

## Conference Report

### **Shared Neurobiology of Autism and Related Disorders 1 U13 NS059269-01 (PI: Steven Moldin) University of Southern California, Los Angeles, CA June 10-13, 2007**

#### Summary

The conference presented a useful model to facilitate research on multiple rare diseases, by which findings across diseases are conceptually integrated to identify shared pathophysiologic mechanisms. The conference assembled 81 researchers and scientific leaders across multiple fields of neuroscience and provided a multidisciplinary discussion of the accumulated evidence, state-of-the-art methodologies and major knowledge gaps in the basic neuroscience of autism and related neurodevelopmental disorders that share common phenotypic characteristics (Fragile X syndrome, Rett syndrome, Angelman syndrome, Tuberous sclerosis and Joubert Syndrome, herein referred to as “neurodevelopmental autism-associated disorders,” or NAD). The conference included 34 talks arranged in the following six scientific sessions: (1) Gene Expression and Epigenetic Mechanisms, Including Genomic Imprinting; (2) Cellular and Systems Biology, Including Protein Characterization, Transport, Signal Transduction & Translational Regulation; (3) Neural Systems, Pathways & Circuits for Social Anxiety & Fear; (4) Brain Structure & Function, Including Neuropathology and Neuroanatomical Connectivity; and (5) Strategies for Prioritizing Potentially Druggable Targets; and (6) Identification of Drug Targets for New Therapeutics.

The presentations and accompanying discussions conveyed the merits and tremendous excitement of molecular, cellular and genomic neuroscience approaches for understanding shared mechanisms common to autism and NAD. Topics covered included: epigenetic mechanisms; presynaptic defects; altered gene regulation through transcription factors; RNA maps of synaptic function; changes in the plasticity and protein makeup of cortical synapses; PI3-kinase signaling and social interaction behavior; and abnormalities in the regulation of synapse development by signaling networks. Potential new insights into the pathophysiology and etiology of autism were provided by talks that revealed a rich source of circuits, molecules and pathways for therapeutic targeting. Strategies for identifying prioritizing potentially druggable targets were identified in scientific talks on novel computational approaches to drug discovery; identification of vasopressin mechanisms; pharmacologic strategies for correcting cognitive-related synaptic defects; and perspectives from industry on drug discovery and development in autism.

Many of the talks and discussion highlighted the value of integrative and multidisciplinary approaches, thereby opening conduits to foster collaborations and networking among young and experienced investigators, while presenting novel and creative routes to investigate the shared neurobiology of autism and NAD. Most importantly, the conference helped to identify cutting-edge approaches in genetics, molecular and cellular biology, developmental biology, neurophysiology, neuroanatomy, and systems and cognitive neuroscience that can be brought to bear to characterize the neural substrates of higher order cognition, communication, fear/anxiety, and attention that are perturbed in autism.

#### Young Investigators Program

The conference supported a Young Investigator Program that permitted 17 junior investigators (women, 47%; underrepresented minorities, 24%) to attend the meeting and present exciting new findings and research approaches that have a high likelihood of accelerating basic

neuroscience and translational research discoveries in autism. The Organizing Committee reviewed abstracts and selected two as Young Investigator Award recipients. These two individuals were given plaques and delivered oral talks during the workshop; the remaining Young Investigators presented posters.

### **Expected Outcomes**

The Organizing Committee is working to develop a conference summary and strategic action plan to establish priorities for future translational research in autism, by which: (1) potential drug targets that emerge from neurobiological research on autism and NAD are identified and prioritized; (2) complementary molecular-targeted assays are developed; and (3) these assays are used in high-throughput screening. This in turn will accelerate the discovery of novel therapeutic strategies and compounds. We expect to publish this summary and strategic action in a leading scientific journal (e.g., *Journal of Neuroscience*). The conference sponsors (NIH - NINDS, NIMH, NICHD, NIEHS; private foundations - Autism Speaks, Fragile X Research Foundation, Rett Syndrome Research Foundation, Southwest Autism Research and Resource Center, Simons Foundation, Tuberous Sclerosis Alliance) have expressed interest in utilizing the recommendations in the strategic action plan to develop research initiatives for several rare diseases.