NOTES FROM THE BENCH

Weill Cornell Autism Research Program (WCARP)

Director's Note

Autism spectrum disorder (ASD) is the most common neurodevelopmental disorder occurring in 1 in 50 individuals. To date, no effective diagnostic markers or pharmacologic treatments exist for ASD. Impaired brain circuits and signaling at synapses, the contacts between neurons, is emerging as one of the causes of autism. The goal of WCARP, a multi-institutional collaborative team, is to utilize patient samples and genetic mouse models to better understand the neurobiological basis of ASD. Faculty with expertise in clinical ASD behaviors, imaging, immunology, neurobiology and drug development are working together to better understand the molecular basis of autism and to support preclinical studies for the development of new diagnostic markers and treatments for patients with ASD. This newsletter reviews recent publications by WCARP faculty members.

Advisory Board's Thanks

We are facing an international epidemic: autism spectrum disorder (ASD). The U.S. Center for Disease Control and Prevention (CDC) has cited that the rate of ASD increased over 289% during the 11 years from 1997 to 2008. In March 2013, the CDC reported that 1 of 50 U.S. children had ASD. The emotional and financial costs of ASD are devastating. A multi-prong attack on this disorder utilizing early recognition and appropriate educational intervention may mainstream up to half of the affected infants and young children. Continuing training for older individuals may lead to gainful employment, but there will be a significant need for effective adult life skill programs and state of the art residences in perpetuity for adults with ASD. Furthermore, more than 25% of individuals with ASD have a significant coexisting disorder such as seizures, severe cognitive impairment or bipolar illness. Given the cost to society of this epidemic, the need for understanding the basic scientific mechanisms of ASD and these related disorders and discovering pathways to developing pharmacologic treatment is crucial in addressing this burgeoning disorder. The bench research undertaken by the scientists of the Weill Cornell Autism Research Program have made preliminary steps in trying to unravel the cruel secrets behind this devastating illness and find successful medical interventions. We applaud the individuals and foundations who financially support our quest for their trust in our endeavors. We give special thanks to the Goldman and Swift Foundations for their generous support.

Research update

The cacna1c Genetic Mutant Mouse Model of Autism and Neuropsychiatric Disorders

Director's Summary: Proper functioning of calcium channels at synapses, the points of contact between neurons, is critical for synaptic function. Genetic mutations in one such synaptic calcium channel gene, cacna1c that codes for the Cav1.2 protein, has been linked to autism and discovered to be a significant risk gene for four other major neuropsychiatric disorders (Bipolar Disorder, Schizophrenia, Depression and ADHD, as reported in the New York Times). In this Weill Cornell Medical College study, using a genetic mouse model, the Rajadhyaksha Laboratory provides direct evidence for the first time that removal of cacna1c in glutamatergic cells in the prefrontal cortex (a brain region known to be impaired in autism and other mood disorders) causes anxiety, a co-morbid condition in ASD. For further reading, visit: nyp.org/komansky/wcarp/papers. Funded by The Hartwell Foundation.
The Cereblon Genetic Mouse Model of Intellectual Disability

Director’s Summary: Intellectual Disability (ID) that commonly accompanies ASD is the most common developmental disability in the United States affecting 1-3% of the population. In 2004, Dr. Joseph Higgins (WCMC faculty) discovered a mutation in the cereblon gene that results in a shorter version of the normal protein in individuals with an inherited form of ID. In this study using a genetic cereblon mouse model, the Rajadhyaksha and Higgins Laboratories demonstrate that, like in humans, mice have deficits in both learning and memory. For further reading, visit nyp.org/komansky/wcarp/papers. Funded by The March of Dimes and The Hartwell Foundation.

Autism and Gastrointestinal Immune Response

Director’s Summary: In this study the Alaedini Laboratory at Columbia University have shown that children with ASD display an increased immune response to gluten proteins of wheat in comparison to children without ASD. The observed antibody response was strongly associated with the presence of gastrointestinal (GI) symptoms, but not with celiac disease, the autoimmune condition triggered by gluten. This study points to a potential mechanism involving immunologic and/or intestinal barrier abnormalities in autism. For further reading, visit nyp.org/komansky/wcarp/papers. Funded by the Department of Defense.

Autism and Infectious Disease

Director’s Summary: In this study, the Alaedini Lab examined the link between autism and Lyme disease. It had been previously claimed that greater than 20% of children with autism are infected with Lyme borreliosis, an infectious disease, implying that antibiotics would be effective in the treatment of autism. This new study convincingly ruled out the presence of a substantive link between autism and Lyme. For further reading, visit nyp.org/komansky/wcarp/papers. Funded by Department of Defense and WCARP.

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