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New Clinical Trial of IGF-1

The Seaver Autism Center has begun a new clinical trial to evaluate the effects of insulin-like growth factor-1 (IGF-1) in children with SHANK3 deficiency. This deficiency, also known as Phelan-McDermid Syndrome (PMS) or 22q13 Deletion Syndrome, results from a mutated or missing copy of the SHANK3 gene. PMS is characterized by global developmental delay, motor skills deficits, delayed or absent speech, and autism spectrum disorder (ASD). IGF-1 is the first medication to be used to treat PMS in a controlled clinical trial.

Seaver Center researchers developed a mouse model lacking a copy of the Shank3 gene in 2010. Since then, they discovered that after

two weeks of treatment with IGF-1, deficits in nerve cell communication were reversed. The nerve cells' impaired ability to adapt to stimulation, a key part of learning and memory, was restored as well. The results from this study inspired the investigators to examine the effects of IGF-1 in humans with the same genetic disorder.

The primary aim of the study is to target core features of ASD, including social withdrawal and language impairment, which will be monitored throughout the trial. "This clinical trial is part of a paradigm shift to develop drugs specifically to treat the core symptoms of autism, as opposed to medications that were developed for other purposes..."

Continued on next page

The Singer Family: Driving for Rebecca

Jon and Michey Singer are the parents of Rebecca Singer. Rebecca is a 15-year-old with Phelan-McDermid Syndrome (PMS), and she is the first participant in the Seaver Autism Center clinical trial of insulin-like growth factor-1 (IGF-1). PMS is a rare genetic disorder that results from a mutated or missing copy of the SHANK3 gene; hallmark symptoms are social, motor and language deficits, and PMS is a known cause of autism spectrum disorder (ASD). The Singer family is deeply committed to autism awareness, and they aim to share their journey and message as much as possible.

Rebecca's brother Sam is a typically developing, funny and smart 12-year-old. He is very sensitive to Rebecca's situation and has shown a lot of maturity throughout their family's

journey. For his charity project, he is raising awareness for children with special needs, and his goal is to spread the message of treating everyone kindly. He named his campaign "ALLR=" and he will be passing out this slogan on patches and note cards. The most important principles of the campaign are to smile and say hi, and to be friendly and accepting no matter what a person's differences may be.

In 2001, the Singers established the Drive4Rebecca foun-



New Clinical Trial of IGF-1 Continued from previous page

poses but were found to also be beneficial for the irritability and aggression that sometimes appear in autism patients,” said Dr. Joseph Buxbaum, Director of the Seaver Autism Center. “Our study will evaluate the impact of IGF-1 vs. placebo on autism-specific impairments in socialization and associated symptoms of language and motor disability.”

Dr. Alex Kolevzon, MD is the Clinical Director of the Seaver Center and the Principal Investigator of this study. He is working with participants, ages 5 through 17, who have SHANK3 deletions or mutations. All participants will undergo two 12-week treatment periods during which they will receive IGF-1 or placebo. All participants will receive active medication during one of the two treatment periods and placebo during the



other. Future trials are also in the planning stages to explore the effects of IGF-1 in ASD without SHANK3 deficiency. The goal is to expand the studies of IGF-1 into larger, multi-centered efforts in order to include as many children as possible.

“We are excited that the researchers at the Seaver Autism Center are undertaking this pilot study to evaluate a possible treatment for SHANK3 deficiency, which may also help everyone with ASD,” said Geraldine Bliss, Research Support Chair of the Phelan-McDermid Syndrome Foundation. “This will be the first clinical trial in Phelan-McDermid Syndrome to emerge from convincing preclinical evidence in a model system.”

Farewell

After almost 10 years at the Seaver Center, I am writing this farewell letter to the many great patients, families, colleagues, and students who have been a part of my professional and personal world in New York. I will be leaving Mount Sinai in June to join the faculty at Rush University Medical Center in Chicago. While the move will bring me closer to family and an exciting professional opportunity, it will take

me away from the many passionate, dedicated people whom I encounter on a daily basis in the New York autism community.

I will miss our patients who taught me so much, including more about the intricacies of the NYC transit system than my family of mechanical engineers. They also include families and parents who exemplified the phrase “grace under pressure”; and clinicians, who despite the many demands of clinical



work, always find time to fit in one more thing. I will also miss the dedicated scientists and graduate students, who do remarkable things everyday

(e.g., locating the hippocampus of a mouse in two seconds flat!). I look forward to continuing my scientific and professional collaborations upon my move, and hope to continue to receive updates from the many families who have been a part of my life at the Seaver Center. I also want to take this opportunity to express my sincerest gratitude for the support of the visionary and dedicated founders of the Seaver Center, Deanna and Hirsch Levine, and to Joseph Buxbaum, my colleagues and dear friends at the Center. To quote the author of one of my son’s favorite books/movies, Peter Pan, “*Nothing is really work unless you would rather be doing something else*”... and for 10 years, I could not imagine doing anything else.

With my sincere gratitude,
Latha Soorya, PhD

Mutations in 3 Genes Linked to Autism Spectrum Disorders

Newswise — Mutations in three new genes have been linked to autism, according to new studies including one with investigators at Mount Sinai School of Medicine. All three studies include lead investigators of the Autism Sequencing Consortium (ASC). The findings, in a trio of papers revealing new genetic targets in autism, are published in the April 4th online issue of the journal *Nature*. The studies provide new insights into important genetic changes and the many biological pathways that lead to autism spectrum disorders (ASD).

Gene mutations are glitches in DNA which can put you at risk for a particular disease. The genes with mutations identified in the studies – CHD8, SNC2A, and KATNAL2 – were discovered with a new state-of-the-art genomics technology known as exome sequencing, where all protein coding regions of the genome, called the exome, are analyzed. The researchers say that with further characterization of the genes and sequencing of genes in thousands of families, they will be able to develop novel therapeutics and preventive strategies for autism.

“We now have a good sense of the large number of genes involved in autism and have discovered about 10 percent of them,” said Joseph Buxbaum, PhD, Director of the Seaver Autism Center and Professor of Psychiatry, Genetics and Genomic Sciences, and Neuroscience at Mount Sinai School of Medicine. “We need to study many more parents and their affected children if we are to uncover the genes important in ASD. As these genes are further characterized, this will lead to earlier diagnosis and novel drug development. This work is crucial for advancing autism treatment.”

In the study, ASC researchers hypothesized that de novo mutations account for a substantial fraction of the risk for autism. De novo gene mutations are mutations that show up in affected children for the first time and result from mutations in the production of sperm or egg.

Founded by Dr. Buxbaum, the Autism Sequencing Consortium is an international group of autism genetics researchers that is working to identify additional genetic causes of autism through large-scale next-generation sequencing. The institutions involved in this study sequenced data from more than 500 families (both parents and the affected child), examining the protein-enriched areas of the genome.

“When the same mutations are found in multiple affected children and none are found in children without autism, we believe that we have identified mutations that collectively affect a higher proportion of individuals with autism,” said Dr. Buxbaum. “Our studies revealed that the proteins encoded by the mutated genes interact with each other far more than expected, demonstrating

significantly greater connectivity than would be expected.”

Two other papers from groups participating in the Autism Sequencing Consortium are also featured in the same issue of *Nature*. Led by Matthew State, PhD, Yale School of Medicine, the first identified several highly disruptive mutations in genes associated with ASD. The results show that multiple variants on one gene identify risk factors for ASD. The second study led by Evan Eichler, PhD at the University of Washington discovered that certain mutations associated with ASD are mainly of paternal origin. Their findings also support previous research showing an increased risk of developing ASD in children of older fathers.

This research conducted at Mount Sinai was supported by grants from the National Institutes of Health and the Seaver Foundation. Dr. Buxbaum coauthored the paper with several Mount Sinai investigators, including Avi Ma’ayan, PhD, Assistant Professor of Pharmacology and Systems Therapeutics; Vladamir Makarov, Computer Scientist, Psychiatry; Guiqing Cai, MD, PhD, Instructor, Psychiatry; Omar J. Jabado, PhD, Instructor, Genetics and Genomic Sciences; Seungtae Yoon, PhD, Assistant Professor of Psychiatry, and Jayon Lihm, PhD student.

Mount Sinai also collaborated on this study with researchers from Massachusetts General Hospital and Harvard Medical School; the Broad Institute of Harvard and MIT; Carnegie Mellon University; Baylor College of Medicine; University of Pennsylvania; Vanderbilt University; Johns Hopkins University; Hudson Alpha Institute for Biotechnology in Huntsville, Alabama; Université Pierre et Marie Curie in France; University of Texas Health Science Center; University of Illinois at Chicago; and University of Pittsburgh.

Co-directed by Drs. Buxbaum and State, the ASC shares all parallel sequencing data in autism samples. Through the efforts of the Seaver Autism Center at Mount Sinai School of Medicine and 19 other institutions across the United States, Canada, Europe, and Asia, the autism genetics community is making great strides toward understanding the genetic changes and biological pathways important in autism susceptibility.

About the Seaver Autism Center

The Seaver Autism Center recently launched the 10,000 Autism Genomes Project, to discover and characterize all the main genes involved in autism. The Seaver Center is the lead site for the initiative. The Center also conducts progressive research studies aimed at understanding the multiple causes of autism spectrum disorders and strives to develop innovative diagnostics and treatments into the provision of personalized, comprehensive



assessment and care for people with ASDs. It includes a multidisciplinary team of experts that uses genetics, molecular biology, model systems, neuroimaging, and experimental therapeutics to work with patients and families. For more information, visit www.SeaverAutismCenter.org.

About The Mount Sinai Medical Center

The Mount Sinai Medical Center encompasses both The Mount Sinai Hospital and Mount Sinai School of Medicine. Established in 1968, Mount Sinai School of Medicine is one of the leading medical schools in the United States. The Medical School is noted for innovation in education, biomedical research, clinical care delivery, and local and global community service. It has more than 3,400 faculty in 32 departments and 14 research institutes, and ranks among the top 20 medical schools both in National Institutes of Health (NIH) funding and by US News and World Report.

The Mount Sinai Hospital, founded in 1852, is a 1,171-bed tertiary- and quaternary-care teaching facility and one of the nation's oldest, largest and most-respected voluntary hospitals. In 2011, US News and World Report ranked The Mount Sinai Hospital 16th on its elite Honor Roll of the nation's top hospitals based on reputation, safety, and other patient-care factors. Of the top 20 hospitals in the United States, Mount Sinai is one of 12 integrated academic medical centers whose medical school ranks among the top 20 in NIH funding and US News and World Report and whose hospital is on the US News and World Report Honor Roll. Nearly 60,000 people were treated at Mount Sinai as inpatients last year, and approximately 560,000 outpatient visits took place.

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Driving for Rebecca Continued from page 1

dation, aimed at increasing autism awareness and supporting education and research. Another very important part of the Drive4Rebecca's mission is to "help families become stronger advocates for their children with special needs." The kick-off event for the foundation was a cross-country drive because it combined Rebecca's love for riding in the car with a fundraising opportunity. Corporations such as Girl Scouts and Build-a-Bear sponsored the event in 2002, and there were several gathering points across the country. Jon loves the Drive4Rebecca, "because it helps bring [together] many more people than just Rebecca."

All funds from the various Drive4Rebecca activities go to the Drive4Rebecca foundation, which helps them to give money to research, advocacy, education, recreational, and service-based organizations, including the Seaver Autism Center. The Drive4Rebecca also gives to the Phelan-McDermid Syndrome Foundation. "I appreciate that they're doing all that they're doing," Jon Singer explains. The Seaver Autism Center thanks the Drive4Rebecca for their trusted support and continuous generosity.

The project that inspired the Drive4Rebecca foundation is Resources for Effective Educational Development (REED) Academy, Inc., a private non-profit school for children with autism spectrum disorders between the ages of 3 to 21. When Rebecca was approaching school age, the Singers were confronted with "huge waiting lists" at all the schools that would provide the education they wanted for Rebecca. Not a family to give up, the Singers asked the Alpine Learning Group, a pioneer of using Applied Behavioral Analysis as a teaching method, if "they could build a new little wing if they somehow got a million dollars." The administrators at Alpine were graciously willing to help the Singers by assisting them in the establishment of a brand new school. The Singers joined five other families interested in this endeavor, and they raised the funds needed to establish REED Academy with help from various groups. At 15, Rebecca is the oldest student, and appropriate services are being added as she gets older.

In 2011, Jon decided he wanted to complete the New York City Triathlon with Rebecca. He had completed the race once before, but wanted to take it to the next level. The Singers started a charity team under the Drive4Rebecca, and they invited the Seaver Autism Center to participate. Dr. Alex Kolevzon, Clinical Director of the Seaver Center, and Sandeep Soorya, husband of Dr. Latha Soorya, Chief Psychologist, completed the race for the Seaver Autism Center. Jon biked and swam on his own, and he completed the running portion with Rebecca. The Drive4Rebecca has formed a team for the 2012 triathlon

as well, and Travis Doyle, friend of the Seaver Center, will be racing as a member of this team.

Also as a part of the Drive4Rebecca foundation, Jon Singer has written and published *The Special Needs Parent Handbook*, a guide for parents on how to advocate for their children with special needs so that "every child can be their best." This handbook is distributed to local libraries across the country through the Advocacy4All initiative, a Drive4Rebecca activity that supports nonprofit advocacy organizations and aims to fund services for any family in need. Jon's current project is *Driven*, a book that he is writing on his life lessons "that can be applied to overcome virtually any obstacle, transforming problems into challenges to be solved." Based on the family's track record, there is no doubt that they will succeed on this project.

As part of the IGF-1 Clinical Trial, Rebecca and the Singers traveled to the Rutgers Sensory-Motor Integration Lab to use three dimensional motion sensors and computer-generated imagery (CGI) technology to measure her gait. This technology also produced an "avatar" of Rebecca in order to examine her gait and will be used to study any changes that result from treatment with IGF-1.

When asked what advice he would give to younger parents of children with special needs, Jon offered, "It takes a long time to get experience. They should talk to other families in other situations with older kids who have been through a lot before. The most important thing is to try to connect with other people, and especially talk to as many people as possible. The more people you can get on your side, the better." He also recommends to "really do whatever you can to work on your relationship with your spouse or significant other, because you need that teamwork at home. It's never easy, but you can get through it." Jon added, "You don't have to worry about negative or bad things happening because they take care of themselves. They happen. Celebrate the positive things, especially the small ones that may be taken for granted. Sometimes getting a kid to look in your direction is huge."

Visit <http://driveforrebecca.org> to learn more and to access several free resources, and visit <http://drivenstory.com> to learn more about *Driven*, Jon's latest endeavor. *The Special Needs Parent Handbook* can be purchased at <http://tiny.cc/parenthandbook>, and visit <http://tiny.cc/seavertriathlon> if you would like to help support the Seaver member of the Drive4Rebecca NYC Triathlon Team.

Seaver Center Athletes

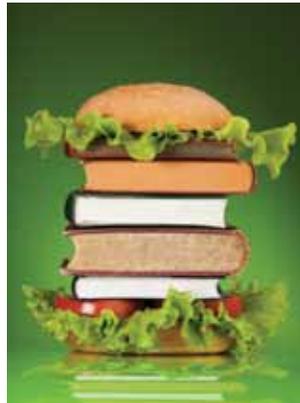
The Seaver Autism Center is proud to join with the Singer family and [Team Drive4Rebecca](#) in the New York City Triathlon on July 8, 2012. All the money raised by the Seaver Autism Center's Team will go to the Center to support active research. We are profoundly grateful to the Drive4Rebecca for their continued generosity.

Help us cheer on our Seaver athletes! Visit <http://tiny.cc/seavertriathlon>.



AUTISM SCIENCE FOUNDATION AND THE SEAVER AUTISM CENTER HOST SCIENCE AND SANDWICHES

Visit these pages to watch interviews with Drs. Joseph Buxbaum (<http://tiny.cc/buxbauminterview>) and Alex Kolevzon (<http://tiny.cc/kolevzoninterview>), PhD Student Rhonda Charles (<http://tiny.cc/charlesinterview>), and a lecture about the SHANK3 gene by Dr. Buxbaum (<http://tiny.cc/buxbaumlecture>).



The Seaver Autism Center would like to thank Mr. Rob Greenfeld and his team at Connections Personnel of NY, Inc. for the Connections Campaign for Autism Awareness Month. We appreciate all of the time and effort they put into this campaign, and the Center is extremely grateful to all those who participated and gave.



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SAVE THE DATE

Sunday, October 14, 2012

PRESENTS

Seaver Autism Center Advances in Autism Conference

PRESENTED BY
Mount Sinai School of Medicine
Seaver Autism Center
for Research and Treatment

COURSE DIRECTOR
JOSEPH BUXBAUM, PHD

CONFERENCE BROCHURE TO FOLLOW

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FEATURING
KEYNOTE PRESENTATION BY DR. SIMON BARON-COHEN,
AND SCIENTIFIC PRESENTATIONS BY DRs. JOSEPH D. BUXBAUM,
WALTER KAUFMANN, AND TIMOTHY ROBERTS.

• **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, Mount Sinai School of Medicine, One Gustave L. Levy Place, Box 1668, New York, NY 10029. Our phone number is 212.241.0961 and our web site is www.SeaverAutismCenter.org.

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



NEW! Seaver Autism Center Distinguished Lecturer Series

The Seaver Distinguished Lecturer Series (DLS) is a unique two-part lecture series featuring a renowned autism researcher and targeted towards parents and professionals alike. Prof. Dr. med. Tobias M. Boeckers, Director of the Institute of Anatomy and Cell Biology at Ulm University, will be the first speaker in this series, and he will present on anatomy and cell biology in autism spectrum disorders. Dr. Boeckers will give two lectures, one specifically for parents and one specifically for professionals. Please see below for information about each.

For Parents: *From proteins of synaptic contacts to model systems for autism spectrum disorders (ASDs)*

Tuesday, May 15, 2012 at 5:30pm

Please join us for a reception immediately following the lecture.

To register, visit <http://tiny.cc/seaverlectureparents> or scan here.



For Professionals: *Molecules and dynamic changes at postsynaptic densities (PSDs)*

Wednesday, May 16, 2012 at 2:00pm

To register, visit <http://tiny.cc/seaverlectureprof> or scan here.



Registration is required.

Location information will be sent to registrants via email.

FOR MORE INFORMATION ABOUT THE LECTURE

SERIES PLEASE CONTACT:

Jessica Brownfeld at jessica.brownfeld@mssm.edu

Help us Learn More about Early Autism Diagnoses

The Seaver Autism Center at the Mount Sinai School of Medicine is collaborating with Columbia University, as well as Carnegie Mellon University, to better identify barriers to early diagnosis of autism spectrum disorders. We invite you to participate in this research by completing a short survey. The survey is specifically for parents of children with ASD and focuses on timing issues, i.e., when parents, family members, and friends began to recognize that a child's development was not proceeding in a typical manner. The survey should take you about 10 minutes to complete. To complete the survey, please visit http://tiny.cc/seaver_card or scan here.



If you have any questions about this research, please contact the office of the Seaver Autism Center research team at 212-241-0961.