Icahn School of Medicine at Mount Sinai

seaver autism center for research & treatment @ mount sinai

Vol.6, No.1, 2015

IN THIS ISSUE

Growth Hormone Treatment Improves Social Impairments in Patients with a Genetic Disorder Known to Cause Autism

A growth hormone can significantly improve the social impairment associated with autism spectrum disorder (ASD) in patients with a related genetic syndrome, according to a pilot study conducted at the Seaver Autism Center and published at the end of last year in *Molecular Autism*.

The study results focus specifically on the use of insulin-like growth factor-1 (IGF-1) to treat Phelan-McDermid syndrome, a disorder caused by a deletion or mutation of the SHANK3 gene on chromosome 22. Along with facing developmental and language delays and motor skill deficits, most people with Phelan-McDermid syndrome also have ASD.

SHANK3 is a focus of research in the field because of its essential role in the function of synapses, the gaps between nerve cells that "decide" whether messages continue along nerve pathways as they regulate bodily processes. While Phelan-McDermid syndrome is a rare disorder, advanced genetic technology has revealed it to be a relatively common cause of ASD.

"Ours is the first controlled trial of any treatment for Phelan-McDermid syndrome," says Alex Kolevzon, MD, Clinical Director of the Seaver Autism Center. "Because different genetic causes of ASD converge on common underlying chemical signaling pathways, the findings of this study may have implications for many forms of ASD."

IGF-1 is a commercially available compound that promotes nerve cell survival, synaptic maturation and synaptic plasticity, the ability of synapses to strengthen or weaken over time, in response to increases or decreases in their activity. It is currently approved by the Food and Drug Administration for the treatment of short stature.

This study is the first to suggest that IGF-1 is safe, tolerable and associated with significant im-

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Recent Events

▶AUTISM SEQUENCING CONSORTIUM MEETING

Leaders of the Autism Sequencing Consortium (ASC), an international autism genetics collaboration led by Joseph Buxbaum, PhD, Director of the Seaver Autism Center, met recently in New York City to discuss new studies and advances in the field. To date, the ASC has sequenced 20,000 exomes, and in a recent study published in *Nature*, identified new autism risk genes. To learn more about the ASC, visit *www.autismsequencingconsortium.org*.

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Core Members of the ASC (L-R): Mark Daly, MD, PhD (Broad Institute of MIT and Harvard); Joseph Buxbaum, PhD (Seaver Autism Center, Icahn School of Medicine at Mount Sinai); Jessica Brownfeld (Seaver Autism Center, Icahn School of Medicine at Mount Sinai); Catalina Betancur, MD, PhD (Univ. Pierre et Marie Curie); Bernie Devlin, PhD (Univ. of Pittsburgh Medical Center); Jeffrey Barrett, PhD (Wellcome Trust Sanger Institute); Edwin Cook, Jr., MD (Univ. of Illinois at Chicago); Silvia De Rubeis, PhD (Seaver Autism Center, Icahn School of Medicine at Mount Sinai); Kathryn Roeder, PhD (Carnegie Mellon Univ.); Michael Zwick, PhD (Emory Univ.); David Cutler, PhD (Emory Univ.); Alison Singer (Autism Science Foundation).

Growth Hormone Treatment

Continued

provement in both social impairment and restrictive behaviors (fascination with one subject or activity; strong attachment to one specific object; preoccupation with part[s] of an object rather than the whole object; preoccupation with movement or things that move) in people with Phelan-McDermid syndrome.

Researchers enrolled nine children aged 5-15 years who were diagnosed with Phelan-McDermid syndrome in a placebo-controlled, double-blind, cross-over design study. All participants were exposed to three months of treatment with IGF-1 and three months of placebo, in random order. Compared to placebo, the IGF-1 phase was associated with significant improvement in social withdrawal and restrictive behaviors as measured by the Aberrant Behavior Checklist and the Repetitive Behavior Scale respectively, both standard behavior scales used to assess treatment effects in ASD.

Preclinical studies of SHANK3-deficient mouse models developed at the Seaver Autism Center and human neuronal models derived from pluripotent stem cells (stem cells that have the capacity to produce several distinct biological responses) of humans with SHANK3 deficiency previously suggested that IGF-1 can reverse synaptic plasticity and motor learning deficits. These studies formed the basis of this clinical trial and the results provide support for the ongoing effort to develop related drug treatments.

"This clinical trial is part of a paradigm shift to develop targeted, disease modifying medicines specifically to treat the core symptoms of ASD," says Joseph Buxbaum, PhD, Director of the Seaver Center. "Results from this pilot trial will facilitate larger studies that more definitively inform efficacy and better targeted therapeutic treatments."

L-R: Alex Kolevzon, MD, Clinical Director of the Seaver Autism Center; and Joseph Buxbaum, PhD, Director of the Seaver Autism Center

This study was funded by the Beatrice and Samuel A. Seaver Foundation and the National Institute of Mental Health.

Recent Awards

ANDREW BROWNE, graduate student and Seaver Fellow in the Seaver Autism Center and Laboratory of Molecular Neuropsychiatry led by Joseph Buxbaum, PhD, recently received the Systems and Developmental Biology and Birth Defects T32 Training Grant for his thesis project entitled, "A systems biology approach to drug discovery in autism." For this project he is generating induced pluripotent stem cells, and then neural cells from blood samples from patients with Phelan-McDermid syndrome. He is performing RNA sequencing on the cells to identify disease-associated expression changes that can be mapped to drugs with known expression profiles.

KARIM IBRAHIM, former extern at the Seaver Autism Center and currently a doctoral student in clinical psychology at the University of Hartford, received the 2014 Student Research Award from the Division of Intellectual and Developmental Disabilities of the American Psychological Association (APA) Division 33 for his dissertation study on the neural mechanisms of social skills training for children with ASD. Karim is one of two graduate students chosen nationally for this award, and his dissertation research was conducted at the Seaver Autism Center under the mentorship of Ting Wang, PhD, Assistant Professor of Psychiatry and Nueroscience. His paper titled, "Neural effects of a CBT social skills treatment on eye gaze processing in children with autism," was presented at the 2014 APA national convention in Washington, DC and was featured in the APA's winter newsletter.

HALA HARONY-NICOLAS, PHD, Seaver Fellow and Instructor in Psychiatry, recently received the International Society for Autism Research Travel Award to attend the 2015 International Meeting for Autism Research.

ALLISON MAHON, a first year medical student at Icahn School of Medicine at Mount Sinai, was awarded a Summer Research Fellowship by the American Academy of Child and Adolescent Psychiatry to study "The Impact of Workplace Social Skills Training on Job Readiness for Young Adults with Autism Spectrum Disorder." She will be mentored by Alex Kolevzon, MD, and Michelle Gorenstein-Holtzman, PsyD, Director of Community Outreach for the Seaver Center.

Recent Events *Continued*

▶"ASK THE EXPERT" AT THE MOUNT SINAI BRAIN AWARENESS FAIR

Earlier this year Ting Wang, PhD (right), participated in the "Ask the Expert" booth at the Third Annual Brain Fair hosted by the Mount Sinai Neuroscience Outreach Program. She answered questions from attendees regarding the brain and neural pathways in individuals with ASD. Fair attendees had the opportunity to learn about the brain and brain health in many different ways.

▶SEAVER AUTISM CENTER AT THE 2015 WALK NOW FOR AUTISM SPEAKS

Jessica Brownfeld, Communications and Marketing Associate, with Emily Fourie and Stacey Lurie, Clinical Research Coordinators, represented the Seaver Autism Center at this year's Walk Now for Autism Speaks.

▶LEADING RESEARCHERS COLLABORATE IN NYC

Leaders in the fields of ASD, epilepsy, and intellectual disability research and advocacy met earlier this year in NYC to discuss collaborations designed to bridge the gaps between research advances in these fields.

▶PRESENTATION AT GOETHE UNIVERSITY

Joseph Buxbaum, PhD (second from right), with colleagues at a recent presentation at Goethe University in Frankfurt, Germany. Dr. Buxbaum presented at the "International Scientific Symposium: Biomarkers and biologically guided therapeutic options of child psychiatric disorders," and his presentation focused on "Translation of genetic findings in ASD into clinical practice."

New Seaver Fellow

THE SEAVER CENTER WOULD LIKE TO WELCOME JOHANN DU HOFFMANN, PHD, NEW SEAVER POSTDOCTORAL FELLOW IN THE DEPARTMENT OF PSYCHIATRY.

In 2014, Dr. du Hoffman completed his PhD at Albert Einstein College of Medicine in the Department of Neuroscience under the mentorship of Saleem Nicola, PhD. At Mount Sinai, he is co-mentored by Joseph Buxbaum, PhD, and Matthew Shapiro, PhD. For this fellowship, Dr. du Hoffmann's research is focused on the behavioral and electrophysiological consequences of Shank3 deficiency with a focus on prefrontal cortical function.

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• **THE SEAVER AUTISM CENTER NEWSLETTER** *brings you timely updates about new developments related to research and treatment of autism spectrum disorders, as well as activities at the Seaver Autism Center. To be placed on our mailing list, please contact SeaverCenterEditor@mssm.edu or The Seaver Autism Center, Icahn School of Medicine at Mount Sinai, One Gustave L. Levy Place. Box 1668, New York, NY 10029. Our phone number is 212.241.0961 and our website is www.SeaverAutismCenter.org.*

• **SEAVER IS CONTINUING TO GO GREEN!** *Please send your email address to seavercentereditor@mssm.edu to receive this newsletter electronically.*

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SAVE THE DATE

JOIN US ON Sunday, October 25, 2015

THE 19TH ANNUAL

Seaver Autism Center Advances in Autism Conference

PRESENTED BY
The Seaver Autism Center for Research and Treatment at the Icahn School of Medicine at Mount Sinai

COURSE DIRECTOR
JOSEPH BUXBAUM, PHD

FEATURING
KEYNOTE PRESENTATION BY ALISON SINGER
CO-FOUNDER AND PRESIDENT
AUTISM SCIENCE FOUNDATION

CONFERENCE BROCHURE TO FOLLOW

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