment Interactions*

One of the earliest grants to the researchers at the M.I.N.D. Institute and the Children's Center for Environmental Health came from the National Institute of Environmental Health Sciences and focused on examining how toxic chemicals may influence the development of autism in children. The cornerstone of the center is an epidemiological study called "Childhood Autism Risks from Genetics and the Environment," or CHARGE. It is the first and largest case-control study of autism, and its goal is to look at the influence of environmental factors, the role of genetic susceptibility and the interplay between the two.

Finally, a CCEH project scheduled to be launched this fall has a new acronym: MARBLES, for Markers of Autism Risk in Babies Learning Early Signs, led by Irva Hertz-Picciotto, Ph.D. The primary subjects in this study will be women who have a child diagnosed with autism and who are pregnant or plan to become pregnant in the near future. The goal is to find out if anything that occurs during pregnancy can be associated with a later diagnosis of autism.

#### *The Autism Phenome Project*

One of the major roadblocks to understanding autism is that it has diverse outcomes. This raises the possibility that there are several types of autism with a variety of causes. The Autism Phenome Project, led by Dr. Amaral, aims to distinguish among subgroups or phenotypes of autism.

So far, more than 50 children have received thorough evaluations of medical history, behavior, environmental exposures, genomics, brain structure and function, immune function, proteomics (the large-scale study of

protein) and metabolomics (systematic study of the unique chemical fingerprints that specific cellular processes leave behind). A sophisticated bioinformatics (use of techniques including applied mathematics, informatics, statistics, computer science, chemistry and biochemistry to solve biological problems usually on the molecular level) core will analyze this complex data to detect patterns that can be used to define different types of autism.

The M.I.N.D. Institute is dedicated to bridging gaps in what is known about autism and other neurodevelopmental disorders to reduce or eliminate challenges for children and their families. While research in this area still has a long way to go, the institute is making significant headway every day toward this goal.

To learn more about UC Davis M.I.N.D. Institute research and events, visit [www.mindinstitute.org](http://www.mindinstitute.org).

*Robert Hendren, D.O., is executive director of the M.I.N.D. Institute.*