Icahn School of Medicine at Mount Sinai

seaver autism center for research & treatment @ mount sinai

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IN THIS ISSUE

NEW NIH GRANT: Optimizing treatment for Individuals with Phelan-McDermid Syndrome and Autism with IGF-1

Recent work suggests that 1-2% of individuals with autism and intellectual disability (ID) have deletions or point mutations in the SHANK3 gene, resulting in Phelan-McDermid Syndrome (PMS), and approximately 85% of people with PMS meet criteria for autism.

Alex Kolevzon, MD, Clinical Director of the Seaver Autism Center, has been awarded a new grant by the National Institutes of Health (NIH) for a new project entitled "Electrophysiological Markers for Interventions in PMS and Idiopathic Autism (iASD)".

One hundred and fifty children will be enrolled in the new study, which will use a genetics-first approach for personalized medicine in a clinical trial of Insulin-Like Growth Factor-1 (IGF-1). Our goal is to establish electrophysiological biomarkers to identify an overlapping subset of children with iASD and evaluate the effectiveness of IGF-1, and the ability of the biomarkers to stratify iASD.

Targeting SHANK3 deficiency in PMS as a specific genetic cause of autism allows us to inform treatment in broader iASD. Preliminary data using visual evoked potentials (VEPs) demonstrate promising links to disease mechanisms in PMS and iASD.

We expect this study to enable us to clarify an underlying neural mechanism in PMS common to subsets of iASD and to validate methods to predict treatment response for future clinical trials.

** Mount Sinai and Joseph Buxbaum hold a shared patent for IGF-1 in Phelan-McDermid syndrome*

CAN BABY TEETH PREDICT AUTISM?

In the recent study published by *Science Advances,* Seaver Autism Center's Avi Reichenberg, PhD, Director of Epidemiology, and a group of scientists used data gathered from baby teeth to study connections between prenatal and early-life toxic exposures and autism diagnosis.

In the study, "Dynamical features in fetal and postnatal zinc-copper metabolic cycles predict the emergence of autism spectrum disorder," Reichenberg along with Manish Arora, PhD and colleagues measured toxic chemicals and exposures by studying the layers of teeth that children shed between the ages of 6 and 12.

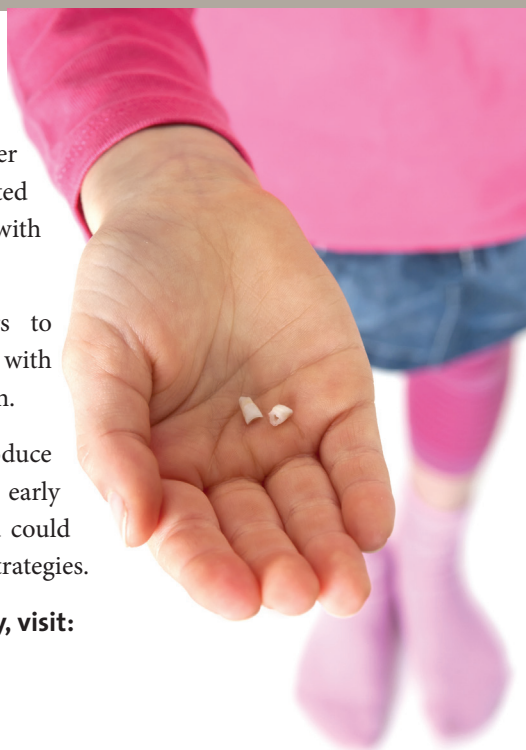
Baby teeth start to develop at the end of the first trimester, and form a new layer each day, similar to the rings on trees. These layers can capture traces of chemicals that document exposures that occurred during fetal development.

Cycles involved in zinc and copper metabolism appear to be dysregulated in autism and seem to be associated with developing the disorder.

The tooth records enable researchers to examine if children who are diagnosed with autism were biologically different early on.

The results of this research could produce a new diagnostic approach for autism early in life, before the disorder appears, and could prompt new treatments and prevention strategies.

For more information about this study, visit: http://bit.ly/BabyTeethAutism



OLIVIA'S STORY

In the early morning hours of January 23, 2009, Andrea & Bob Papageorgiou experienced one of the greatest joys of their lives as they welcomed their twin daughters Olivia and Ava into the world.

When the girls were about six months old, their parents noticed that they were not reaching some of their developmental milestones. They got both girls Early Intervention services for prematurity and, out-patient OT, PT and speech therapies.

The Papageorgiou family

Around the age of 4, Ava was discharged from out-patient therapies since she had met milestones, while Olivia was still struggling.

Olivia's doctor then recommended whole exome genetic testing, which identified her Phelan-McDermid Syndrome (PMS) diagnosis. There was a relief in finally receiving the diagnosis, but they found that most doctors do not even know what PMS is.

The Papageorgiou's attended the 2016 Phelan-McDermid conference where they met and heard Alex Kolevzon, MD speak. They were excited to discover that at the Seaver Autism Center at Mount Sinai, Olivia would be able to participate in the longitudinal assessments and natural history study of PMS. The family was able to meet with the Seaver Center staff and Dr. Kolevzon in September 2016. The testing performed has been invaluable to the family. Collaborating with the Mount Sinai experts on PMS has made a meaningful and positive difference in Olivia's life.

Olivia's progress at age 9 has been astounding. Every day the family is amazed with her growth and look forward to what tomorrow will bring

Read the full Papageorgiou family story online: http://bit.ly/OliviaStory

SEAVER ELS INSTITUTE UPDATE

First announced in April of this year, the collaboration with the Els for Autism Foundation has officially kicked off! Seventy people from the school and community, ranging in age from 4-22, have already expressed interest in participating in research. Of that total, 38 have already completed initial screening tests and 5 participants have been enrolled and completed initial study visits.

Our first project collects genetic samples, through saliva from individuals with autism and their family members, as well as phenotypic information about the individuals through parent reports.

Recruitment for our second project is also underway. This project examines the efficacy of a manualized early intervention program implemented by Els clinicians. It involves data collection at four time points to assess change, including clinical assessments and electrophysiological measures, such as EEG and eye tracking tasks.

Beginning in August, Seaver Clinical Research Coordinator, Audrey Rouhandeh, has been on-site full-time in Jupiter, FL, where she and the research team completed training for the newly installed EEG equipment.

For more information, please contact Audrey: audrey.rouhandeh@mssm.edu

MORE PAGES TO THIS CHAPTER...

The funding for our Population-based Autism Genetics and Environment Study (PAGES) study has been renewed for five more years. In its first five years, more than 1,300 individuals with autism were studied to understand how often diseases occur in different groups of people and why.

In the next five years, we will be taking a deeper look at autism severity and genetic burden, while also integrating environmental factors.

NEW FACULTY AND STAFF

ANDREA BOITNOTT, BS

Andrea Boitnott, recently graduated from Bates College with a Bachelor's of Science in Neuroscience and double minor in Chemistry and Educational Studies. She joined the Seaver Center as a research associate in Dr. Silvia De Rubeis's lab, where she will be conducting research on intellectual disability caused by a mutation in the DDX3X gene. One of the projects she will be working on is characterizing a mouse model of DDX3X syndrome, by following mice throughout development and adulthood.

HANNAH GROSMAN, BS

Hannah Grosman joined the Seaver Center in July of 2018 after working as a Clinical Research Coordinator at the Marcus Autism Center. Hannah is thrilled to continue her training working dually in the Foss-Feig Lab examining electrophysiological biomarkers in the rare disorders population seen at the center as well as on studies exploring family genetics and the female protective effect in autism.

SARAH LYNCH, BS

Sarah Lynch joined the Seaver Center in June 2018 as a Communications and Marketing Associate. Her responsibilities include various forms of internal and external communication and event management to enhance awareness of the Center. Sarah graduated from the Pennsylvania State University with a degree in Public Relations and previously worked as a senior account executive at G&S Business Communications.

CHRIS MCLAUGHLIN, BS

Chris McLaughlin joined the Seaver Center in June 2018 after graduating from Williams College in May with a major in biology. As a Research Coordinator in the Foss-Feig Lab, he will be working on studies investigating sensory and perceptual functioning in autism.

DANIELLE MENDONCA, BS

Danielle Mendonca joined the Seaver Center in June 2018 as an Associate Researcher after graduating from New York University in January 2018 with a degree in Neural Science. Her research will investigate the role of DDX3X in the pathogenesis of intellectual disability.

LARA TANG, BS

Lara Tang joined the Seaver Center in July 2018 as a Research Coordinator after graduating from Harvard College with a degree in Human Evolutionary Biology. At Seaver, she will be working on the rare genetic disease program that is investigating intellectual disability and autism caused by variants in the ADNP, FOXP1 and DDX3X genes.

DÉVINA UNG, PHD

Dévina Ung is a postdoctoral fellow in the lab of Dr. Silvia De Rubeis. She will be focusing her work on studying the neurobiology of DDX3X, a novel sex-specific gene associated with intellectual disability. She will use translational approaches to characterize the role and the pathophysiology of DDX3X during brain cortical development using a new DDX3X mouse model.

Mount Sinai

Seaver Autism Center for Research and Treatment

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

RARE DISEASE RESEARCH PROGRAM IS NOW STUDYING DDX3X SYNDROME

At the Seaver Center, we have expanded our research program on rare genetic diseases to include DDX3X syndrome, a condition caused by mutations in the DDX3X gene and associated with intellectual disability, autism and other neurodevelopmental, neurological, and medical features. DDX3X syndrome is thought to account for up to 2% of unexplained intellectual disability in females, making it one of the more common known causes of intellectual disability.

Our research aims to advance knowledge about this syndrome through coordinated clinical and pre-clinical research programs, led by Dorothy Grice, MD, and Silvia De Rubeis, PhD, respectively. The clinical component includes a comprehensive battery of evaluations by experts in psychiatry, psychology, medical genetics, and neurology, with the aim of studying DDX3X syndrome across the lifespan to better understand how the developmental aspects of this condition may change over time. The clinical research program is translated to the laboratory through studies of patient-derived stem cells and research involving animal models.

If you are interested in learning more, please contact Lara: lara.tang@mssm.edu.

You're Invited

25th Anniversary Luncheon

A benefit for the
Seaver Autism Center for Research and Treatment

Honoring
The Beatrice & Samuel A. Seaver Foundation trustees
John Cohen & Hirschell Levine

Thursday, November 1, 2018
Noon to 2:00

The Roosevelt Hotel
45 East 45th Street
New York, NY

For more information, visit: bit.ly/Seaver25th