Inside this issue

Letter from the Director 2
Research Impact 3-6
Postdoctoral Fellows 7-9
Events 10-11
Spring 2022 Events Overview 12
Dear Friends,

We launched the Simons Center for the Social Brain (SCSB) on January 1, 2012, with a unique mission: to understand the neural mechanisms underlying social cognition and behavior, and to translate this knowledge into better diagnosis and treatment of autism spectrum disorders. While SCSB was funded by the Simons Foundation Autism Research Initiative (SFARI), I was encouraged by Gerry Fischbach, then SFARI director, to not focus exclusively on autism. We agreed that a broad view of brain development and function spanning diverse approaches would be essential for understanding autism.

We proposed two watchwords for the center: collaboration and community. SCSB would emphasize collaborative research across MIT and even other Boston-area institutions in its programs, and aim to build a sense of community, not only through its research, but also through events that would span research talks and build awareness of autism and brain disorders. Now, even as we complete 10 years since our founding, our impact on MIT and Boston continues to grow (see graphic on page 3).

For the first 5 years, we funded annual seed grants that required two investigators as co-PIs, usually researchers who had not previously worked together. By sifting the best of the many ideas the seed grants generated and working with SFARI, we started multi-year targeted projects that included teams of faculty researchers working collaboratively on a common question, using complementary approaches and techniques. We have now organized six projects (see graphic on page 6), each involving a major team proposal and plan of research, rigorous peer review, regular meetings including data sharing and plans, and often collaborative publications. The impact of these projects ranges from discoveries crucial for understanding brain systems and mechanisms to findings that are shaping clinical trials for subsets of autism spectrum disorder (see story on page 4).

Our postdoctoral fellows program has been exceptional in the range and quality of our awardees (see story on page 7). From the program’s inception, we have required each applicant to have a primary and a secondary mentor. We continue to provide our Simons Fellows active career guidance and any other kind of support they need. A significant proportion of our previous fellows are now faculty members in universities or have research positions, and they are steadily expanding the pool of autism researchers worldwide.

Last but not least, our events—including colloquia by external speakers and lunch seminars by internal speakers—are now a fixture on the Boston neuroscience scene (see story on page 10). Somewhat to my surprise, their reach has only grown during the two years of Covid when we have met via Zoom webinars and meetings. We look forward to at least a partial return to in-person meetings and socials that are important for sustaining a sense of community.

Situated at MIT, we have been influenced by Sidney Brenner’s dictum: Progress in science depends on new techniques, new discoveries and new ideas, probably in that order. Our cover story features just some examples of the center’s contributions; please also visit our website [https://scsb.mit.edu] and our prior newsletters for a more comprehensive list. There, you can learn more about the wide range of technologies, discoveries and ideas—and, importantly, the people—that we have supported.

Perhaps the most important contribution of SCSB has been to shape the landscape of research around fundamental brain mechanisms and their relationship to brain disorders. Brain disorders with even ‘simple’ causes, such as a single genetic mutation or focal injury, have complex manifestations that are unlikely to be understood by studying the disorder alone. And fundamental brain mechanisms find expression in a wide range of neural and cognitive functions. A mechanism-based understanding of a brain disorder needs to begin with basic neurobiology but cannot stop there. Indeed, a brain disorder provides a test-bed for examining fundamental ideas and discoveries, with the potential for significant impact on human lives.

SCSB is proud to have contributed to this emerging and exciting synergy, at MIT and beyond, and we look forward to building on it in future.

At the end, I wish to acknowledge two people who have been instrumental for our work: Eleana MacPhail, our Administrative Manager, and Alexandra Sokhina, our Events Coordinator. Eleana and Alexandra have been part of SCSB for a long time, and their dedication and energy are vital components of our success.

Mriganka Sur
Newton Professor of Neuroscience
Director, Simons Center for the Social Brain
“They were willing to take a big leap of faith,” Sur said of Jim and Marilyn Simons.

Intrigued by the couple’s invitation, Sur and five other professors (Mark Bear, John Gabrieli, Ann Graybiel, Pawan Sinha and Susumu Tonegawa) proposed a set of initial research projects that, in 2005, the couple funded as The Simons Collaboration for Autism. The scientists discovered they could indeed apply their labs’ talents to autism-related research (in fact, Simons-supported studies in the Bear and Sur labs during that time have both advanced research that has reached phase III clinical trials). And so, in 2009, after the Simonses founded the Simons Foundation Autism Research Initiative (SFARI) to catalyze autism research globally, the fledgling MIT venture grew to become the Simons Initiative for Autism Research, including new support for research seed grants and postdoctoral fellowships.

By 2011, Sur had become inspired to transform the experiment into a vision. To better rise to the challenge of autism’s complexity, he wanted to break the traditional mold of single labs working on single projects by creating a collaborative community of autism researchers across all of MIT and even beyond. Involving numerous genetic variations and molecular

**Research Impact**

_Over a decade, SCSB has built a thriving community for autism research at MIT_

David Orenstein

Hundreds of influential scientific papers. A bustling calendar of lectures and talks. A collaborative ensemble of more than 120 scientists and trainees. After the first 10 years of the Simons Center for the Social Brain, evidence of MIT’s dedication to advancing the understanding, diagnosis and treatment of autism and related disorders is unmistakably apparent. But what may be most remarkable about the scope and quality of the Center’s impact is that it arose from scratch. The vibrant and productive community SCSB has built was once nothing more than a wish.

“In 2003, Chuck Vest, then president of MIT, asked me as the head of the Department of Brain and Cognitive Sciences whether there was anybody at MIT working on autism, and I said I don’t think so, why do you ask?,” said Mriganka Sur, Newton Professor of Neuroscience at MIT and director of SCSB. “He said ‘We have this very famous alumnus, Jim Simons, and he is very interested in promoting research on autism. He would like MIT to be engaged in autism research if we are interested’.”

If there was interest, it had yet to be pursued. Whatever MIT might contribute to the field was entirely prospective.

By 2011, Sur had become inspired to transform the experiment into a vision. To better rise to the challenge of autism’s complexity, he wanted to break the traditional mold of single labs working on single projects by creating a collaborative community of autism researchers across all of MIT and even beyond. Involving numerous genetic variations and molecular

**SCSB by the Numbers**

<table>
<thead>
<tr>
<th>2012–2021</th>
<th>SCSB has supported</th>
<th>SCSB serves as a bridge connecting</th>
</tr>
</thead>
<tbody>
<tr>
<td>318</td>
<td>83 investigators</td>
<td>14 Boston-area institutions.</td>
</tr>
<tr>
<td></td>
<td>47 postdoctoral fellows.</td>
<td>At MIT alone, it supports 16 departments, laboratories and centers.</td>
</tr>
</tbody>
</table>
SCSB became the first MIT research center focused on a brain disorder.

Impactful research

Since then, researchers in 16 MIT departments and 14 collaborating institutions have published more than 300 scientific papers with SCSB support, many of which have been major contributions in their own right. Seed grants made in early years of the center, for instance, helped to support Professor Feng Zhang’s development of the revolutionary CRISPR gene editing technique and Associate Professor Gloria Choi’s groundbreaking studies explaining how infection of a mother during pregnancy can result in aberrant development of social and repetitive behaviors in her offspring. Postdoctoral fellowship support (see p. 7) has supported many more discoveries.

Overarching many such examples, however, are long-term lines of research in which the Center’s targeted projects have developed, sustained and advanced progress on highly consequential cross-cutting questions in the field. One project has examined the importance of a critical brain region, the thalamic reticular nucleus, where many autism risk genes are highly expressed and disruptions in them produce hyperactivity and dysfunctions in attention, and sleep. A current project seeks to determine whether marmosets might serve as a highly informative and practical animal model of autism. The first targeted project delved deeply into the neural consequences of a prominent autism mutation in a gene called Shank3. The results of this project not only yielded fundamental insights into how it disrupts the development of neural connections, or synapses, but has also led to the development of potential therapeutic approaches.

Investigating 16p11.2 deletion

Another targeted project, a similarly deep examination of the consequences of a genetic aberration, a deletion on chromosome 16 called 16p11.2, has yielded both a defining behavioral characteristic and a mechanism-based potential treatment now undergoing clinical testing.

In 2012, Bear had become a leading expert on the neurophysiological consequences of mutation in a gene called FMR1, which leads to Fragile X syndrome. By showing that disruption of FMR1 led to excess
Fedorenko and Kanwisher collaborated to lead another targeted project examining language in autism (along with MIT Professors Rebecca Saxe, Edward Gibson, Laura Schulz and Joshua Tenenbaum). Their goal was to understand how “pragmatic” linguistic abilities—interpretation of language in social contexts—may differ in people with autism. The project produced many beneficial outcomes, including 23 papers contributing discoveries to the field. Though the project formally ended in 2017, Fedorenko said she’s still following up on findings the team made. For instance, in 2020, her team published the discovery that people with autism (and neurotypical people with many autism-like traits) showed reduced lateralization of language processing, meaning that both hemispheres of the brain contributed more equally than is typical. The right hemisphere’s unusual participation, however, appears to play a maladaptive role.

Meanwhile, targeted project collaborator Nancy Kanwisher and then research scientist Ev Fedorenko were studying 16p11.2 at an entirely different level. They were investigating observations that people with the deletion exhibited speech and language problems. They wanted to know whether such issues truly characterize the condition and, if so, precisely how. Working to develop precise, reliable measures in volunteers with the condition, they published two papers over the next several years demonstrating that only a specific manifestation, which they termed “childhood apraxia of speech” (CAS), was indeed characteristic of the disorder. People with 16p11.2 deletion had difficulties with speech articulation, or being able to produce and sequence speech sounds, Fedorenko said.

Building on these findings, SFARI is now supporting a clinical trial of R-baclofen for people with 16p11.2 deletion. Importantly, improvement in CAS is one of the main measures in the trial.

“Developing methods to provide accurate and precise characterization of cognitive phenotypes in autism is of critical importance,” said Fedorenko, who is now an Associate Professor at MIT. “I am thrilled that we were able to do this for individuals with 16p deletions with respect to articulatory abilities.”

### Pragmatics of language

Fedorenko and Kanwisher collaborated to lead another targeted project examining language in autism (along with MIT Professors Rebecca Saxe, Edward Gibson, Laura Schulz and Joshua Tenenbaum). Their goal was to understand how “pragmatic” linguistic abilities—interpretation of language in social contexts—may differ in people with autism. The project produced many beneficial outcomes, including 23 papers contributing discoveries to the field. Though the project formally ended in 2017, Fedorenko said she’s still following up on findings the team made. For instance, in 2020, her team published the discovery that people with autism (and neurotypical people with many autism-like traits) showed reduced lateralization of language processing, meaning that both hemispheres of the brain contributed more equally than is typical. The right hemisphere’s unusual participation, however, appears to play a maladaptive role.
“This work has inspired an exciting new direction in my group: trying to understand the contributions of the right hemisphere to language processing—a still much-debated question,” said Fedorenko, who said that incorporating studies of autism into her broader research on the neuroscience of speech and language has been rewarding. “SCSB has definitely been a major motivator for working with individuals with 16p11.2 deletion and with autism. I had previously only worked with neurotypical individuals and individuals with acquired brain disorders, such as stroke aphasia. Because of SCSB, my research program expanded in the direction of autism research.”

The problem of prediction

Sinha credits his interest in autism to the early conversations he had participated in with Sur and the Simonses back in 2003. The center that emerged has supported his research ever since its founding, leading to many milestones. In particular, in 2014, he led an influential paper (cited hundreds of times), hypothesizing that a common feature that might underlie the diverse behavioral traits in autism is an impairment of predictive abilities. Predictive Impairment in Autism (PIA) would skew a person’s sense of what to expect from experience and make it harder to appropriately apportion attention to the most salient stimuli.

SCSB seed grants funded his first experiments to test this hypothesis, and today he leads the newest targeted project with Professors John Gabrieli at MIT and Jesse Snedeker at Harvard. The collaborative aspect of the targeted project, he said, is valuable.

“To the extent that PIA is a broad hypothesis, it is necessary for us to systematically carve out the extent of its applicability – what aspects of autism might be fruitfully thought of as linked to a predictive challenge and which others may be quite unrelated?,” Sinha said. “Having two wonderful colleagues with expertise in domains that no single lab possesses has been crucial for this enterprise. For instance, John’s neuroimaging work is showing that, while sensory habituation is impacted in a manner consistent with PIA for social stimuli, non-social stimuli are not similarly affected.”

Bear agreed that SCSB has succeeded in generating a sustained, productive community at MIT dedicated to advancing knowledge about autism and related disorders and advancing diagnosis and treatments.

“It’s been a wonderful catalyst,” he said. “You create these magnets and you hope good things come of them. You bring people together around a common interest and you hope the whole is greater than the sum of the parts... People dedicated their own resources and people turned their focus to autism in a way they probably would not have.”

And so, where autism was once a remote notion at MIT, it is now a central focus of a large, lively, productive, and collaborative community of researchers.

SCSB Targeted Projects and their timelines
**Postdoctoral Fellows**

**SCSB fellowships propel a new generation of autism researchers**

David Orenstein

Xin Tang can demonstrate how much his Simons Center for the Social Brain postdoctoral fellowship meant just by pointing to his 2019 paper in *Science Translational Medicine*, in which he developed an innovative method of screening for drugs with the potential to treat the autism-like disorder Rett syndrome. Four figures illustrate experiments in one SCSB mentor’s lab and the other two illustrate work in the lab of his other SCSB mentor. In addition to its funding support, the fellowship gave him the opportunity to blend the complementary proficiencies of the labs of Professors Rudolf Jaenisch and Mriganka Sur, providing him with what he needed to make a significant translational advance.

Tang said his fellowship work also helped him earn a SFARI Bridge to Independence Award and land his current job as an Assistant Professor at Boston Children’s Hospital and Harvard Medical School. There, he continues to pursue the discovery of autism therapeutics. By further digging into the mechanisms by which his drug screen hits appear to help restore a healthier balance of excitation and inhibition among neurons, he is finding that they affect molecular pathways that might matter not only to Rett, but also other disorders. He credits the SCSB fellowship with helping him develop a more translational emphasis in his work, after he originally came to MIT with a focus on basic biology.

“At the beginning of your postdoctoral training, your research can go in many directions,” Tang said. “This grant was a good affirmation of this direction that gave me so much more confidence to pursue a drug discovery approach that was very much uncharted.”

Tang’s experience reflects that of many of the other 47 young researchers who have been named to SCSB fellowships during the center’s first 10 years. For instance, among the program’s 41 alumni, 13 hold faculty positions at universities around the world, another 26 are otherwise engaged in academic research and two are working in industry.

The benefits of the program for fellows range from the practical, including two years of financial support and mentorship from two prominent senior researchers, to the more personal. Like Tang, former and current fellows alike praise the inspiration, validation, collaboration and community that earning the competitive award provides.

‘An outstanding motivation’

Alex Major, a current fellow mentored by MIT Professor Earl Miller and Boston University Professor Nancy Kopell, said the fellowship has enabled him to delve more deeply into his long-standing interest in autism.

“Autism has always been an interest of mine; however, I had not been professionally involved until I began my postdoc here at MIT,” he said. “This has been an outstanding motivation for me to dive into the literature and learn about this complex and heterogeneous condition. It has also been a great opportunity to chat with some of my friends with autism about their experience, from both a scientific and personal perspective.”

Major studies “predictive coding,” the means by which the brain applies expectations to filter incoming
sensory information. For instance, predictions can de-emphasize what’s usual and mundane in a situation to help us focus on what might be new and important. To endow us with this capability, high frequency “gamma” brain rhythms among neurons in the outer surface of our brain encode sensory information, but these are regulated by lower frequency “alpha/beta” rhythms that carry our expectations. These alpha/beta rhythms are produced by neurons in deeper layers of the brain’s cortex. In people with autism, these lower frequency signals appear disrupted, potentially impairing the predictive filter and leading to a feeling of sensory overload. Major is testing this hypothesis in animal models by selectively deactivating different layers to observe the cognitive effects that causes.

Major, who is looking ahead to establishing his own academic lab in a few years, said the fellowship is very helpful in not only inspiring and supporting his research, but also in connecting him with a diverse array of fellow researchers.

“Being a part of the Simons community has also allowed me to meet fellow trainees and past Simons fellows,” he said. Moreover, “The dual mentorship structure is a very useful aspect of the fellowship. It is both a chance to network with another PI and provides experience in a different neuroscience sub-field.”
Her work included not only formulating a theoretical view of the phenomenon, but also empirical studies of individuals with autism using functional magnetic resonance imaging. She plans to continue this work in her new position as an Assistant Professor at the Faculty of Medicine at Bar-Ilan University in her native country, Israel.

“While autism isn’t the main line of research in my lab, thanks to the Simons Fellowship I realized the importance of studying autism from various aspects, so I am still expanding this branch of my research,” she said.

The inspiration, training and career advancement provided to each Simons fellow has the potential to impact the field and benefit people with autism for decades to come.
Events

SCSB events central to building a sense of community

David Orenstein

When Mriganka Sur proposed the Simons Center for the Social Brain to Jim and Marilyn Simons, a pillar of the plan was that the center would not only foment individual discoveries, but also a sustained exchange of ideas and inspiration across MIT and partner institutions.

“I suggested that our deliverables will not only be papers, publications and discoveries, but also a community and a style of doing research that will be collaborative,” Sur said.

One way the SCSB builds collaboration and community is by funding targeted projects that bring together labs with different approaches around the same big question. Another way the Center forges connections is by hosting regular meetings for past and present SCSB fellows to gather as a community. But nothing brings the whole community together more than its numerous colloquia, lunch talks and other events that have ceaselessly provided hundreds of local scientists the chance to learn, present, network, and simply be social.

Learning opportunities

Over the Center’s first decade, more than 130 leading scientists from around the globe have spoken at the SCSB colloquia. This series is the longest-running seminar series on brain disorders in the Boston area. Another 100+ SCSB member scientists have spoken at the more internally-focused lunches.

“These events have been fantastic!” said MIT Associate Professor Ev Fedorenko, who has been a researcher in the SCSB for almost its entire history, both when she held positions at Massachusetts General Hospital and at MIT. “They bring together researchers who investigate autism from all sorts of perspectives and at all the different levels from cellular/molecular to cognitive/computational. I have learned a tremendous amount by attending these and have connected with the autism research community worldwide.”

Like Fedorenko, former SCSB postdoctoral fellow Xin Tang, now an Assistant Professor at Boston Children’s Hospital and Harvard, said event speakers have introduced him to new ideas. While Tang’s graduate and postdoctoral research focused on cellular and molecular phenomena in cell cultures, he said SCSB talks have helped him learn the value colleagues who assess human behavior and cognition place on very different techniques, such as eye tracking and recording brain rhythms with EEGs.

Researchers can learn as much from being at the podium as being in the audience. Like Fedorenko and Tang, Professor Pawan Sinha has also delivered talks at SCSB events.

Temple Grandin, Ph.D.
Author of The Autistic Brain, Thinking in Pictures, and other books
Delivering a talk on “Helping Different Kinds of Minds Succeed”
Sur agreed, “Through sets, sounds, images and art, they powerfully conveyed the emotions of her son and her team as they work together to understand Clovis and the impact each has on the other.”

**Chances to connect**

Events are not only chances to learn but also chances to connect, which can be particularly important for young researchers. Current SCSB postdoctoral fellow Alex Major, for instance, said he looks to events to help him learn from the experiences of colleagues as he navigates his career path. These include special lunches just for postdoctoral fellows.

“The most impactful Simons Center events to me have been visits from past Simons fellows that are now in faculty positions,” Major said. “Hearing about their recent experience and advice has helped me feel more prepared for my applications when I reach that stage in a couple of years.

“Professor Sur creates a welcoming culture in the Simons community,” Major continued. “Past trainees always express their gratefulness for their time with SCSB and are enthusiastic to pass down advice to younger members such as myself.”

Now entering its 11th year, the SCSB events calendar continues as strong as ever with six colloquia set for the spring semester (see page 12). And because the Covid-19 pandemic has moved them online, it’s never been easier to register and join this vibrant community as it continues to learn and connect.

“I have thoroughly enjoyed participating in SCSB events,” Sinha said. “I have had the opportunity to present our work on multiple occasions and also host visitors. These have been invaluable experiences, giving me very useful feedback and also building cross-lab linkages that may have been difficult to create otherwise.”

**Embracing experience**

Complementing the research talks are special colloquia where parents or other caregivers share their experiences with autism.

One of such events titled “Autism, Interdependence and Reciprocity” featured a parent, Nathalie van Bockstaele, together with a set of people who work or have worked with her and her adult son Clovis in various capacities.

As an MIT alumna and a long-time Cambridge resident, van Bockstaele said she has been especially sensitive to the way the local image of autism has evolved in the last 30 years. She saw the creation of the Simons Center as a major step forward within the Institute.

“Thanks to Mriganka’s open-minded vision, we had a chance to present our approach to the MIT community and beyond,” she said. “Interacting with autism makes the universal interdependence among human beings blatant, and it calls for recognizing the reciprocal nature of any relationship.”

---

**Ron Suskind**  
Author of *Life, Animated: A Story of Sidekicks, Heroes, and Autism*

Delivering a talk on “Mapping the substructures of common affinities for ASD population to create tools for intellectual and emotional growth”

---

**Nathalie van Bockstaele, with Jason O’Keefe, Elise L’Herault, Michael Jauquet, Noa Alon, Pablo Friedmann, Jocelyn Odóna Holm, Jackie Lee**  
At the event “A show and tell about: Autism, Interdependence and Reciprocity”
Upcoming Events: Spring 2022

Colloquium Series

**FEBRUARY**
16 - Afonso C. Silva, Ph.D.
University of Pittsburgh

**MARCH**
9 - Linda Richards, Ph.D.
Washington University
30 - Pamela Feliciano, Ph.D.
Simons Foundation Autism Research Initiative (SFARI)

**APRIL**
13 - Liuba Papeo, Ph.D.
Institut des Sciences Cognitives “Marc Jeannerod”
27 - Juan Carlos Izpisua Belmonte, Ph.D.
Salk Institute

**May**
18 - Julia Kaltschmidt, Ph.D.
Stanford University

General Info:
Time: 4PM–5PM
Location: Zoom Webinar, registration required

Lunch Series

February 11, 2022 – **Alex Major, Ph.D.**
Simons Postdoctoral Fellow, Earl Miller Laboratory, Picower Institute, MIT

March 18, 2022 – **Michael Segel, Ph.D.**
Simons Postdoctoral Fellow, Feng Zhang Laboratory, Broad Institute of MIT and Harvard

April 22, 2022 – **Chenjie Shen, Ph.D.**
Simons Postdoctoral Fellow, Guoping Feng Laboratory, McGovern Institute, MIT

May 6, 2022 – **Ann Graybiel, Ph.D.**
Institute Professor, Department of Brain & Cognitive Sciences, McGovern Institute, MIT

General Info:
Time: 12PM–1PM
Location: Zoom Meeting, registration is not required

All events are open to public, please visit our website for all upcoming events: scsb.mit.edu/events

We urge you to support the Simons Center for the Social Brain (SCSB) at MIT. Your gift will fund groundbreaking research into causes, mechanisms and treatments of neurodevelopmental disorders including autism spectrum disorders (ASD). The center supports laboratories that study the brain at multiple levels spanning molecular, circuit and computational mechanisms of brain function and cognition. Our programs include funding for innovative, collaborative team projects and postdoctoral fellowships, as well as events that reach a wide audience.

Please consider making a gift: Simons Center for the Social Brain - Autism Research Fund 3836050

Credits:
Contributing Writer: David Orenstein
Editing: Taylor Johns
Cover Art and Design: Wing Ngan, Ink Design

SCSB team:
Director: Mriganka Sur | msur@mit.edu
Administrative Manager & Director of Development: Eleana MacPhail | ericci@mit.edu
Events Coordinator & Administrative Assistant II: Alexandra Sokhina | asokhina@mit.edu

Simons Center for the Social Brain
43 Vassar Street, Cambridge, MA 02139
http://scsb.mit.edu