

ICare4Autism International Autism Conference

'Autism: Cutting Edge Research and Promising Treatment Approaches'



Albert Einstein College of Medicine Robbins Auditorium



in conjunction with Montefiore Medical Center

Wednesday, June 5th, 2013
Agenda
Robbins Auditorium
Welcoming Remarks: Joshua Weinstein, Ph.D., M.B.A.
President & Founder, International Center for Autism Research and Education ICare4Autism
Eric Hollander, M.D. Director of the Autism and Obsessive Compulsive Spectrum Program at Albert Einstein College of Medicine/Montefiore Medical Center and Chairman of the ICare4Autism Advisory Council
Bruce J. Schwartz, M.D. Deputy Chairman & Clinical Director, Professor of Clinical Psychiatry, Department of Psychiatry and Behavioral Sciences, Montefiore Medical Center
~~~~~~Keynote Address~~~~~~~~~
Taking a Fresh Look at Autism: Chronic Dynamic State, not Fixed Trait Martha Herbert, M.D., Ph.D.
Assistant Professor of Neurology at Harvard Medical School, Pediatric Neurologist at the Massachusetts General Hospital in Boston, Director of the TRAN-
SCEND Research Program (Treatment Research and Neuroscience Evaluation of Neurodevelopmental Disorders)
Dialogue with the presenter and the audience
Exploring the Immune-Brain Interactions in Autism: A Look at Cytokines-Chemokines Networks Carlos A. Pardo, M.D.
Associate Professor, Department of Neurology and Pathology, Johns Hopkins University School of Medicine
A Role for 5-hydroxymethylcytosine in ASD?
Nathaniel Heintz, Ph.D. Investigator, Howard Hughes Medical Institute, James and Marilyn Simons Professor, Laboratory of Molecular Biology, The Rockefeller University
Activated Mast Cells Secrete "Innate Pathogens" Causing Focal Brain Inflammation Reversed by methoxyluteolin
Theoharis C. Theoharides, MS, Ph.D., M.D., FAAAAI
Professor of Pharmacology, Internal Medicine and Biochemistry; Director, Molecular Immunopharmacology and Drug Discovery Laboratory; Department of Molecular Physiology and Pharmacology at Tufts University School of Medicine
Communication Deficits in Rett's Syndrome
Aleksandra Djukic, M.D., Ph.D.  Director, Tri-State Rett Syndrome Center, Associate Professor of Neurology and Pediatrics, Montefiore Medical Center, Albert Einstein College of Medicine
Inflammation, Temperature and Personalized Therapeutics of ASD
Eric Hollander, M.D.
Director of the Autism and Obsessive Compulsive Spectrum Program at Albert Einstein College of Medicine/Montefiore Medical Center and Chairman of the
ICare4Autism Advisory Council
Dialogue with the presenter and the audience
Lunch On Your Own  Special Ways and Techniques (SWAT) for Achieving Meaningful Inclusion
Stephen Shore, Ed.D.
Assistant Professor, Dept. of Special Education, Adelphi University, member of the ICare4Autism Advisory Council
Protein Biomarkers in Autism Spectrum Disorders
Alisa G Woods, Ph.D., M.S  Director, Autism Research Program, Laboratory for Biochemistry and Proteomics, Clarkson University
Electrophysiological Mapping of Sensory Processing and Multisensory Integration in Autism
Sophie Molholm, Ph.D.
Associate Professor, Muriel and Harold Block Faculty Scholar in Mental Illness, Departments of Pediatrics and Neuroscience, The Sheryl and Daniel R. Tishman
Cognitive Neurophysiology Laboratory, AECM
Diagnosis and Treatment of Autism at Birth Gary Steinman, M.D., Ph.D.
Chairman, Dept. of Biochemistry, Touro College of Osteopathic Medicine
Language, Writing, and Conduct Disorder in the Autistic Spectrum
Daniel Orlievsky
School of Psychology. University of Buenos Aires. Infantile and Adolescent Psychiatric Hospital, Buenos Aires. Argentina
ICare4Autism Global Autism Initiatives



### Joshua Weinstein, Ph.D., M.B.A. - Founder & CEO of ICare4Autism

Dr. Joshua Weinstein has been an educator and administrator for over four decades. He holds a Ph.D., two Masters Degrees in Educational Administration and Supervision and an MBA in Executive Administration. He has been the CEO in healthcare, social services, and business corporations. He's the president and founder of ICare4Autism, Shema Kolainu-Hear Our Voices and Tishma for children with autism in Jeru-

ICare4Autism Global Autism Initiatives. ICare4Autism's mission is to drive the worldwide research necessary to discover the etiology of autism and its biologic and environmental causes. The organization is currently focusing on the development of the Global Autism Center, which will be located in Jerusalem at Mount Scopus. The Center will be comprised of the ICare4Autism Research Institute (a global research center), ICare4Autism Academy (the world's first advanced professional school of autism studies), ICare4Autism Model School (a school that will apply the latest research to meet the educational needs of students across the spectrum), and ICare4Autism Foundation (an organization engaging a global community of scientists, educators, and advocates). The Global Autism Initiatives include Workforce Development, Africa Awareness and Intervention, ICAP4Autism, ICare4Autism Legal Dept and Joint Projects with the World Health Organization.



# Eric Hollander M.D. - Chairman of the ICare4Autism Advisory Council

Dr. Hollander is Director of the Autism and Obsessive-Compulsive Spectrum Disorders Program, and Clinical Professor of Psychiatry and Behavioral Sciences at the Albert Einstein College of Medicine and the Montefiore Medical Center. Dr. Hollander has served as principal investigator for a number of federal grants, including the NIH Greater New York Autism Center of Excellence, the NIMH Research Training Grant in Psychopharmacology and Outcomes Research, and the Orphan Product FDA studies of adult and childhood autism; and of Foundation grants such as the Simons Foundation studies on TSO and on fever in ASD. He served as Chair of the DSM-V Research Planning Agenda for Obsessive Compulsive Behavior Spectrum Disorders, and is an Advisor to the DSM-V Anxiety, Obsessive-Compulsive Spectrum, Post-Traumatic and Dissociative Disorders Workgroup, and the Behavioral and Substance Addictions Workgroup.

Inflammation, Temperature and Personalized Therapeutics of ASD. Our group has examined the underlying mechanisms of a fever response

and involvement of the immune-inflammatory system in ASD via four approaches: 1. Oxytocin vs placebo in ASD: (oxytocin not only has potent effects on social cognition and lower order repetitive behaviors but also has effects on obesity and wound healing; clinical response may be magnified in syndromal forms of ASD - tuberous sclerosis and Prader Willi Syndrome), 2. Hyperthermia: children with ASD are compared at temperatures of 102 degrees vs 98 degrees on clinical measures, biomarkers, and gene expression profiling, 3. LC/NE function as an outcome of maternal stress is examined by a milnacipran vs placebo trial of ASD, 4. TSO (trichura suis ova; a helminth) vs placebo is examined in adult ASD on clinical measures and biomarkers.



### Martha Herbert, M.D., Ph.D.

Dr. Herbert's main research interests are in addressing autism as a "dynamic encephalopathy" (changable) rather than a "static encephalopathy" (fixed for life) and in how environmental vulnerability affects brain and body health and function. She therefore takes three approaches: 1) a whole body systems biology view of how autism emerges — or not — in infants at high risk for autism (she has an older sibling on the spectrum); 2) combining multi-modal brain imaging and biomarkers to study of the interface between metabolic/immune disturbances and altered brain signaling, which could be the "ground zero" of autism for many, and 3) applying these approaches to the systems biology of improvement and recovery in autism as well as other disorders and situations where complex systems are multiply challenged. She is the author

Taking a Fresh Look at Autism: Chronic Dynamic State, not Fixed Trait. Autism has been considered a genetically caused and fixed, lifelong brain deficit. However emerging science is making that framing of autism outdated. There is more than genes and brain, there is lots of variability even for any one individual, and it is not in itself a "deficit." An emerging model includes environment and physiology as well as genes, and looks at strengths as well as difficulties. It may well be that what we call "autism" is not the fixed output of a static wiring diagram but the moment-to-moment recreation of atypical patterns of brain wave oscillations that arise from a brain with differences in cell and tissue physiology. Emerging multi-scale systems biology points us toward a whole-body dynamic model of autism where many aspects of life can be made easier so that each person has the best chance to reach their optimal potential.



## Carlos A. Pardo, MD

Dr. Pardo is a clinical neurologist and neuropathologist and currently an Associate Professor of Neurology (Division of Neuroimmunology and Neuroinfectious Disorders) and Pathology (Neuropathology) at Johns Hopkins University School of Medicine in Baltimore, Maryland. He is the principal investigator of the Neuroimmunopathology Laboratory, and neurologist at the Multiple Sclerosis and Transverse Myelitis Centers at Johns Hopkins Hospital. His clinical specialization is on neuroimmunological and Infectious disorders of the nervous system, with particular focus on autoimmune disorders of the CNS and neurological complications of HIV infection.

Exploring the Immune-Brain Interactions in Autism: A Look at Cytokines-Chemokines Networks. There is growing evidence that neuroglia play important roles in pathogenic mechanisms associated with autism spectrum disorders (ASD). Studies of neuroglia as well as profiles of mmune mediators (e.g., cytokine/chemokines) in brain tissues from patients with ASD disclose an increased activity of microglia and astroglia. Interestingly, neuroglia responses coincide with changes in the profiles of innate neuroimmune responses such as those from cytokines/ chemokines and Toll-like receptors signaling pathways. Interestingly, studies in blood and cerebrospinal fluid from patients with ASD also show that selected subsets of these immune mediators are differentially expressed. These findings support the view that innate immune responses mediated by neuroglia along with cytokines/chemokines responses constitute non-genetic factors in the interaction between the environment and central nervous system responses that may play critical roles in the pathogenesis of ASD.



## Nathaniel Heintz, Ph.D.

Dr. Heintz graduated from Williams College with a B.A. in biology in 1974. He received his Ph.D. from the State University of New York, Albany, in 1979 and then worked as a postdoc at Washington University in St. Louis until 1982. He came to Rockefeller as assistant professor in 1983 and was named associate professor in 1987, professor in 1992 and James and Marilyn Simons Professor in 2006.

A role for 5-hydroxymethylcytosine in ASD? Research in Dr. Heintz's laboratory aims to identify the genes, circuits, cells, macromolecular assemblies and individual molecules that contribute to the function and dysfunction of the mammalian brain. Dr. Heintz and his colleagues have developed a suite of novel approaches based on the manipulation of bacterial artificial chromosomes (BACs) to investigate the histological and functional complexities of the mammalian brain in vivo and to understand how these mechanisms become dysfunctional in disease.



service" from the New England Medical Center.

Theoharis C. Theoharides, M.S., Ph.D., M.D., F.A.A.A.I.
Dr. Theoharis Theoharides is the Director of the Molecular Immunopharmacology and Drug Discovery Laboratory, as well as a Professor of Pharmacology, Biochemistry and Internal Medicine at Tufts University, Boston, MA (www.mastcellmaster.com)
He received all his degrees from Yale University from where he was awarted the "Winternitz Price in Pathology." He also received a Certificate in Global Leadership from the Fletcher School of Law and Diplomacy, and the "Oliver Smith Award "recognizing excellence, compassion and

Activated Mast Cells Secrete "Innate Pathogens" Causing Focal Brain Inflammation Reversed by methoxyluteolin. Mast cells participate through cytokine release in acquired and innate immunity, as well as inflammation involved in the pathogenesis of atopic dermatitis and autism, but the triggers and the specific mediators released are unknown. We reported that the peptide neurotensin (NT), found in the brain, gut and skin, is significantly increased in the serum of autistic children (n=20; 3 years old) along with significantly more mitochondrial (mt)DNA for Cytochrome B (p=0.0002), as compared to normally developing controls (n=12). These biomarkers may characterize an autistic phenotype since over 50% of patients have eczema and food allergies. Here we report that human LAD2 cultured mast cells stimulated by IgE/antilgE, since over 50% of patients have eczema and food allergies. Here we report that human LAD2 cultured mast cells stimulated by IgE/antigE, NT, or substance P (SP) secrete mt components including mtDNA without cell death. Purified LAD2 mt components trigger release of (a) histamine, IL-1β, IL-8, PGD2 and TNF from mast cells, (b) vascular endothelial growth factor (VEGF) from human keratinocytes, (c) human microvascular endothelial cells, as well as (d) IL-6 from human microglial cells. When mtDNA from LAD2 cells was injected ip in rats, it was detected in rat serum within 4 hr indicating that extravascular mtDNA could enter the systemic circulation. Pretreatment with the flavonoid methoxyluteolin inhibited these processes. Mitochondrial components secreted from stimulated live mast cells may act as "innate pathogens" contributing to the pathogenesis of inflammatory diseases and may serve as targets for novel treatments (Supported by NIH R01AR47652, the National Autism Secretary and Sec National Autism Society and Safe Minds).





## Aleksandra Djukic, M.D., Ph.D.

Dr. Aleksandra Djukic is an Associate Professor of Clinical Neurology and Pediatrics at Albert Einstein College of Medicine and the Director of the Tri-State Rett Syndrome Center at the Montefiore Medical Center, one of the largest Rett Syndrome clinics in the U.S. Dr. Djukic specializes in the evaluation and treatment of children with cognitive impairment disabilities with a special expertise in girls with Rett Syndrome. Her commitment to education and outreach about Rett Syndrome, and continuity of care for each patient from infancy through adolescence and adulthood is evident by her vision of developing the Rett Syndrome Center at the Montefiore Medical Center. Communication Deficits in Rett's Syndrome. Dr. Djukic has received funding from the NIH to study how much Rett girls understand spoken language, as well as to study receptive language abilities using a new 'system identification' approach. Together, these studies are integral components of her mission "to focus on what girls with Rett can do", and also reveal the need for more customized testing for girls with Rett syndrome to more accurately assess their intellectual abilities and psychological state. Specifically it has been found that it is a medical necessity for these girls to have access to eye-gaze speech-generating computers in order for them to demonstrate their mental abilities and to communicate with their families.



Stephen Shore, Ed.D. - Member of the ICare4Autism Advisory Council
Diagnosed with "Atypical Development and strong autistic tendencies" and "too sick" for outpatient treatment Dr. Shore was recommended brightest with Applications and strong autistic relationships and too strong and with children and talking about life on the autism spectrum, Stephen presents and consults internationally on adult issues pertinent to education, relationships, employment, advocacy, and disclosure as discussed in his books Beyond the Wall: Personal Experiences with Autism and Asperger Syndrome, Ask and Tell: Self-advocacy and Disclosure for People on the Autism Spectrum, the critically acclaimed Understanding Autism for Dummies, and the newly released DVD Living along the Autism Spectrum: What it means to have Autism or Asperger Syndrome.

Special Ways and Techniques (SWAT) for Achieving Meaningful Inclusion. Through the development and use of educational accommodations as extensions of good teaching practice, participants will learn easy to implement, practical solutions for including student with disabilities in regular education - For example affording a student unable to stand still and sing in chorus class another way of meaningful



# Alisa G Woods, PhD, MS

Dr. Alisa G Woods received her PhD in neurobiology from the University of California, Irvine, completed post-doctoral work in neuroanatomy as an Alexander von Humboldt Fellow at the University of Freiburg, Germany and received her Master's degree in Mental Health Counseling at the University of Massachusetts, Boston. She initiated the psychiatric biomarker research program at Člarkson University in Potsdam NY, where she is currently a Research Assistant Professor in the Department of Chemistry and Biomolecular Science. The longterm goal of her research is to understand the connections between biochemistry and behavior in neurodevelopmental and psychiatric

Protein Biomarkers in Autism Spectrum Disorders. Autism spectrum disorder (ASD) diagnosis is increasing, with 1/88 children believed to be affected by the disorder. Treatment and understanding of ASD causes is a pressing health concern. ASD protein biomarkers may provide clues about ASD cause. Protein biomarkers for ASDs could be used for ASD diagnosis, subtyping, treatment monitoring and identifications. tifying therapeutic targets. Here we analyzed the sera from 7 children with ASD and 7 matched controls using Tricine gel electrophoresis (Tricine-PAGE) and liquid chromatography-tandem mass spectrometry (LC-MS/MS). Overall, we found increased levels of apolipoproteins (Apos) ApoA1 and ApoA4, involved in cholesterol metabolism and of serum paraoxanase/arylesterase 1, involved in preventing oxidative damage, in the sera of children with ASD, compared with their matched controls. All three proteins are predicted to interact with each other and are parts of High Density Lipoproteins (HDLs). Our data suggests that in children with ASD, cholesterol metabolism is dysregulated. Our results also support current theories that ASDs may involve increased oxidative stress responses



### Sophie Molholm, Ph.D.

Dr. Molholm is Associate Professor in Pediatrics and Neuroscience at Albert Einstein College of Medicine, and the Muriel and Harold Block Faculty Scholar in Mental Illness. Dr. Molholm's research is focused on understanding how children with autism process and integrate sensory-perceptual information, if this differs from typically developing children, and how this ultimately relates to expression of the phenotype. She is pursuing projects in both high-functioning and low-functioning individuals, using high-density recordings of the electrical activity of the brain. Dr. Molhom also directs the Human Clinical Phenotyping Core of the Einstein IDDRC. She receives support from NIMH, NSF, the Sheryl and Daniel Tishman Foundation and the Nathan Gantcher Foundation.

Electrophysiological Mapping of Sensory Processing and Multisensory Integration in Autism. Unusual sensory symptoms have long been noted in individuals with ASDs. Several of the longstanding as well as contemporary theories of ASDs, such as weak central coherence theory of Frith and Happe and enhanced perceptual functioning theory proposed by Mottron reflect the notion that individuals with ASD do not process or integrate sensory inputs in the same manner as those with typical development. Electrophysiological recordings of the brains response to sensory inputs provide a powerful test of differences in sensory processing and multisensory integration. I will discuss the use of electrophysiology to interrogate brain function in ASD, and present findings of data showing marked differences in sensory processing and multisensory integration in autism. Potential implications, including the possibility that disordered neural connectivity partially accounts for these processing differences, will be considered.



# Gary Steinman, M.D., Ph.D.

Dr. Steinman is the Chairman of the Department of Biochemistry at Touro College of Osteopathic Medicine. He has published a total of 4 books, holds 5 patents, and has 55 research articles and chapters

Diagnosis and Treatment of Autism at Birth. Several observations have pointed to the role of depressed IGF at birth, CNS dysmyelination, and the appearance of autism. Studies are ongoing to document the neonatal level of IGF and the probability of autism developing later. Possible modes of prevention and treatment will be discussed.



### **Daniel Orlievsky**

Daniel Orlievsky is a Child and Adolescent Psychologist that has been working for more than 35 years as a therapist. He created and he is the Director of the Rehabilitation Through Writing Project Program at the Infantile and Adolescent Psychiatric Hospital "Dra. Carolina Tobar García", in Buenos Aires since 1997.

Orlievsky is Director of an Outreach Program about Language Habilitation Through Writing in PDD, is Professor of Child Psychology and since 2001 he has been Co-Director of Research Projects related to Writing and Language in Autism at the School of Psychology of the University of Buenos Aires, he also runs the Program at the Pediatric Mental Health Unit at the Hospital Italiano in Argentina. Language, Writing and Conduct Disorder in the Autistic Spectrum. Since it is supposed that written language is acquired after oral language it is common not to teach writing to patients with severe developmental disorders that lack language or whose language is sufficiently disturbed so as to presume lack of comprehension. However, the cases studied showed us that this strategy is possible for a series of them. It is possible to invert the order as a function of the child's capabilities and predispositions to allow for a smooth transition from written to spoken language that is tailored to the individual. We consider it interesting that some patients could develop some functional language at a much older age than previously considered possible. Finally, the cases studied showed us significant changes in their conduct after the acquisition of writing.

# **About Our Sponsors**

This ICare4Autism and Albert Einstein College of Medicine presentation is Co-Sponsored by Shema Kolainu- Hear Our Voices School and Center for Children, Montefiore the University Hospital for Albert Einstein College of Medicine, and Coronado Biosciences

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BioAdvantex Pharma manufactures PharmaNAC effervescent N-actetylcysteine tablets supplied to a study in children with autism conducted by Stanford University. Published in the June 2012 issue of Biological Psychiatry, the study reports that children taking doses up to 3 tablets of PharmaNAC daily, containing 2700mg of n-acetylcysteine had improvements in irritability and repetitive behavior.



The Sluis Academy is a wholly Canadian owned company that offers a unique program of adaptive physical education in conjunction with development of social skills in persons with special needs, most specifically, with those persons exhibiting symptoms of autism and fetal alcohol syndrome.



With special thanks to Albert Einstein College of Medicine for hosting the event and to Shema Kolainu – Hear Our Voices, School and Center for Children with Autism.

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