seaver autism center
for Research & Treatment at Mount Sinai
NEWS

The 25th Annual Advances in Autism Conference

For its milestone year, we hosted the 25th annual Advances in Autism Conference in the spring. Presented online on Tuesday, May 18, the virtual conference attracted over 500 academic experts in the field of autism, healthcare professionals, parents, and community groups. This year, the focus of the conference was Quantifying Autism.

The ability to pinpoint and objectively measure biological and behavioral changes is crucial to develop treatments for any condition or disorder, including autism. These measurable indicators are known as biomarkers and they are vital to advance diagnoses, understand typical and atypical biological processes, individualize optimal treatments, and gauge responses to therapeutic interventions, such as the reduction or elimination of symptoms.

Researchers are developing biomarkers to quantify autism through EEG, imaging, and more. Our expert speakers helped educate attendees about what is needed from all stakeholders to increase the feasibility of clinical trials and individualized therapies for individuals with autism.

Seaver Center Director of Drug Discovery and Development, Ana Kostic, PhD, started the conference with a presentation that addressed why translational biomarkers are challenging to identify in autism.

We were privileged to host a roster of exceptional guest speakers, all experts from various institutions and disciplines, who presented the latest information about: Genetic Liability for Autism and Infant Brain Development (Jessica Girault, PhD), Using Neuroimaging to Understand Sensory Processing (Elysa Marco, MD), EEG Biomarkers for Clinical Trial Readiness (Shafali Jeste, MD, FAAN), Sleep Uncovered: An Unexplored Window into Neurodevelopmental Disorders (Ashura Buckley, MD), Considerations in Measurement of Social-Communication Behavior, (Somer Bishop, PhD), and the Importance of Patient Organization Collaboration (Sandra Bedrosian-Sermone).

We closed out the conference with a panel of the day's speakers, co-moderated by Seaver Center Director, Joseph Buxbaum, PhD and Seaver faculty member, Jennifer Foss-Feig, PhD. Speakers answered questions that were submitted online from the audience throughout the day.

Thank you to our event sponsors and donors that made the conference possible and free to attend for all!

Seaver Seminar Series

We are hosting an online Seaver Seminar Series that features both internal and external speakers presenting exciting and emerging bodies of work. Presentations cover a broad spectrum of basic and clinical research on autism and related neurodevelopmental disorders. Common themes include, but are not limited to, genetics, genomics, epidemiology, stem cell biology, and rodent models.

These meetings connect researchers from around the world, help attendees stay current with the latest research advances in the autism field, and spark new ideas and translational collaborations.

The series is hosted on the World Wide Neuro platform and occurs biweekly on Wednesdays at 11am. For more information on the Seaver Seminar Series, please contact the Series Director, Dr. Silvia De Rubeis: silvia.derubeis@mssm.edu or visit: **https://www.world-wide.org/Neuro/Seaver-Autism-Center/**.

Another Virtual Autism Awareness Month

Our Center made the most of our virtual celebration of Autism Awareness Month again this year! Throughout April, we shared a special social media campaign that highlighted the unique changes and challenges that families impacted by autism and related disorders faced throughout the COVID-19 pandemic. This campaign engaged our research families and members of the community to share their experiences, the difficulties and the unexpected silver linings.

We also collaborated on a social media campaign with Mount Sinai Health System, which included autism focused infographics and a Facebook Live Q&A segment with our Director of Drug Discovery and Development, Ana Kostic, PhD.

Our clinical team hosted two free webinars focused on Optimizing Primary Care Visits for Children with Autism and Self-Care for Caregivers.

Unfortunately, going virtual meant that we had to miss another year of spending quality time with our research families at Family Appreciation Day. However, we planned a special 'Messy Morning' of activities with the help of the Long Island Children's Museum. The virtual class hosted on Sunday, April 25 welcomed families from across the US, many who would not have been able to attend the traditionally in-person event.
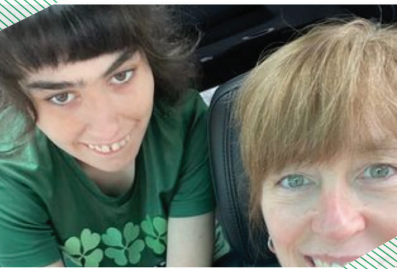
Each family that registered to attend received a special care package with all the materials to participate in the guided lessons to make Oobleck and Clean Mud. It was a treat to see so many familiar smiling faces having fun online together.

Charlie and Chloe Cleveland enjoying Messy Morning

The Clevelands' finished Oobleck and Clean Mud

AUTISM AWARENESS MONTH

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O'BOYLE FAMILY

COVID-19 PANDEMIC

AFTER THE FIRST 2 WEEKS OF THE LOCKDOWN MY DAUGHTER (20 YEARS OLD) BECAME SEVERELY DEPRESSED, STAYED IN BED MOST OF THE DAY AND EVENTUALLY BECAME CATATONIC.

AUTISM

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by difficulties in social communication as well as restricted interests and repetitive behaviors.

COMMON SYMPTOMS

Autism can present very differently from individual to individual. Common symptoms may include:

Social

- Limited eye contact
- Not responding to name
- Not initiating or responding to social bids
- Limited interest in people
- Difficulty understanding physical boundaries
- Overly familiar with strangers

Communication

- Limited verbal communication
- Limited nonverbal communication (gestures)
- Unusual intonation or volume when speaking
- Repeating words or phrases
- Difficulty with pragmatic language (e.g., back-and-forth conversation)

Restricted, repetitive behaviors or interests

- Difficulty with transitions or changes in routine
- Sensory hyperreactivity (overresponsiveness), hyporeactivity (underresponsiveness), and seeking (unusual interest in sensory aspects of the environment)
- Intense interest or extensive knowledge in something specific
- Motor mannerisms (e.g., hand flapping, spinning, rocking)
- Self-injurious behaviors (e.g., hitting self, head banging)

RISK FACTORS

Researchers have identified **102 genes** associated with risk for autism.

The Seaver Autism Center for Research and Treatment at Mount Sinai studies three of the identified top single-gene causes of autism – ADNP, FOXP1, and SHANK3 – and an additional X-linked gene, DDX3X, that is believed to be the most common genetic cause of intellectual disability in girls.

TREATMENT

Primary and first-line treatments include intensive **behavioral and educational therapies** that promote the development of social and communication skills commonly observed in individuals with autism.

There are currently no pharmacological treatments for these symptoms. However, there are some medications that can be used to help manage associated symptoms in individuals with autism such as anxiety, epilepsy, and depression.

Specific interventions should be tailored to each individual's needs and may include both behavioral and pharmacological interventions.

Mount Sinai

ARTEMIS BRIASOULI, MD, MPH

Artemis is a Postdoctoral Fellow in the Janecka Lab at the Seaver Center. Her background includes degrees in Medicine and Public Health, and two years of scientific research in pediatric brain tumor epigenetics at Johns Hopkins School of Medicine. She employs Mendelian Randomization methods to interrogate potential causal effects of abnormal gestational length on autism, as well as other neurodevelopmental disorders.

LAUREN DIERDORFF

Lauren graduated from Tulane University in 2020 and is a second-year PhD student in the De Rubeis Lab, where she is investigating the brain-wide neural populations altered in the mouse model of DDX3X syndrome. With her secondary mentor Dr. Foss-Feig, Lauren's work has a translational focus and ultimately aims to bring new treatments for neurodevelopmental disorders.

NICHOLAS CORDERO

Nicholas joined the Seaver Center in June 2021 under an NIH Diversity Supplement and is currently a second-year undergraduate student at the Sophie Davis School of Biomedical Education. As a member the Harony-Nicolas Lab, he works to create a map of neuronal populations that project to the paraventricular nucleus of the hypothalamus.

MICHAEL FLORES

Michael graduated from New York University in 2021 with a BA in Biology. He joined the De Rubeis Lab in July. The lab investigates the cellular, molecular, and developmental functions of DDX3X, an autism risk gene that is critical for cortical neurogenesis. In the future, Michael hopes to pursue a PhD in neuroscience.

CAROLINA CAPPI, PhD

Carolina is a postdoctoral fellow who joined the Buxbaum and Grice Labs in 2021. Carolina received her BS from São Paulo State University and a doctorate in Psychiatric Genetics from University of São Paulo Medical School (USP). During her PhD she did an internship at Yale University, where she applied network analysis techniques to identify risk genes in the first exome sequencing study of obsessive-compulsive disorder (OCD) parent-child trios. Under the mentorship of Dr. Buxbaum and Dr. Grice, her research is focused on identifying risk genes and biological pathways for neurodevelopmental disorders, including autism and OCD.

KAYLEIGH KANGAS-DICK, PhD

Kayleigh is a former Seaver extern, returning for postdoctoral fellowship, having obtained her PhD in School Psychology from Teachers College, Columbia University. Her predoctoral clinical background includes supervised experience in providing assessment and treatment services for children, adolescents, and young adults with attentional, behavioral, anxiety, mood, learning, and autism spectrum disorder, as well as youth in foster care. In collaboration with and under the supervision of Dr. Foss-Feig, current research efforts involve investigating the clinical utility of a new measure designed to capture autism symptom heterogeneity, as this may allow for better precision in clinical diagnostics, while facilitating more targeted, data-driven treatments and progress monitoring.

LEXIE MASSA

Lexie graduated from Middlebury College in 2021 with a BA in Neuroscience and joined the Seaver Autism Center as a Clinical Research Coordinator in the summer of 2021. Lexie coordinates a longitudinal project examining genotype and phenotype data from participants who have Phelan-McDermid syndrome, in order to better understand the early biomarkers and progression of the rare disorder.

MONICA SCHREIBER

Monica graduated from UC Berkley in 2019 with a BA in Public Health. As a Clinical Research Coordinator in the Foss-Feig Lab, Monica organizes the EXPAND study, which seeks to validate a new diagnostic measure for autism. In her role, she manages and maintains various clinical studies and works with visiting patients and families. In the future, Monica hopes to work as a health care provider with a special emphasis on Community Health models of care.

DAVID PARK

David graduated from Columbia University in May with a BA in neuroscience. He is an Associate Researcher at the Seaver Center, working with Brett Collins, the lab manager, to help manage the laboratory and assist in studies.

URVASHI THOPTE, MA

Urvashi graduated from Columbia University with a Master's in Biotechnology in December 2020, and joined the Lalli Lab as an Associate Researcher in July. The lab focuses on developing high-throughput genomic technologies in iPSC-derived neuronal cells to study the underlying genetic causes of autism and find effective therapies.

MARIA NAVA PALMA

Maria graduated from the University of California, Santa Barbara with a BS in Global Studies and a minor in Applied Psychology. She is the Spanish-speaking Clinical Research Coordinator at the Seaver Center working with Dr. Foss-Feig and Dr. Trelles to evaluate a family-focused intervention program for children with autism designed to teach functional skills, promote independence, facilitate academic learning and inclusion in all areas of life in partnership with the Ann Sullivan Center in Perú. She also works with Dr. Buxbaum in collecting DNA samples from Latinx populations to identify risk factors in autism.

JADYN TRAYVICK

Jadyn graduated from Yale University in 2021 with a BS in Psychology. As a Clinical Research Coordinator in the Foss-Feig Lab, Jadyn manages the administrative, recruitment, and data-collection aspects of EEG and eye-tracking for all research studies and coordinates the SCAN neuroimaging study for adults with autism. She hopes to pursue a doctorate in Clinical Psychology after her time in the lab.
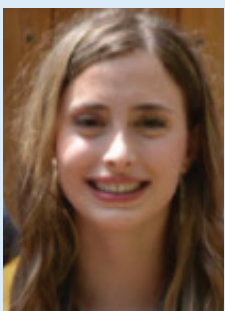
MEGAN SARDIS

Megan graduated from Yale University in May and joined the Seaver Center as a Clinical Research Coordinator in June 2021. She has a background in and passion for working with children on the autism spectrum. Megan will be working on various studies related to a range of psychiatric conditions, including autism and OCD.

Seaver Team Grant Success!

2021 proved to be another challenging year, but that did not stop our team from making strides! We are so proud of their relentless efforts to secure additional funding for their research projects. Below are a few notable achievements:

DDX3X Support

The Development of Cortico-Cerebellar Circuits in a Genetic Form of Intellectual Disability grant has been funded by the **National Institute of Neurological Disorders and Stroke (NINDS)**. With this grant, Dr. Silvia De Rubeis and her lab will look at how the cerebellum develops and communicates with the cortex in a mouse model of DDX3X syndrome. With the project, she hopes to understand if and how motor and cognitive deficits are linked in DDX3X syndrome. Postdoctoral Fellow and member for the De Rubeis Lab, Adele Mossa, PhD, also received funding from the **2021 Uplifting Athletes Grant**. Adele will expand on Dr. De Rubies' work, considering the evidence of cerebellar alteration in patients with DDX3X syndrome, their motor deficits, and the emerging role of the cortico-cerebellar circuits in autism. Through this work, the team expects to achieve a greater understanding of the circuit-level alterations in DDX3X syndrome and explore possible therapeutic targets.

Oxytocin Projections and Modulation Impacting the Supramammillary Nucleus

The oxytocin hormone is an important chemical messenger that controls some behaviors and social interaction. Oxytocin projections from the paraventricular nucleus (PVN) have been found in several brain regions that comprise the "social memory brain circuit." The Harony-Nicolas Lab has identified the presence of oxytocin neurons in the PVN as a major modulator of social recognition memory (SRM), in this instance, the ability for a rodent to distinguish between familiar and unfamiliar rodents.

Keerthi Thirtamara Rajamani, PhD, a Postdoctoral Fellow in the Harony-Nicolas Lab, has identified a novel posterior hypothalamic region called the supramammillary nucleus (SuM) as a critical point for regulating hippocampal-dependent learning and memory processes. He has been awarded the **Mindich Child Health and Development Institute (MCHDI) 2021 Trainee Pilot Grant** to study the impact that the oxytocin projections from the PVN to the SuM brain regions have on SRM.

SRM involves a multitude of cognitive and behavioral processes, and deficits in SRM have been implicated in several psychiatric disorders, including autism. However, the neural circuitry underlying this form of behavior is not fully understood and it is unclear if oxytocin projections from the PVN have a role in both the acquisition and/or consolidation of social memory. Through a prestigious **Brain Behavior Research Foundation's NARSAD Young Investigator Grant**, Keerthi will also begin to dissect the role of oxytocin in different aspects of social memory. He will employ a rodent model of autism, the *Shank3*-deficient rat, to examine if activation of the oxytocin projections from the PVN can reverse the long-term SRM deficits that were previously reported in this model. Completion of this project will determine the role that oxytocin neurons play in SRM.

Connecting Rare Genetic Mutations in Autism to Common Biological Pathways

International studies led by Dr. Buxbaum and colleagues, have identified over 102 genes, that if changed, strongly contribute to autism. Studying these genes separately is a daunting, if not impossible, task. The Brain Foundation awarded a **Brain Investigator Research Grant** to Joseph Buxbaum, PhD, to initiate an alternative, more effective approach. Co-Investigator Matt Lalli, PhD, also received a **Brain Behavior Research Foundation's NARSAD Young Investigator Grant** to help support the massive undertaking. Recently, Dr. Lalli developed a rapid and powerful method to study the function of many genes simultaneously.

This approach allows our team to study how autism-linked mutations change nerve and brain development. These mechanism biological "pathways" are important targets for new treatments since they reflect changes that are shared across many individuals with autism, including those without any known gene mutations. This method will enable direct comparison of the findings across autism genes and the ability to identify groups of genes that act through common mechanisms.

These grants will enable our team to apply this new technology to understand how many of the top autism risk genes affect nerve and brain cell development, and to group the findings into a smaller number of common pathways. Identifying a smaller number of these common pathways would guide the development of therapeutic treatment strategies for broad groups of individuals with autism. Once grouped, the team will apply a computational drug repurposing approach to search for already existing compounds that would be predicted to revert altered autism pathways to a healthy state.

2021 Young Investigator Top Draft Pick
DRAFTED!
Adele Mossa, PhD
Seaver Autism Center
#WeTackleRare
DDX3X syndrome

Mount Sinai

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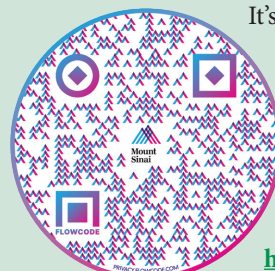
PHILANTHROPY MAKING AN IMPACT

An unfortunate fact about scientific and clinical research is that it is expensive. At the Center we are always looking for new ways to increase philanthropy in order to keep making progress for individuals with autism.

This year, our annual Seaver Celebration fundraiser took on a new format, a virtual video premiere. The 24-minute film premiered on November 9, and features our honorees, Anthony "Tony" and Mary Lou Cancellieri and some of the remarkable families who participate in our research, like the Egerton-Warburtons. Their son Rowland has ADNP syndrome, a leading single gene cause of autism. Viewers see what a day in their life is like and get a glimpse of a groundbreaking clinical trial.

We chose to recognize the Cancellieris for their tremendous support in the autism community and commendable efforts to inspire action to truly impact the lives of individuals with autism. Together, they have a vision of improving medical care

for individuals with autism. Our Center worked closely with Tony and his team to design and build an autism-friendly space at the Mount Sinai South Nassau Emergency Department, and to develop training videos for health professionals to work with individuals on the spectrum. These videos are now being deployed across the Mount Sinai Health System.

A special thanks to all of the sponsors and donors who helped contribute to the success of the virtual event. The video premiere helped us raise over $200,000 to support our autism and related rare disorder research.

It's not too late to be a part of the Celebration! Watch the video, donate, and learn more about the honorees: **http://giving. mountsinai.org/ SeaverCelebration**

Scan to support the Seaver Center.

Our Center also participated in the 2021 Falmouth Road Race as a Numbers for Non-Profit team. Our small, but mighty team of five runners raised over $4,800 at the 7-mile race in August.

*Seaver Team Runners:
Laura Sloofman and Hannah Walker*