



IN THIS ISSUE

1 SEAVER AUTISM CENTER HIRES DIRECTOR OF DRUG DISCOVERY AND DEVELOPMENT

DELETION OF THE KH1 DOMAIN OF FMR1 LEADS TO TRANSCRIPTIONAL ALTERATIONS AND ATTENTIONAL DEFICITS IN RATS

2 GRANT AWARDED TO STUDY TRANSFER OF ZIKA VIRUS FROM MOTHERS TO CHILDREN

INSAR ANNUAL MEETING RECAP

3 AUTISM AWARENESS MONTH

TOP ACHIEVEMENTS FOR SEAVER GRADUATE STUDENT

4 ADVANCES IN AUTISM CONFERENCE SAVE THE DATE

Seaver Autism Center Hires Director of Drug Discovery and Development



We are advancing efforts to translate our research findings to novel therapeutics. To lead this effort, we hired Ana Kostic, PhD to be the Director of the Drug Discovery and Development program at the Seaver Autism Center.

The landscape of medicine is changing. The world knows more now than ever before about genetic mutations and autism. At the Seaver Autism Center, we focus on five of the top genes that represent the most common single-gene causes of autism that are now called: ADNP, DDX3X, FOXP1, Fragile X

and Phelan-McDermid syndromes.

When given the same medication, people with gene mutations like these often respond in different ways than others – leading to the need for precision medicine.

In 2018, after reflecting on the state of the field, emerging technologies and evolving approaches to autism research, our Center implemented a new strategic plan with a vision to be the international leaders for precision medicine in autism and related disorders.

We needed someone to spearhead our Drug Discovery and Development initiative who understood our scientific language and could translate it to strategic partners in the pharmaceutical and biotechnology sectors.

It took over a year, but we found the person with the experience and vision needed to lead the program. Dr. Kostic is a clinical scientist with

expertise in drug development, biomarkers, and patient selection. After receiving her PhD and postdoctoral training in molecular and cell biology at Columbia University, she spent over a decade in the biotech and pharmaceutical industry, working in various roles across pre-clinical, clinical and precision medicine at Regeneron Pharmaceuticals and as the Senior Director of Translational Medicine at Kiniksa Pharmaceuticals.

The main focus of her research will be to identify potential drug candidates for treatment of autism, design experimental strategies for testing in neuronal cell systems and animal models, as well as discovery and validation of molecular biomarkers in autism.

We believe that precision medicine is essential to making a positive impact in the lives of individuals with autism and related rare disorders.

Deletion of the KH1 Domain of FMR1 Leads to Transcriptional Alterations and Attentional Deficits in Rats

Researchers at the Seaver Autism Center discovered that a rat model being used to study Fragile X syndrome (FXS), which was previously thought to lack the fragile X mental retardation protein (FMRP), does in fact express most of the sequence – excluding the crucial KH1 domain that is responsible for a main function of the protein.

FXS is a leading genetic cause for autism. The

syndrome is a neurodevelopmental disorder caused by mutations in the FMR1 gene that leads to the lack of expression of FMRP.

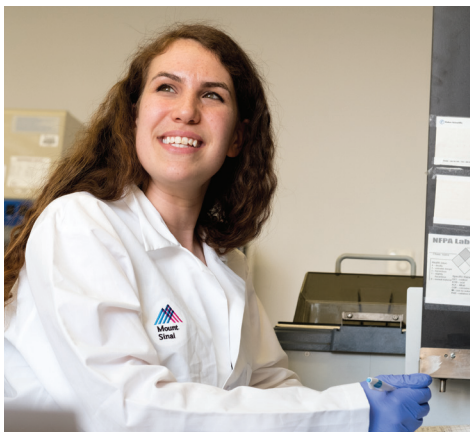
“We observed that deleting the KH1 domain from the FMRP protein in a rat is sufficient to cause deficits in attention, similar to those reported in individuals with Fragile X syndrome,” said Carla Golden, first author and Seaver Autism Center graduate student at

the Icahn School of Medicine at Mount Sinai.

The KH1 deletion also causes alterations in gene expression in the medial prefrontal cortex – the brain region that is essential for attention.

Published in *Cerebral Cortex*, this paper shows that the dysregulated genes are enriched in

Deletion of the KH1 Domain of FMR1 Leads to Transcriptional Alterations and Attentional Deficits in Rats CONTINUED



two clusters that are preserved across healthy rat and human subjects, which suggests that people are equally likely to be vulnerable for having these molecular differences.

Though the rodent model has a different gene and protein expression than originally reported, it still models the FXS disorder. The findings in this paper indicate that attentional testing might be a reliable cross-species tool for investigating new potential therapies for FXS.

With this enhanced understanding, future research can focus on potential molecular and behavioral targets for therapeutic treatment.

Carla was supported by a Seaver Graduate Fellowship.

To read the full paper, visit:
<http://bit.ly/KH1-FXS>

Grant Awarded to Study Transfer of Zika Virus from Mothers to Children

Elodie Drapeau, PhD, Assistant Professor at the Seaver Autism Center and her collaborator, Jean Lim, PhD, Associate Professor in the Department of Microbiology at Mount Sinai, have been awarded a NIH Exploratory/Developmental Research (R21) Grant to seek the understanding of how maternal antibodies transferred to a fetus enhance the severity of Zika infection in newborns.

The Zika virus is a flavivirus that has recently caused a large-scale outbreak in South and Central America and continues to spread. Often transferred to humans by mosquito bites, Zika attacks the nervous system of adults and can also be passed from mother to child in utero.

Children born to mothers infected with Zika during pregnancy have been shown to suffer from numerous defects, including: intellectual disabilities, movement and balance problems, vision and hearing loss, speech and mental delays and seizures – but what causes the wide-array of the severity of these conditions is still unknown.

Dr. Lim's initial research found that an earlier infection of a related flaviviruses such as dengue virus (DENV) can enhance Zika pathogenesis – a phenomenon known as antibody-dependent enhancement.

In both mice and humans, maternal antibodies are transferred from mother to offspring through the placenta. Because Zika circulates in many regions around the world where DENV circulates, children born to DENV-immune mothers will have circulating DENV antibodies at the time of birth.

This study hypothesizes that maternally-transferred DENV-specific antibodies enhance Zika damage to the neonates. The team will use rodent models with a humanized immune response protein to research the effects that antibodies transferred from mothers – previously affected by DENV, who also contracted Zika – have on their offspring.

Learning how environmental factors interact to cause developmental delay will help increase the understanding of autism and associated disorders.

INSAR Annual Meeting Recap

The International Society for Autism Research (INSAR) Annual meeting was held May 1-4 in Montreal.

There was a significant commitment to enhance underrepresented research disciplines at the 2019 meeting. Under the leadership of Joseph D. Buxbaum, PhD, Seaver Autism Center Director and INSAR Co-Program Chair and Executive Committee Chair, the meeting expanded its study topics to create balance and promote translational research between, biological and medical sciences, psychology and other disciplines.

Keynote speakers, Kathryn Roeder, PhD, Jason Lerch, PhD, Elizabeth Berry-Kravis MD, PhD, and Vikram Patel, MBBS, PhD, echoed that effort by offering their knowledge on genetics, neuroimaging, neurobiology, clinical trials and global health in autism and associated disorders.

INSAR 2019 was the largest annual meeting yet – over 2,000 abstracts were submitted for posters, panels and oral sessions and attendance grew to over 2,500 individuals, representing research from over 50 countries.

Over 15 members from the Seaver Autism Center were selected to present updates on our research that ranged from gut microbiome and rare genetic disorders, to biomarkers, diagnostic whole exome sequencing and more.

As planning begins for next year's annual meeting, INSAR will continue to focus on expanding research disciplines and mandating submission diversity. In addition to addressing cutting-edge themes in autism research, panel proposals will also be required to reflect a diversity of viewpoints and/or approaches, gender, geography, ethnicity and career stage.

We look forward to the autism research progress that will be represented at the meeting next year. The 2020 Annual Meeting will be held at the Washington Convention Center in Seattle, Washington on May 6-9.

Autism Awareness Month

The Seaver Center celebrated Autism Awareness Month by connecting with families and spreading knowledge about the disorder and our Center.



On April 7th, we hosted our annual Family Appreciation Day to thank the amazing families and children who have participated in our research studies. This year, we continued the tradition with performances by magician JP Laramee and the Little Maestros musical group. Seaver staff members volunteered to help make the day special by painting faces, decorating cookies, crafting custom picture frames and being the paparazzi for the photo booth.

The event celebrated attendees with a fun filled afternoon where they were able to connect with similar families.

Beyond the event, we hosted information tables at Mount Sinai Hospital to give employees and visitors a chance to meet and engage with our lab and clinical team members.

Throughout the month, we shared a special social media campaign that highlighted

the incredible siblings of some of our research participants. This series shared the experiences they have growing up in families affected by autism and the related rare genetic disorders, FOXP1 and ADNP syndromes.

Mount Sinai Health System also produced a Facebook Live segment that featured our Genetic Counselor, Maureen Mulhern, discussing the genetics of autism.

We look forward to April each year, when the world rallies around and celebrates the mission we work tirelessly towards year-round.



Top Achievements for Seaver Graduate Student

Carla Golden, a PhD candidate studying the neurobiology of attention deficits in Fragile X syndrome at the Seaver Autism Center, has been acknowledged for her tremendous involvement during her time as a student at the Icahn School of Medicine at Mount Sinai.

She has been honored with the:

2019 Award for Science Advocacy

This Graduate School Achievement is awarded to a graduating PhD student who permeates all levels of society with scientific endeavors and inspires the next generation of young people to pursue a STEM career.

Some of Carla's advocacy accomplishments

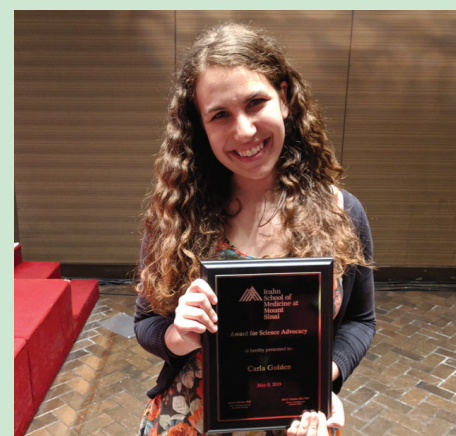
include: creating a fellowship application course, Mentoring over 10 undergrads and co-directing the Mentoring in Neuroscience Discovery at Sinai (MiNDS).

Phillip Hausfeld Memorial Scholarship

This award recognizes a particularly outstanding graduate student at Mount Sinai who is pursuing a PhD in Neuroscience.

Excellence in Curricular Development Award

Awarded for Carla's curriculum development for the Principles of Scientific Proposals course, which educated fellow students about the essential components of grant writing.



Congratulations, Carla – the contributions that you have made to the field of science are an inspiration to us all!



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23RD ANNUAL

Seaver Autism Center Advances in Autism Conference

TOPIC

Drug Discovery and Development in Autism

What Clinicians, Parents and Researchers
Need to Know

PRESENTED BY

The Seaver Autism Center for
Research and Treatment

NEW LOCATION

Apella
450 East 29th Street
New York, NY 10016

COURSE DIRECTOR

Joseph D. Buxbaum, PhD

SAVE THE DATE
FRIDAY, SEPTEMBER 20, 2019

seaver autism center for research & treatment @ mount sinai

For more information please contact:
annualconference@seaverautismcenter.org