Recent Findings from Research at the Seaver Autism Center

NEW MOUSE MODEL FOR AUTISM

A team of researchers, led by Joseph Buxbaum, PhD, Director of the Seaver Autism Center, created and studied a mouse model that has a loss of one copy of the shank3 gene. The team discovered that nerve cells communicate less effectively when one copy of the shank3 gene is missing. In addition, missing a copy of this gene hinders normal nerve-cell learning processes. This finding could explain how the loss of a copy of shank3 contributes to the behavioral manifestations of autism and the related Phelan-McDermid Syndrome. Dr. Buxbaum said, “Armed with this information, we are beginning to test drugs in these mice that are aimed at treating the syndrome at its root cause, improving nerve cell communication.”

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The team from Mount Sinai included Ozlem Bozdağlı, MD, PhD, Takeshi Sarkerai, MD, PhD, Patrick Hof, MD, and Qiang Zhou, PhD, as well as Jacqueline Crawley, PhD, of the National Institutes of Health.

Dr. Buxbaum explains, “We know that the shank3 mutation plays a central, causative role in forms of autism and in Phelan-McDermid Syndrome, but we wanted to learn

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The First International Phelan-McDermid Syndrome (PMS) Foundation Symposium was recently co-hosted by the Foundation together with the Seaver Autism Center. Scientists, clinicians, and parents of children with PMS came together to discuss active research and progress in the development of novel therapeutics for people with PMS. Presenting from the Seaver Autism Center was Ozlem Bozdağlı Gunal, MD, PhD, who discussed initial results of a biological treatment in a model system of PMS. Joseph Buxbaum, PhD moderated a roundtable discussion. More information about topics discussed at the Symposium can be found at www.shank3gene.org.
more about how it does this.” Mice were genetically engineered to lack one copy of SHANK3—comparable to patients who have a SHANK3 mutation on one copy of the gene. The team analyzed both nerve cell and brain activity, and examined social behaviors in the mice.

The researchers identified impaired nerve cell communication in the SHANK3 group, and noted that the nerve cells and synapses experienced altered functional and structural plasticity. At the Laboratory of Behavioral Neuroscience at the NIH, Dr. Crawley observed a decreased level of social interaction between male and female SHANK3 mutant mice.

“These results have helped us identify a pathological mechanism behind the neurobehavioral manifestations of autism and related syndromes,” said Dr. Buxbaum. “We hope and expect that, like other developmental disorders such as Fragile X syndrome, the use of mouse models will lead directly to clinical trials that can benefit patients.”

A report of this study is available for free through the open-access journal *Molecular Autism* at the following link: http://www.molecularautism.com/content/1/1/15/abstract.

This study was sponsored by the Seaver Foundation, a special multi-investigator grant given to co-authors Drs. Buxbaum, Crawley, Hof and Zhou from the Simons Foundation, and by a generous gift from Paulina Rychenkova, PhD, and William Gibson.

**Seaver Center Athletes**

The Seaver Autism Center is proud to join with the Singer family and Team Drive4Rebecca in the New York City Triathlon on August 7, 2011. Half of all the money raised by the Seaver Autism Center’s Team will go to the Center to support active research, while the other half will be donated to Drive4Rebecca’s continuing projects.

*Help us cheer on our Seaver athletes!*

Visit http://www.crowdrise.com/TeamDriveForRebecca/fundraiser/seaverautismcenter.
The results of the study, published in *Psychological Science*, confirmed the researchers’ hypothesis. “Our data show that oxytocin selectively improves social cognition in people who are less socially proficient, but had little impact on more socially proficient individuals,” Dr. Bartz said. The men who were originally more socially proficient remained that way, and scored well on the empathic accuracy task whether they received oxytocin or the placebo. The participants who were originally less socially proficient scored poorly if they had been given the placebo but significantly better if they had been given oxytocin, so much so that their scores matched those of the more socially proficient men. Dr. Bartz said, “While more research is required, these results highlight the potential oxytocin holds for treating social deficits in people with disorders marked by deficits in social functioning, such as autism.”

This important research was covered by several media outlets, including an interview with Dr. Bartz and Jon Hamilton on National Public Radio (NPR) News during the Health section of the Morning Edition on Jan. 3.

Dr. Bartz and her colleagues have received a grant through the National Institute of Mental Health to continue their research on the impact of oxytocin beyond this study, specifically in adults with ASD.

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**News & Events**

**JOEL ELKES RESEARCH AWARD**

Dr. Buxbaum was recently awarded the prestigious Joel Elkes Research Award from the American College of Neuropsychopharmacology (ACNP). Every year the College presents this award to a scientist who has made a significant clinical or translational contribution to neuropsychopharmacology.

**TEXTBOOK OF AUTISM SPECTRUM DISORDERS**

The new *Textbook of Autism Spectrum Disorders*, co-edited by Dr. Alexander Kolevzon, covers available treatment approaches for autism spectrum disorders (ASDs) and is designed for practitioners, as well as parents of individuals with ASDs who are looking to understand biomedical and behavioral treatment options. The textbook is available on www.amazon.com.

**UJA FACULTY LINE, AUTISM COMMUNITY CONSULTATION**

Michelle L. Gorenstein-Holtzman, PsyD, returned to the Seaver Autism Center team to join the clinical faculty and serve as a liaison between the UJA Federation and the Seaver Autism Center. Dr. Gorenstein-Holtzman is consulting with community agencies on social and recreation programming for children with ASDs, including a new consultation relationship with the Brooklyn Autism Spectrum Disorders Initiative (BASDI) programs. Additionally, Dr. Gorenstein-Holtzman is arranging and providing staff training and par-
ent workshops related to research in ASD.

Dr. Gorenstein-Holtzman was most recently a Postdoctoral Fellow at Premier Healthcare in New York. Prior to that she was a Psychology Intern at Mount Sinai. She received both her PsyD and MA in general psychology from Ferkauf Graduate School of Psychology at Yeshiva University.

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**UJA Federation grant expands funding to support faculty line in community consultation**

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**Ongoing Research**

**PHELAN-McDERMID SYNDROME**
- This study is designed to comprehensively evaluate subjects with 22q13 deletions/SHANK3 mutations clinically and genetically to fully characterize this syndrome and clarify the prevalence of ASD and other features. The overall goal of this work is to explore clinical heterogeneity and to develop meaningful outcome measures for use in clinical trials.
- Participants in this study have 22q13 deletions/SHANK3 mutations.

**EFFECTS OF OXYTOCIN ON SOCIAL PERCEPTION IN ADULTS WITH ASDs**
- This study examines the critical role that oxytocin plays in social behavior and social cognition in adults with ASD.
- Participants in this study are physically healthy adults (ages 18–45) who meet diagnostic criteria for ASD.

**STUDYING THE EFFICACY OF SOCIAL SKILLS GROUP IN CHILDREN WITH ASDs**
- This study is designed to evaluate changes in behavior and in the brain associated with social skills treatment in children.
- Participants in this study are children with ASD, ages 8–11.

If you would like more information about these studies, please contact Jessica Zweifach at 212.241.2826 or jessica.zweifach@mssm.edu.