seaver autism center
for Research & Treatment at Mount Sinai
NEWS
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Study of More Than 150,000 People Identifies More Genes Strongly Linked to Autism and Neurodevelopmental Disorders

The latest landmark study by the Autism Sequencing Consortium (ASC), "Rare coding variation provides insight into the genetic architecture and phenotypic context of autism," was published in *Nature Genetics* on August 18

The research uncovered more than 70 genes that are very strongly associated with autism and more than 250 with strong links to the condition. The analysis is the largest of its kind to date and includes more than 150,000 participants, 20,000 of whom have been diagnosed with autism.

The results offer the most comprehensive look yet at diverse forms of genetic variation in autism and in more broadly defined neurodevelopmental conditions. The insights shed light on the molecular roots of brain development and neurodiversity, and provide new avenues for future research on the biology of autism.

"We know that many genes, when mutated, contribute to autism and in this unprecedented study, we were able to bring together multiple types of mutations in a wide array of samples to get a much richer sense of the genes and genetic architecture involved in autism and other neurodevelopmental conditions. This is significant in that we now have more insights as to the biology of the brain changes that underlie autism and more potential targets for treatment," said co-senior author Joseph D. Buxbaum, PhD, Director of the Seaver Autism Center and co-founder of the ASC.

These analyses indicate that there are shared genetic risk factors between autism and other neurological and psychiatric disorders.

Based on the study findings, Dr. Buxbaum said a precision medicine approach to autism would benefit patients, as treatments that work for individuals carrying a mutation

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Exciting Grant Funding

Autism Sequencing Consortium

This year, we received exciting news that the ASC's third R01 grant has been funded by the National Institute of Mental Health (NIMH). Since Dr. Buxbaum co-founded the ASC in 2010, our collaboration with international scientists who share autism samples and genetic data has grown to over 50 sites. As mentioned above, our latest published analysis identified more genes associated with risk for autism, bringing the total of known genes – that if mutated are known to significantly increase risk for autism – to over 250. Now over 12 years later, this level of continued NIMH support confirms the quality of this work and validates the vision for a collaborative genetics-first approach that we had at the start of this great exploration, proving it to be valuable and providing the greatest understanding of the disorder that has ever been known.

Genomics of Autism in Latinx Ancestries

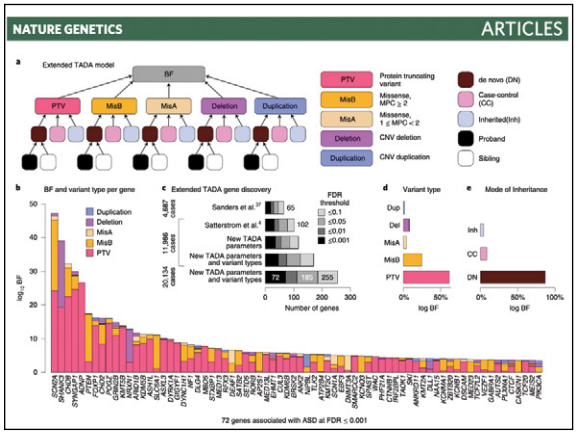
Despite our large-scale genetic analyses, there remains a number of unanswered questions, one of which is whether its genetic architecture differs across ancestral populations. Notably, there has been no systematic effort to investigate this in Hispanic and Latina/Latino populations, the largest minority population in the United States (~60 million, 18% of the total population), and growing rapidly. To increase inclusion of under-represented populations in genetic studies, we received an NIMH R01 grant to focus on the Genomics of Autism in Latinx Ancestries (GALA). The GALA study will investigate genetic risk for autism in people of Hispanic/Latinx ancestry by recruiting at least 1,600 additional Hispanic/Latinx autism trios, thereby expanding our existing sample set of well-characterized Hispanic/Latinx autism samples.

Gene Study CONTINUED

in one gene may not work in other individuals carrying a mutation in a different gene.

"A critical takeaway is that autism has many genetic mutations driving it and thus genetic testing is warranted, not just for the benefit of families and individuals at risk for autism spectrum disorder, but also to drive development of therapeutics," said Dr. Buxbaum. "The more we can advance therapeutics, based on the targets identified in these genetic findings, the more people we have the potential to help, which could have a significant impact in addressing autism and developmental delay worldwide."

The findings result from a collaboration involving scientists and datasets from the Autism Sequencing Consortium, the Simons Foundation Powering Autism Research initiative, the Lundbeck Foundation Initiative for Integrative Psychiatric Research, the Population-Based Autism Genetics and Environmental Study, and the Center for Common Disease Genomics at the Broad Institute of the Massachusetts Institute of Technology and Harvard.



Seaver Center Director Honored as a 2022 Jacobi Medallion Awardee

Joseph D. Buxbaum has been selected as a 2022 Jacobi Medallion recipient.

The Jacobi Medallion is one of the highest honors that the Mount Sinai Health System bestows upon current or former colleagues. The recipients have made exceptional contributions to Icahn Mount Sinai, the Health System, the Mount Sinai Alumni Association, or the fields of medicine or biomedicine.

Dr. Buxbaum is a renowned molecular geneticist who is being recognized for his research that aims to understand the molecular and genetic basis of autism and other neurodevelopmental disorders, with the goal of developing novel therapeutics.

The Jacobi Medallion award ceremony and cocktail and dessert reception was hosted at The Plaza Hotel on Tuesday, June 21.

(Top Row L-R) Dr. Talia H. Swartz, Dr. Naomi Luban, Dr. Sandra Masur, Dr. Annetine Gelijns, Dr. Dennis Charney, Barbara Niss, Dr. Rosalind Wright, Dr. Carlos Cordon-Cardo, **(Bottom Row L-R)** Dr. Joseph D. Buxbaum, Dr. Yvette Calderon, Dr. Jean-Frederic Colombel, Dr. Reena Karani, Dr. Ebby Elahi, and Dr. Joanne Stone attends the 2022 Mount Sinai Jacobi Medallion Awards Ceremony at The Plaza Hotel on June 21, 2022 in New York City. *(Photo by Bennett Raglin/Getty Images for Mount Sinai Health System)*

Congratulations to the other 2022 Jacobi Medallion Recipients: Yvette Calderon, MD, MS; Jean-Frederic M. Colombel, MD; Carlos Cordon-Cardo, MD, PhD; Ebby Elahi, MD, MBA, FACS, MSSM '96, MSH '00; Annetine C. Gelijns, PhD; Reena Karani, MD, MHPE, MSH '02; Naomi LC Luban, MD, MSSM '72; Barbara J. Niss, BA, MA; Joanne L. Stone, MD, MSHCDL; Rosalind J. Wright, MD, MPH

Another Virtual Autism Awareness and Acceptance Month

During Autism Awareness and Acceptance Month in April, we leveraged our networks to help increase awareness about autism and our research. This year, to highlight our sensory work, we created a social campaign that focused on sensory facts. We worked with the Mount Sinai Health System social team to have our Chief Psychologist, Dr. Paige Siper, PhD, featured in a Facebook Live Q&A video that was promoted and broadcasted from their account. The interview echoed the importance of understanding sensory processing differences and how they are related to autism. The Facebook Live video was adapted into a blog article and sent to the Health System's HealthCast eNewsletter for patients. The blog also included two special video projects: 1.) An emotional Health System PSA video, that featured a family impacted by ADNP syndrome from our Center and how the first-ever drug trial for ADNP syndrome that we conducted "changed their lives in ways they will forever be chasing" and encouraged families to get genetic testing; and 2.) A video at the emergency department of Mount Sinai Beth Israel, highlighting the sensory kits our team developed to improve the patient experience in a medical setting.

Our team hosted another interactive virtual program for our annual Family Appreciation Day. On Sunday, May 1, we partnered with the Guggenheim Museum to host 'A Day At The Guggenheim.' The developmentally appropriate 1.5-hour virtual session included a virtual exploration of the Guggenheim's Kandinsky exhibition and an online class to create inspired artwork. Care packages with Seaver branded water bottles, Seaver branded maracas for music breaks, and all the art materials were delivered to each participant's home before the virtual event. We had 28 families (with over 50 children) from across the country (NY, NJ, CT, IL, VA, CO, GA, FL, PA, KY & MD) participate, again far-extending our local reach when the event was hosted in-person.

The 26th Annual Advances in Autism Conference

The 2022 annual Advances in Autism Conference was held on Tuesday, May 24. Initially, we were planning to host the meeting as a hybrid event, but days before the event NYC was declared a high-risk area for COVID-19 transmission. For the safety of our attendees, we converted the Conference into a fully virtual event.

The program focused on Convergence in Autism: From Many Genes to Few Pathways. Our accomplished speakers presented their work that explained how finding out what pathways are involved in the disorder, and identifying what step of the pathway is affected in each individual, can lead to more personalized strategies for the diagnosis and treatment of autism.

We had over 460 attendees from around the world join the live event. The presentations and Q&A recordings are now available to view on the online Conference portal:
https://media.rampard.com/20220524

Presentations include: 100s of Genes Identified in Autism (Joseph D. Buxbaum, PhD), Connecting Rare Autism Mutations to Common Pathways (Matthew Lalli, PhD), Using Frogs to Translate Autism Genetics to Actionable Biology (Helen Willsey, PhD), Scalable Investigation of Autism Risk Genes in the Developing Brain (Xin Jin, PhD), Building the Human Cortex: Molecular Logic of Neural Circuit Formation and Evolution (Nenad Sestan, MD, PhD), Studying Convergence in Autism Using 3D Models of Brain Development (Aaron Gordon, PhD), and Redefining Autism – Using the Neuroanatomy to Create Autism Subgroups (Jacob Ellegood, PhD).

Thanks to our amazing sponsors, we were also able to secure funds to support the event and ensure it is free to attend for all.

New Staff

RHEA CHANDLER, MPH

Rhea graduated from John Jay College in May 2019 with her MPH. She joined the Administrative team at the Seaver Center in May 2022 and works with Dr. Buxbaum as his assistant as well as providing general administrative support for the Center.

LILY COHEN

Lily graduated from New York University's Applied Psychology program in May. In June she joined Drs. Behrang Mahjani and Dorothy Grice's team as a Clinical Research Associate in the OCD, Tics, and Related Disorders Program.

KATE FRIEDMAN

Kate, who also goes by Katie, graduated from Vanderbilt University in May and joined the Seaver Autism Center as a Clinical Research Coordinator. Her studies focus on rare diseases related to autism, including an investigation of the natural history of Phelan-McDermid syndrome.

SEULGI JUNG, PHD

Seulgi joined the Mahjani Lab at the Seaver Center as a Postdoctoral Fellow in March 2022. During his PhD course in University of Ulsan College of Medicine in South Korea, his research focused on identification of common genetic variants related to autoimmune and infectious disease in East Asians using genome-wide association studies. With his mentors, Drs. Mahjani, Buxbaum, and Grice, he is investigating genetic causes of OCD on de novo, rare, and copy-number variants identified using whole-exome sequencing datasets.

KIRSTEN LONG

Kirsten graduated from Middlebury College in February of 2022 with a BA in Neuroscience and Psychology. She joined the Foss-Feig Lab in June as a clinical research coordinator, focusing on a project that validates a new autism measure that will allow for a targeted clinical treatment in the future.

PRAISE OLA

Praise graduated from Alcorn State University in May 2022 with a BA in Biochemistry. 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, Praise hopes to pursue a MD/PhD in neuroscience.

ARABELLA PETERS

Arabella graduated from Emory University in 2022 with a BA in Psychology and a BA in Linguistics. As a Clinical Research Coordinator in the Foss-Feig Lab, Arabella manages the administrative, recruitment and data-collection aspects of EEG and eye-tracking for all research studies. After her time at the Foss-Feig Lab, Arabella plans to pursue a doctorate in Clinical Psychology.

THARIANA PICHARDO

Thariana graduated from Amherst College in 2022 with a BA in Psychology and Political Science and joined the Seaver Center as a Spanish-speaking Clinical Research Coordinator in the summer of 2022. Thariana organizes the GALA project in Dr. Buxbaum's Lab, which helps investigate the genetic risk factors in autism by conducting research in Latinx communities, which have often been excluded from research. In the future, she hopes to keep working with underserved communities and pursue a doctorate in Clinical Psychology.

HAILEY SILVER, MA

Hailey graduated from Teachers College at Columbia University in 2022 with a Master's in Clinical Psychology. As a Clinical Research Coordinator, Hailey manages studies focusing on rare diseases related to autism and other neurodevelopmental disabilities and collects biomarker data via VEP, EEG, and eye-tracking for these participants.

XURAN WANG, PHD

Xuran is an Assistant Professor in the Buxbaum Lab. Xuran's main research interest is developing statistical methods and computational tools for cutting-edge biotechnologies and genetic problems. Her research spans from Mendelian randomization to single-cell deconvolution and single-cell gene expression network constructions. Before joining the Seaver Center, Xuran earned her PhD in Applied Mathematics and Computational Science at University of Pennsylvania and worked as a postdoctoral fellow in the Roeder Lab at Carnegie Mellon University.

Mount Sinai

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

Summer 2022 Class of Seaver Undergraduate Research Scholars

After a successful spring class, the Seaver Autism Center was thrilled to welcome the 2022 Summer Class of Seaver Undergraduate Research Scholars.

This year's summer program was made possible in part by a generous sponsorship by MaxWell Biosystems.

Seaver Undergraduate Research Scholars program is committed to eliminating barriers and increasing access to education and careers among students from (URiSM) and/or economically disadvantaged backgrounds. Our Scholars are matched with a Seaver faculty mentor and hosted in their lab, giving them a unique opportunity to gain diverse skills, build confidence in interacting with scientific mentors, and boost their competitiveness when applying for subsequent academic positions.

Sponsor a student or contribute any amount to help us continue to train the next class of scientific leaders in autism research and welcome much-needed diversity to our scientific ranks!

http://giving.mountsinai.org/goto/Seaver

Meet the Summer Scholars:

Winston Li

FROM: Brooklyn, NY
COLLEGE: Stony Brook University
CLASS: Senior
SEAVER PI: Dr. Ana Kostic
FOCUS AT SEAVER: Identify effective drugs for autism with known genetic causes and analyze their therapeutic potential in other subtypes of autism.

Alexa Von Mueffling

FROM: NYC, NY
COLLEGE: Barnard College, Columbia University
CLASS: Rising Junior
SEAVER PI: Dr. Silvia De Rubeis
FOCUS AT SEAVER: Understanding the cortical alterations in a mouse model of DDX3X syndrome. This work will contribute to defining the cellular mechanisms causing DDX3X syndrome.

Jacqueline Cho

FROM: Queens, NY
COLLEGE: Brown University
CLASS: Rising Junior
SEAVER PI: Dr. Nan Yang
FOCUS AT SEAVER: Using human stem cell-based models to study DDX3X syndrome, specifically the molecular and biochemical mechanisms underlying its etiology.

Frankie Garces

FROM: Larchmont, NY
COLLEGE: Bowdoin College
CLASS: Senior
SEAVER PI: Dr. Matthew Lalli
FOCUS AT SEAVER: Interrogating the role of SHANK3 in human neuron morphology using CRISPRi.

Kenzo Senaha Kimura

FROM: Parkland, FL and São Paulo, Brazil
COLLEGE: New York University
CLASS: Senior
SEAVER PI: Dr. Magdalena Janecka
FOCUS AT SEAVER: Identifying genetic differences associated with environmental and sociodemographic factors in autism.