

# IMPACT REPORT 2021

Stories of our mission in

*Research*

*Service*

*Training*

*& Outreach*



*Advancing knowledge of human development,  
developmental disabilities, and neurodegenerative diseases*





## From the Director

The Waisman Center continues to recover from the pandemic. With your help, our researchers, clinicians and staff continue to advance research on intellectual and developmental disabilities (IDD) and neurodegenerative diseases and serve the thousands of children and families who seek specialized care through the Waisman Center Clinics.

The impact of your support is tangible and continues to sustain the Waisman Center through these uncertain times. I am deeply grateful for your commitment and shared vision of our core mission — improving the lives of individuals and families through research, service, training and outreach.

The pages of this year's impact report highlight some of the people who inspire our work as well as the researchers, clinicians, and community who carry out our mission.

You are an invaluable partner in our progress. On behalf of the entire Waisman community, thank you for your support.

Best wishes for 2022!

A handwritten signature in blue ink, appearing to read 'Qiang Chang', with a long, sweeping underline.

Qiang Chang, PhD  
Director, Waisman Center  
Profesor, Medical Genetics & Neurology



# Waisman Center Board of Visitors & Friends of the Waisman Center

The **Waisman Board of Visitors** was established in 1996 to: provide perspective and important connections with the business community and public policy makers; assist the Waisman Center in strengthening partnerships with the private sector; provide an advocacy network; and guide major fundraising efforts.

*Phil Blake*

*Jay Loewi*

*Jay Smith*

*Walter Dewey*

*Harold F. Mayer*

*Thomas E. Terry*

*Sheri Edison*

*John McClure*

*Judith B. Ward*

*Timothy Erdman*

*Steve Mixtacki*

*Paul M. Weiss*

*Scott Kelly*

*Carmen Skilton*

Founded in 1975, the **Friends of the Waisman Center** is a nonprofit 501(c)(3) organization that supports the Waisman Center through fundraising, volunteer efforts, and community outreach. The Friends raise awareness and support for the center through three community fundraisers: a spring benefit; a golf outing; and the Waisman Whirl Run, Walk, & Roll for All Abilities.

*Linda Berman*

*Annette Helmer*

*Eric Lund*

*Robert Bishop*

*Eric Horler*

*Christina*

*Jody Bleck*

*Scott Hoselton*

*Martin-Wright*

*Joan Burns*

*Barbara Illman*

*Dan McGown*

*Drew Cheers*

*Sherri Kliczak*

*Carmen Skilton*

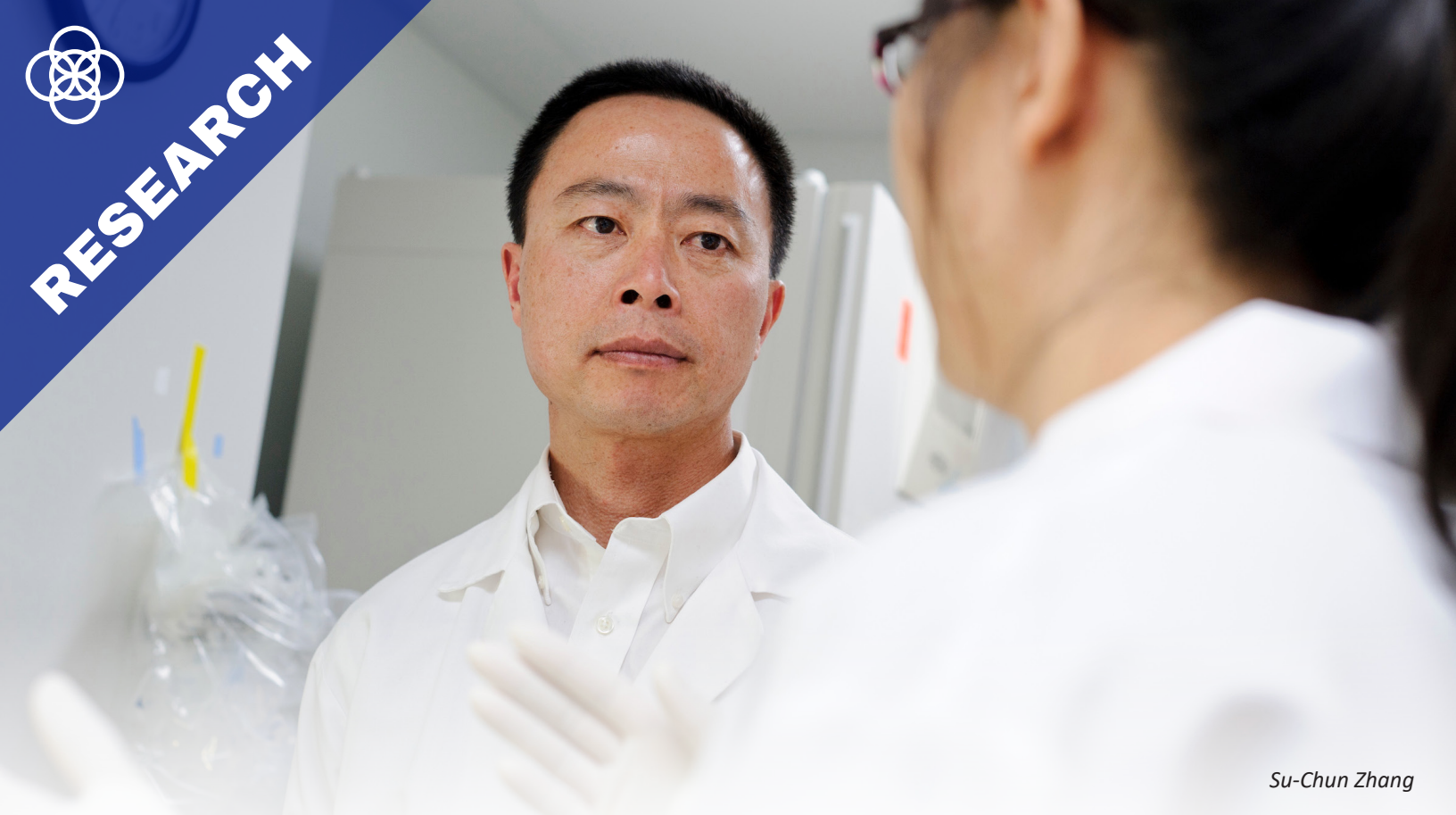
*Nancy Hansis*

*Scott Kornstedt*

*Guy Stratton*

*Kendall Harrison*

*Gary Kuter*



*Su-Chun Zhang*

## Pioneering research brings potential Parkinson's disease treatment one step closer

**O**ver two decades of fundamental research in Parkinson's disease led by **Su-Chun Zhang, MD, PhD**, professor of neuroscience and neurology at the University of Wisconsin-Madison and Waisman investigator, has culminated in the development of a promising stem cell-based treatment for the disease. The treatment is now entering into human clinical trials.

Zhang is a pioneer in stem cell research. He was the first in the world to direct embryonic stem cells into human brain cells, specifically neurons, in 2001. "We hoped that the cells would someday be useful for treating patients," says Zhang.

Since then, his lab has developed essentially all types of neural cells, which they use to study disease processes and design therapeutics. As a trained physician, Zhang's purpose has always been moving his research to the clinic. Now, he is closer than ever.

Zhang's recent Parkinson's work, done in collaboration with other researchers on campus and published in *Nature Medicine*, found that monkeys with Parkinson's-like symptoms showed significant

improvement in motor function, brain activity, and mood after receiving a graft of neurons derived from induced pluripotent stem cells (iPSC).

iPSCs are stem cells reprogrammed from skin or blood samples, that are then instructed to become other types of cells. In this case, the cells are differentiated into neurons that release dopamine — a chemical in the brain that is deficient in Parkinson's. The lack of dopamine makes it progressively harder to control movement, a common symptom of Parkinson's. Zhang had the idea for this study in 2008. However, because it was a novel study in monkeys, no government funding agency was willing to fund it. Finally, with a small grant from the Parkinson's Disease Foundation, they were able to test if the stem cell grafting worked in monkeys. "And I think that piece of data convinced the NIH to give me money to start [the present experiment]. And that's how we started," says Zhang.

"And then it takes a really long time, because we want to mimic the clinical situation, meaning the monkeys develop Parkinson's, for a few years, and then we do the transplantation [of dopamine releasing neurons],"



explains Zhang. The experiments were done in older monkeys with Parkinson's-like symptoms such as persistent slow movement, postural and gait imbalance, slight tremors and impaired gross motor skills, as well as depressive symptoms. This closely mimics Parkinson's in a clinical setting.

Scientists then used a novel approach where the monkeys received a graft of dopamine neurons made from their own stem cells— known as autologous transplantation. The cells were specifically grafted at the striatum, a region of the brain involved in motor control that lacks dopamine signaling in Parkinson's.

Half of the monkeys received autologous grafts, while the other half received grafts developed from stem cells obtained from other monkeys, also known as allogeneic transplantation.

All of the monkeys that received autologous grafts showed a substantial improvement in motor function, including increased amount of movement, speed, and fluidity.

“Our original expectation was that some will work, some will not. But they all worked. That was a good surprise,” says Zhang, impressed by the striking number of monkeys that showed recovery over 24 months after receiving autologous grafts.

Along with motor function outcomes, monkeys that received autologous grafts of stem cells had extensive growth in dopamine neuron axons – part of the neuron that transports signals – and increased dopamine activity as measured by positron emission tomography (PET), an imaging modality.

These behavioral and anatomical benefits were not observed in monkeys that received allogeneic grafts.

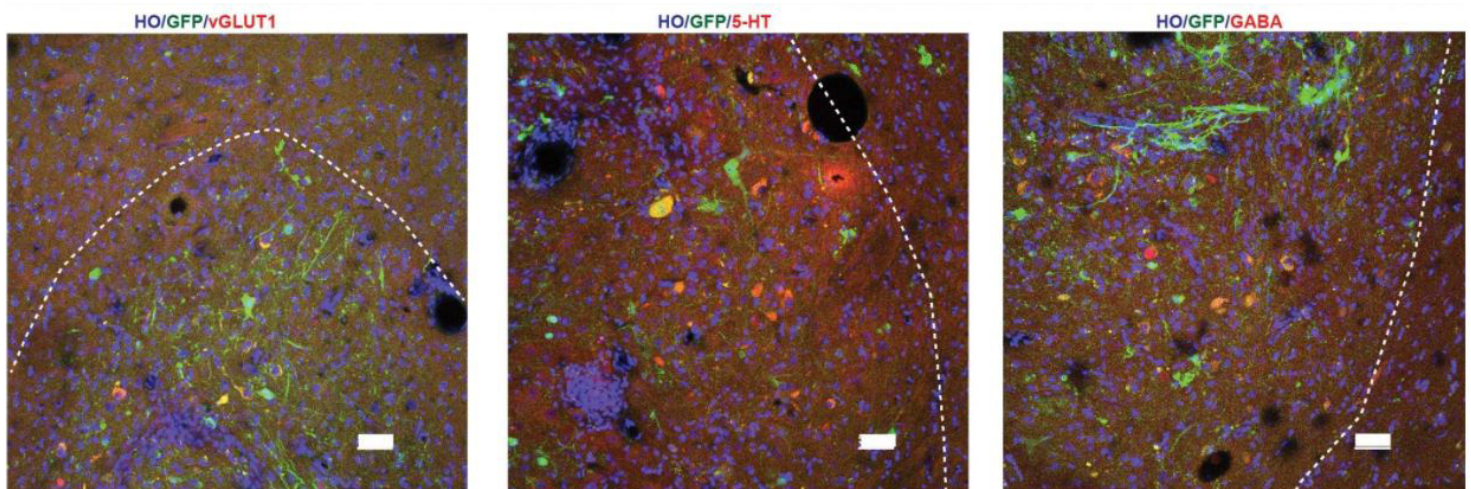
One downside to allogeneic grafts is that often times the body, recognizing cells as foreign, will activate the immune system to reject them. This was the case in this study. Monkeys receiving allogeneic grafts had ongoing inflammatory and immunological response up to 1.5 years after receiving the cells. This increase was not seen with autologous grafts.

Typically, rejection of the cells can be avoided by suppressing the immune system, which increases the chance of an infection.

For Zhang, the main take away points of this study are that “number one, the stem cell therapy for Parkinson's disease, and potentially other neurological disorders works. Number two is that, if we are taking the autologous transplantation strategy, then it does not require immunosuppression, that actually helps, because it alleviates the pain for patients.”

Right when the research group was getting ready to wrap up and finish the study, Zhang realized there was one more important aspect of Parkinson's they had not looked at. “When I was revising the paper, I asked my collaborator, ‘Did we look back on whether there is a mood change?’” This question, says Zhang, added three more months to their already long process. The encouraging results were worth the wait.

To their surprise, autologous grafts mitigated depressive symptoms in monkeys. “That was completely unexpected,” says Zhang.

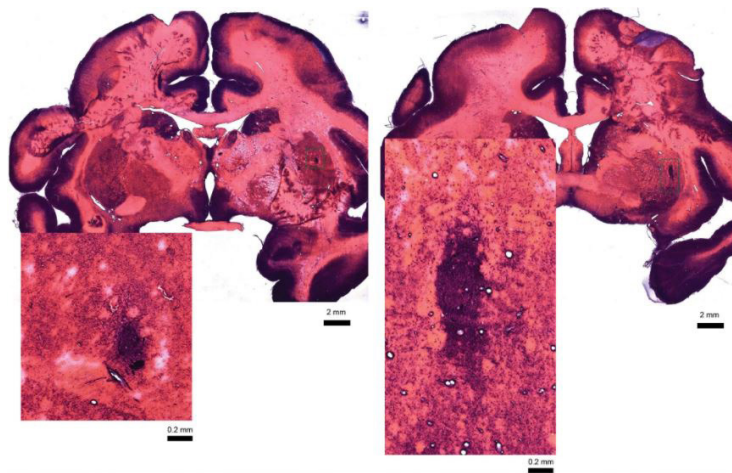


The image above shows the neurons found in the grafts implanted in monkeys. Each image marks for three different types of neurons – glutamate, serotonin, and GABA releasing – that were found in the grafts in smaller populations in addition to dopamine neurons.



Even though Parkinson's disease is regarded as a movement disorder, mood changes are another common symptom.

Zhang remembers having dinner with a colleague who had late-stage Parkinson's disease. "When he tried to pick up his food, he began trembling, that's the typical symptom," says Zhang. "He struggled to even pick up the food to get it to his mouth. You can see how debilitating the disease is, and you can imagine how this impacts their mood."



This image shows the brain section of one monkey that received allogeneic grafts (left) and one that received autologous grafts (right), highlighted in the square. Allogeneic grafts had clear boundaries – showed in the zoomed in square – while autologous grafts merged with the host tissue.

Zhang believes that the positive effect on mood observed in the monkeys that received autologous grafts could have been caused by a response to an improvement in motor symptoms. However, he believes the main reason for this improvement is the fact that the target regions grafted with new dopamine releasing neurons, also interact with areas related to mood and reward besides being involved in motor control.

"And I think that it turns out to be also very informative. When we design our clinical trial, we could potentially also target some of these [mood regulating] regions," says Zhang.

Such a comprehensive study, including behavioral tests, brain imaging, histological analysis, and cell grafting experiments, required collaboration among multiple labs within the Waisman Center and other departments at UW-Madison.

"That's the beauty of being in academia, and also being in Wisconsin, right? That's part of the reason I have stayed in Wisconsin for 25 years. Because it's a fairly collaborative environment," says Zhang, who has collaborated with other researchers at UW-Madison including Marina Emborg, PhD, and Bradley Christian, PhD.

Two decades and numerous research studies later, they are ready to move forward with clinical trials.

"I think the data is strong enough. I think it's also very solid. It makes me really, really confident to move on", says Zhang. Currently, Zhang and colleagues are in the process of designing clinical trials for autologous grafts to be tested as a treatment for Parkinson's in humans.

Upon approval from the Food and Drug Administration (FDA), they expect to take skin cells from selected individuals with Parkinson's disease, transform them into iPSCs to then reprogram them into dopamine releasing neurons. Lastly, they would graft the cells back to the patients' brain and follow up two years later.

One of Zhang's hopes is to also implement this therapy in other types of neurological disorders that he studies such as Alzheimer's, spinal cord injury, and Huntington's disease. "Ideally, it should also work for other neurological disorders. But each disease is different," says Zhang. "There are many issues that you still need to solve for each of the diseases. But that's why we work on one at a time."

The progress toward clinical trials is the culmination of more than twenty years of basic research and the beginning of a promising therapeutic approach for a disease that currently has no standard treatment.

"It has been a very long journey," says Zhang, to achieve these encouraging results. "If we compare today with what we saw 20 years ago, yeah, there is a gap. We expected something to happen much earlier. But the reality is, it takes a much longer time," says Zhang. The timeline has been impacted over the years by challenges to stem cell research with government restrictions and funding shortages. "But in the end, we're getting there. We are actually moving toward the clinic."





# TRAINING



*(L-R) Audra Sterling, Doug Dean, Lauren Bishop & Sigan Hartley*

## Postdoctoral program equips a new generation of scientists in IDD research

**A** pillar of the Waisman Center is investing in the next generation of research leaders through training and education. For more than 26 years, the center's Postdoctoral Training Program in Intellectual and Developmental Disabilities Research has helped shape the careers and research paths of 53 postdoctoral researchers through multidisciplinary training in social, epidemiological, behavioral and biobehavioral research on intellectual and developmental disabilities (IDD).

Postdoctoral fellows, who are funded through this program by a grant from the National Institute of Child Health and Human Development (NICHD) come from a wide range of academic backgrounds and are trained in understanding the neurocognitive, social, affective, communicative and family processes in relation to IDDs. "A big focus of our training program is the idea that the future research leaders in the field of IDD are going to need the tools to work in

multi-disciplinary teams in order to tackle the big problems in IDD." says Sigan Hartley, PhD, director of the program who is an associate professor of human development and family studies and a Waisman Center investigator.

Prior to Hartley, Len Abbeduto, PhD, now the director of the UC Davis MIND Institute, initiated the training grant in 1995. He was followed by Marsha Mailick, PhD, Emeritus Vice Chancellor for Research and Graduate Education and former director of the Waisman Center, who led the program from 2011 to 2017.

As part of the program, the fellows receive training in planning and conducting independent research, research collaboration, and securing funding. "I think the fellowship really helped outline some of the stepping stones I needed in order to get funding and how to establish myself as an early career



professional,” says Geovanna Rodriguez, PhD, who was part of the fellowship from 2017-2019 and is now an assistant professor of school psychology at the University of Oregon.

During her time as a fellow at Waisman, Rodriguez studied bullying and victimization experiences of children with autism spectrum disorder (ASD), as well as family level factors that affected the trajectory of internalizing symptoms in ASD. Currently, at Oregon, her research focuses on mental health outcomes within adolescents with ASD. Rodriguez is a co-principal investigator on a recently funded federal grant through the Office of Special Education Programs aimed at improving school-based mental health supports for high school students with disabilities. This grant could not have been possible without the mentorship and training



provided at Waisman. Her training highlighted the importance of creating integrated and high-quality systems of care for students with disabilities, says Rodriguez.

Other research areas that trainees study include Down syndrome, cerebral palsy, auditory perception, fragile X syndrome and early profiles of atypical development.

Fellows also attend seminars on research design and analysis, research ethics, race/ethnicity and culture, professional development and methods in IDD research. “We want to make sure fellows spend time thinking about research ethics, what it means to be a socially responsible scientist, and the importance

of ensuring that science is inclusive, reflective of the wide spectrum of individuals with IDD, and responsive to feedback from self-advocates and community stakeholders,” says Hartley.

A vital part of this training is the mentor-mentee relationship. Trainees are matched with mentors “who can help propel [their success] even more and, through the program, give them the skills to succeed,” says Hartley, who mentored Rodriguez during her time as a fellow.

For Rodriguez, her professional development and growth stemmed from her experience working with the mentors at Waisman as part of the fellowship. “Their mentorship and experience were invaluable in terms of my confidence as a researcher and helping me develop a research agenda,” says Rodriguez. Many of the lessons and skills Rodriguez learned at Waisman she now applies in her current position.

***“Their mentorship and experience were invaluable in terms of my confidence as a researcher and helping me develop a research agenda”***

Geovanna Rodriguez

Her experience during the fellowship helped shape the mentor she is today. “I think some things that I’ve taken from [Waisman] informed how I see myself as a mentor and advisor and helping researchers develop those skill sets. So that’s been something very valuable to me,” says Rodriguez.

The program helped emphasize to Rodriguez the importance of collaborations in research. “I really do try to integrate interdisciplinary collaborations and perspectives because that was something I uniquely experienced at the Waisman Center,” says Rodriguez. “It’s just having that interdisciplinary lens and collaboration model and that’s something that I tried to replicate [at Oregon].”

Many fellows, such as Rodriguez, obtain outstanding positions. Most, says Hartley, go on to tenure track



positions at universities, become research scientists, research professors, or have research leadership positions at agencies such as the CDC.

A handful of past fellows have obtained positions at the University of Wisconsin-Madison, and continue to be a part of the Waisman Center as principal investigators with independent research labs such as Audra Sterling, PhD, associate professor in communication sciences and disorders, Brittany Travers, PhD, associate professor in kinesiology, Douglas Dean III, PhD, assistant professor in pediatrics, Lauren Bishop, PhD, assistant professor in the School of Social Work, Leann DaWalt, PhD, director of UCEDD, and Hartley herself. "These are huge, nationwide competitions and they're the ones flourishing to the top," says Hartley.

For Hartley, getting to work with postdoctoral students such as Rodriguez is one of her favorite things about her job. "Getting to see them develop their confidence, develop their own area of scholarship. And just getting to support them in that process is so rewarding."

During the 2021-2022 academic year, the training program includes: Robbie Dembo, PhD, (mentored by Marsha Mailick and Leann DaWalt); Marianne Elmquist, PhD, (mentored by Katie Hustad, Audra Sterling, and Jenny Saffran); Helen Long, PhD, (mentored by Katie Hustad); and Jenny Phan, PhD (mentored by Hill Goldsmith).

The fellowship is supported by grant T32 HD 007489 of the National Institute of Child Health and Human Development (NICHD) along with generous support from the Terry Family Foundation.

## Postdoctoral Training Program in Intellectual and Developmental Disabilities Research at the Waisman Center

### T32 Alumni with research labs at the Waisman Center



**Lauren Bishop, PhD**

Aging and Health Equity in Autism and Developmental Disabilities (AHEAD)



**Sigán Hartley, PhD**

Hartley Lab for Development in Down syndrome, fragile X syndrome and autism spectrum disorder



**Doug Dean III, PhD**

Developing Brain Imaging Lab



**Audra Sterling, PhD**

Research in Neurodevelopmental Disabilities Lab (RIDDLE)



**Leann DeWalt, PhD**

Lifespan Family Research



**Brittany Travers, PhD**

Motor Brain and Development Lab





SERVICE



Madeline Barger

## New autism group therapy series changes lives

*Note: Lizzie Oster feels strongly about being referred to as an autistic person rather than a person with autism. The language in this piece reflects that preference.*

Elizabeth “Lizzie” Oster was 16 when she was diagnosed with autism. Most autistic people are diagnosed young, typically between the ages of four and five according to the Centers for Disease Control and Prevention, and can start treatment and therapy early. For Lizzie, this wasn’t how it went. It took years, a slew of misdiagnoses and many ineffectual therapists before the idea of autism was brought to the table. Lizzie endured physicians that didn’t understand her, a brief inpatient hospital stay and nearly impossible communication with her parents. All of those years that Lizzie went without a diagnosis meant huge amounts of time lost where she and her family could have benefitted from treatment.

For Lizzie and her family, her autism diagnosis was a relief. “It was really, really difficult before we had the diagnosis,” Rick Oster, Lizzie’s dad, says. A

diagnosis meant that they could begin to understand how Lizzie’s brain works, learn from therapy with autism specialists and finally figure out how to communicate and support one another. This long and difficult journey then brought the Oster family to the Waisman Center with the hope that the center’s Autism Treatment Programs would be a good fit for Lizzie. “We had gone other places and hadn’t gotten good results,” Rick says. At this point in their journey, the Oster family really needed a win.

The family began therapy with **Madeline Barger, MS, LMFT, BCBA, CST**, the Waisman Center’s Autism Treatment Programs’ lead behavior analyst, a Wisconsin licensed behavior analyst, licensed marriage and family therapist and an AASECT certified sex therapist. Madeline’s treatment style immediately resonated with the family. “The difference we noticed immediately was the Waisman Center takes a more holistic family approach,” Michelle Oster, Lizzie’s mom, says. “With many of the previous therapies, Lizzie would just go off and we would have no idea what they were working on or



what we could do to support her. Madeline and the Waisman Center really taught Rick and me about our family, how best we could support Lizzie and how we could understand her too.”

Michelle, Rick and Lizzie credit Madeline and the Waisman Center with saving their family. “Our one-on-one sessions [with Madeline] changed our whole family and our lives,” Rick says.

With the help of therapy and treatment with Madeline, Lizzie has done things she never thought she could. She always felt as though graduating high school was an impossible goal and now she is a sophomore in college. “I would have a mantra of I’m doomed,” Lizzie says. “I would genuinely repeat that for extended periods of time while rocking and being unable to cope.” Madeline helped to break some of those cycles for Lizzie and build in coping mechanisms that she can use to help her through life.

With Lizzie now in college and beginning the challenges of transitioning into adult life, Madeline thought Lizzie would be a good fit for the newly constructed autistic adult treatment series developed at the Waisman Center to support young adults through life transitions. Madeline is the lead provider for teens and adults in the Waisman Autism Treatment Programs. As such, Madeline launched this unique group treatment series specifically designed to help fill a gap in treatment for older autistic people.

“The reason we started with adults is based on a high community demand and clinical need. This 2021 group is specifically an adult women’s group as autistic women often report later-in-life diagnoses. Late diagnoses tend to lead to less effective treatment interventions and [the women] often come to us with pretty intense trauma histories prior to their autism diagnosis,” Madeline says. “We want to finally take those steps

to support autistic adults with access to appropriate and autism-informed healthcare, which is really lacking in the community.”

As someone diagnosed late, Lizzie experienced firsthand this gap in autism treatment for young adults. Prior to coming to the Waisman Center, Lizzie did see an autism specialist but found her particularly unhelpful as her program was designed around treating autistic children. “She showed me resources to teach autistic people but it was really designed for autistic children,” Lizzie says. “It was horrible and kind of infantilizing as well.” One of Madeline’s goals with this group program is to help address the lack of support for autistic young adults.

Another of the group therapy program’s goals is to provide education and support around the skills needed to transition into adulthood. This goal led to the unique trimester design of the treatment series.

The year-long group therapy series is split into three different curriculums, each designed to address an important challenge of experiencing adulthood. “We utilize three different evidence-based programs in our adult group,” Madeline says. The first is Transitioning Together which is a psycho-education model specifically focused on adult transition. The Transitioning Together program was developed at the Waisman Center by **Leann DaWalt, PhD**, a senior scientist, Waisman investigator and director of the center’s University Center for Excellence in



*Rick, Lizzie & Michelle Oster*



Developmental Disabilities. The program is based on more than 20 years of longitudinal research from the Lifespan Family Research Lab led by **Marsha Mailick, PhD**, emeritus vice chancellor for research and graduate education, at the Waisman Center.

The second is a customized group version of the UCLA PEERS® (Program for the Education and Enrichment of Relational Skills) program. The important and unique third trimester, called Advanced Adult Relationships, is specifically designed by Madeline Barger, who has rare and specialized training which allows her to provide systemic sexuality education and treatment to autistic people. This program allows individual group participants to meet their individual advanced adult relationship goals toward not only dating but also intimacy, partnering, and general sexuality education. According to Madeline, there is currently no other program like this in the United States.

community and engage in family problem solving in a group context,” Alyssa says. “Then within the PEERS® program and the Advanced Adult Relationships curriculum, the goal is to talk about the same type of social skills that Madeline is discussing and having parents support their young adults in those areas.” The parents are taught how to help and support their children as their children learn to walk into adulthood.

The Oster Family says they have reaped enormous benefit from the autism group therapy series with one of the biggest benefits being a sense of belonging and community. “I think it’s cool because I haven’t been able to meet a lot of other autistic people other than sort of at a glance and never females,” Lizzie says. “It’s been really nice for me to meet some other autistic girls and see how they interact because I feel like sometimes watching someone else, you can recognize your behaviors in them.”

***“Madeline and the Waisman Center really taught Rick and me about our family, how best we could support Lizzie, and how we could understand her too.”***

Michelle Oster

Transitioning Together builds the basis for fostering self-efficacy, social engagement, and problem solving. The UCLA PEERS® program delves into the social skills needed such as initiating conversations and building and maintaining friendships. Advanced Adult Relationships is best delivered after the initial foundation of social relationships is built and targets skills needed to foster healthy adult relationships including dating and sexual intimacy. Each of these three programs are successfully run as stand-alone programs, but together form the year-long treatment series offered at the Waisman Center. And as Madeline works with the young adults, **Alyssa Walsh, PhD**, a licensed psychologist in the Autism Treatment Programs, runs a concurrent parent group to help teach parents the best ways to support their young adults. **Sara Warner, PsyD**, licensed psychologist, also joins Alyssa in running the parent group.

“For Transitioning Together, the goal of the parent group is to reduce family stress, build a sense of

Rick and Michelle find great relief in the community the group therapy series has gathered around them. There is a peace in talking with other parents who simply understand the struggles of having an autistic child without Rick and Michelle needing to explain. “We are learning from the other parents as well. Having those shared resources and that forum to share, because all our girls are late diagnosed and are high functioning on the autism spectrum, is really helpful,” Michelle says. “Sometimes I am just too tired to explain and I don’t have to do that with the parents in group. They understand and that’s a good feeling.”

This is the first year this year-long autism group therapy series has run at the Waisman Center and Madeline and Alyssa are excited by the results they are seeing. Madeline and Alyssa’s unique combination of licensures, that allow them to provide both psychotherapy and behavioral therapy, is unusual in the autism treatment world. But, Madeline and Alyssa have found that being able to provide both services in a group setting



is uniquely benefitting their patients. “So far, our group members are already reporting decreased anxiety levels and they’re increasing their targeted participation goals. They’re talking more and sharing more,” Madeline says. “They report excitement at the possibility of cultivating new social skills toward creating and maintaining friendships and more intimate relationships. They’re all really invested in this.”

Madeline and Alyssa have big plans for the autism group therapy series. They want to build a larger and more robust training program around the group therapy series in order to cultivate more clinicians who can provide this type of therapy and boast the combination of licensures needed to do it. Madeline and Alyssa know that the unique construction of their programming offers something special and they want to make it available for many more autistic young adults who could benefit from it.

“At the moment we are small in number at the Waisman Center Autism Treatment Programs specific to serving adults. But we are mighty in drive, experience and clinical skill,” Madeline says. “We hope over time to have more staff so that we can do more and build something bigger.”

For right now though, the group therapy series is more than the Oster family could have hoped for. “I don’t know what we would do without this young adult transition program,” Michelle says. “I kind of feel like you either get in somewhere early or you’re like Lizzie. You might get just enough help to get by and then you’re released into the wild. We’re so grateful that we could be a part of this program.”



**CLINIC  
UPDATE**

## New undiagnosed disease clinic opens at the Waisman Center

**T**he UW Center for Human Genomics and Precision Medicine at the UW School of Medicine and Public Health recently opened its first patient clinic, the UW Undiagnosed Genetic Disease Clinic at the Waisman Center. The clinic, one of 11 specialty clinics at the Waisman Center, is for people with undiagnosed genetic diseases, creating a vital hub in a global community of experts dedicated to solving medical mysteries with state-of-the-art

technologies for people whose conditions remain undiagnosed despite an extensive prior clinical workup.

The clinic has a three-fold mission: to provide a diagnosis to patients who in many cases have searched for years for an answer about what is causing their conditions, to better understand the conditions once they are identified, and to discover new genes which can cause human disease.

The clinic has a core staff of medical geneticists, genetic counselors, and researchers working in partnership with researchers and lab technicians at the Wisconsin State Laboratory of Hygiene and the Biotechnology Center at UW-Madison as well as Stanford University and The Hospital for Sick Children in Toronto, Canada. In addition, multiple UW Health clinical consultants are contributing their expertise about specific management and treatment strategies.

“Madison is becoming part of an international network of researchers and clinicians that focuses on rare genetic diseases,” Stephen Meyn, MD, PhD, the director of the UW Center for Human Genomics and Precision Medicine, says. “We’re working to give patients access to the latest technology and expertise here at UW, but also from this global community.”





OUTREACH



*Tiaunta Martin & Family*

## Waisman Center's SaferKids Program gives peace of mind to families

**T**iaunta Martin is a proud mom of three boys. They are bright-eyed, energetic, and usually a whirlwind of chaos. Her middle son, Benjamin or Benji for short, is a rambunctious six-year-old who keeps Tiaunta constantly on her toes. "He's the sweetest adorable child in the world. Very hyper and outgoing, sometimes a little too much. But, he is the most precious child," Tiaunta says.

Benji was recently diagnosed with autism at the Waisman Center and, along with his endearing smile and bubbly personality, Benji had some behaviors that were leaving Tiaunta fearful for her son's safety. He would run out the front door while no one was watching. Go through the knife drawer or chemical closet. Or climb into the refrigerator. Having two other children to look after and a full-time job, Tiaunta could not always have both eyes on Benji. She was always worried for his safety.

While at the Waisman Center with Benji, Tiaunta mentioned her concerns to one of the clinic's family navigators. That's when she was told about the Waisman Center's SaferKids Program. The family navigator explained to Tiaunta that the grant could

help provide her with some tools and resources to make it easier to keep Benji safe. "In my heart, I knew this was the perfect program for us," Tiaunta says.

The Waisman Center's SaferKids Program, in partnership with the Safety Center at the American Family Children's Hospital, helps provide safety equipment and resources to children with disabilities and their families referred through several programs at the Waisman Center. Children with disabilities, such as autism in Benji's case, may present a variety of behavioral issues that can endanger their safety and it can be hard for parents to manage those behaviors without assistance. The grant was established to provide these families with equipment to make it easier to keep their child safe.

"It started with concerns that we were hearing. These children had a lot of safety concerns and no real access to funding to help pay for safety items," says **Michelle Schumacher, MSSW**, a social worker and family navigator at the Waisman Center. Schumacher is also the coordinator for the SaferKids Program, which is currently part of the Wisconsin

Care Integration Initiative at Waisman. “The grant is primarily focused on helping medically underserved families whose children are ages birth-to-five who have developmental concerns, primarily autism, which puts them at increased risk for wandering and other safety concerns.”

Children with autism engage in many of the potentially dangerous behaviors that other young children do such as getting into drawers or closets they aren’t supposed to or playing with electrical sockets. The issue becomes that children with autism may have trouble understanding safety issues due to communication, attention, and learning difficulties. Kids with autism are also prone to wandering and will often leave the home unaccompanied without their parents’ knowledge. There are many reasons a child may wander but common ones include that they enjoy running, they want to go somewhere they enjoy, or they are trying to escape a stressful situation. These behaviors can be upsetting for parents, especially if they cannot afford safety equipment to help prevent the behaviors. That’s the gap the SaferKids Program is looking to fill.

Once a family is referred to the program, they have a consultation with an expert from the Safety Center at the American Family Children’s Hospital. The consultation is used to determine which equipment could provide the most benefit to the family and tailor the products to the family’s specific needs. “Things like door locks, door alarms and appliance locks are quite common. Furniture brackets to keep heavy furniture

from tipping over. Gates are also pretty common,” Schumacher says. “They can also provide things like temporary ID bracelets so parents know that, if their child wanders, whoever finds them has a way to identify them.” When the family and expert have decided on an array of products, they are then shipped directly to the family’s house with detailed instructions on how to install them.

“The process is so easy, easier than I thought,”

Tiaunta says. “I thought I was going to have to fill out forms and do all this paperwork but it was just a phone call and a little bit of information. They ask you what you feel you need and deliver it right to your doorstep.” She now has a gate in her kitchen, alarms on the front and back door, alarms on her front windows, safety doorknobs on the basement door and chemical closet and electrical outlet covers.

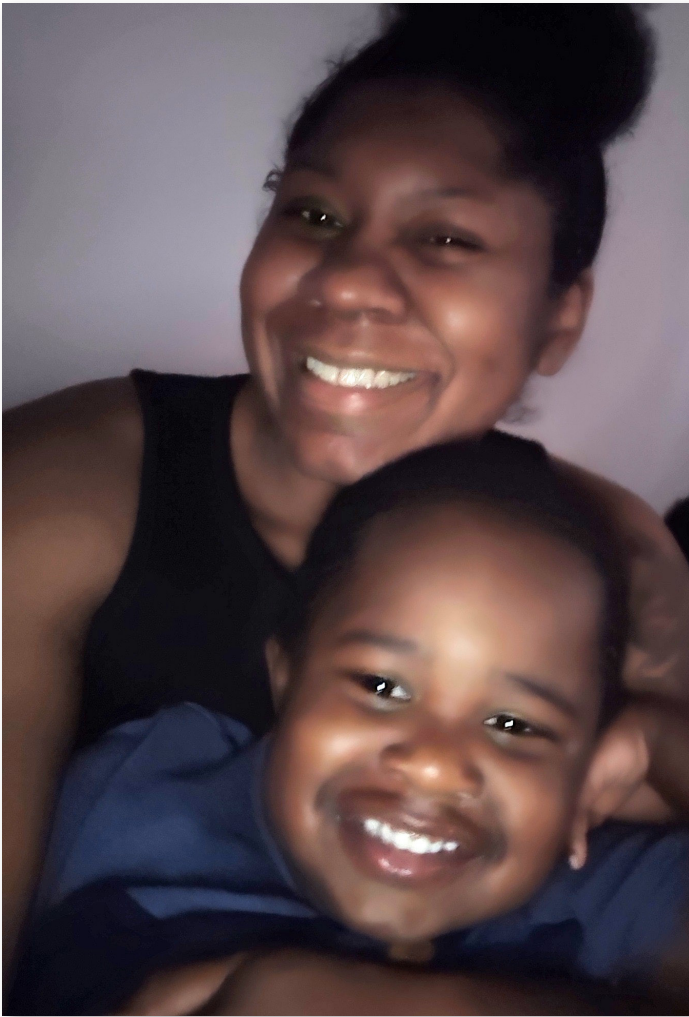
“The products aren’t just keeping Benji safe, they’re teaching him what’s not okay,” Tiaunta says. “They’re teaching him boundaries. He’s a visual learner, so he knows that all this is there because it’s not okay.” Without the SaferKids Program, Tiaunta says she would not have been able to afford the myriad of products she now uses to keep Benji safe.

Demetria Travis, a mother of seven, started to become increasingly worried about her son AJ’s safety after she found him sitting in their oven. AJ, who is three, was diagnosed with autism early and likes to get into everything. “He’s a very bright, very smart kid full of laughter and bubbles. But he is also a runner. He’s a climber. He’s just on the go,” Demetria says. And with seven kids to look after, Demetria could not keep her eyes glued to AJ at all times.



Benji





*Demetria & AJ*

"I received the referral [to the SaferKids Program] and someone called me and asked what my concerns were with AJ, and I said everything," Demetria says. "He climbs on everything. He likes to sit in the oven. He knows how to open doors. He does everything he's not supposed to. And they said we have some things that will help you out."

Now, with an oven latch, furniture brackets, cabinet locks, safety doorknobs, electrical outlet covers, and door alarms, Demetria can rest a little easier

***"The families that have responded, have said overwhelmingly that they are really satisfied with their services and they have overwhelmingly rated the safety information and products they have received as very helpful."***

Michelle Schumacher

knowing that the products will keep AJ safe when she can't give him her undivided attention. Similar to Tiaunta, Demetria says that, without the grant, she could not have afforded all of the products she now uses around the house.

The SaferKids Program was designed to fill in support gaps for families that may be struggling to obtain safety products for their children with developmental disabilities before they have access to other funding. Schumacher is incredibly pleased that the grant is doing that successfully. "The families that have responded [to our survey], have said overwhelmingly that they are really satisfied with their services and they have overwhelmingly rated the safety information and products they have received as very helpful," Schumacher says.

Families also report that they feel respected when communicating with the Waisman Center and the Safety Center at the hospital. Knowing that you will be treated with respect and kindness is an important component in helping families obtain the support that they need. For Tiaunta and Demetria, the grant has provided them with some peace of mind and extra ways to keep their children safe.

"When places have programs that help people out like this, that's something I like to see. Because in other states, they don't have stuff like this," Tiaunta says. "It's amazing all the stuff [the grant] is able to help with and I think it's a really great program."

*The SaferKids Program is made possible through the philanthropic support of the Evjue Foundation, the Green Bay Packers Foundation, and the Friends of the Waisman Center.*



*"The products aren't just keeping Benji safe, they're teaching him what's not okay," Tiaunta says. "They're teaching him boundaries. He's a visual learner, so he knows that all this is there because it's not okay."*

Tiaunta Martin



## SaferKids Program

The Waisman Center's SaferKids Program helps provide families with children who have developmental disabilities with safety products to help keep the child safe.

27

45

So far, of the 45 families referred to the program, 27 have received safety equipment.

The 92% of the families said that they felt very respected when talking about safety concerns with staff.



The same 92% of the families said that they are very satisfied with the services, safety products, and the safety information they received.



### Comments from Families on the SaferKids Program

"It was very helpful. Very grateful for the products."

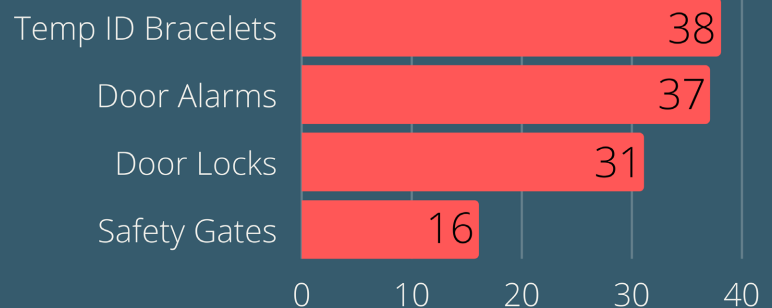
"We were able to get items I couldn't afford."

"Our new neighborhood has a law enforcement officer. After the officer learned of our safety concerns, he now checks in with us every day. The equipment we received has been so helpful!"

"It has put us at ease that she won't fall down a staircase or out a window."

"Allowed us to collaborate and come up with alternatives for safety that first my child's needs."

### Most Common Products



*"He climbs on everything. He likes to sit in the oven. He knows how to open doors. He does everything he's not supposed to. And they said we have some things that will help you out."*

Demetria Travis





## Celebrating the Manlick family's ten years of research participation

**J**ames Manlick is going to homecoming this year and he simply can't contain his excitement. A huge smile lights up his face as he talks about the dance. As a senior in high school, this will be his last opportunity to attend. Since the moment he found out homecoming would be happening, he has been pestering his mom, Sharon, about picking up his ticket and his suit. "He's been all about when am I going to get my ticket," Sharon said, smiling.

School is a favorite of James', especially riding the bus to and from. So, going to homecoming is simply the cherry on top. While James' obvious joy for life and bright smile are utterly contagious, things haven't always been as easy as waiting for homecoming to arrive. He was diagnosed at a young age with fragile X syndrome (FXS).

FXS is a genetic disorder caused by a mutation in the gene FMR1. It is the leading inherited cause of intellectual disability. The condition causes developmental delays, learning disabilities, and social and behavior issues. An FXS diagnosis can be confusing and come with many challenges, so Sharon's first instinct was to gather as much information as possible. That hunt for information brought the family to the Waisman Center almost a decade ago. "We were seeking what help was available in the state of Wisconsin and how we can get better connected to the fragile X community resources," Sharon said.

Upon arriving at Waisman, Sharon and James became involved in research taking place at the center. They have remained deeply involved ever since their very first study. "I remember the first time



that we came to the Waisman Center and it has just kind of blossomed from there,” Sharon said.

The Manlick family has been participating in research at the Waisman Center for almost ten years now. They have shown a drive and dedication to participate in and contribute to research that is not often seen in families. Both James and Sharon are impressively passionate about furthering the work being done on FXS not just for James, but for every other person with FXS. “We want to help advocate

***“We love visiting the Waisman Center so, whenever they like us to come, we will be there,” Sharon said. “It really is all about how we can do our part as best as we can.”***

where we can,” Sharon said. “We feel this is what we need to do to help others and try to make a difference.”

**Audra Sterling, PhD**, an associate professor of communication sciences and disorders and a Waisman Center investigator, has been studying language development in people with FXS in order to develop more effective and accurate assessment tools. All of the research studies that the Manlicks have participated in over the years have been part of her research. For Sterling, working with the Manlick family over an extended period of time has not only been a pleasure but has helped to inform her research.

“They are so open and willing to share their life experiences. And those things help us as researchers know where we need to be thinking about the field. Of course, we are going to plan our studies based on what data is out there and what’s important but none of that really matters if it’s not meaningful to the families,” Sterling said. “So, they’re giving us insight into what their lives are like and sharing this time with us. They help us think about what’s important to James and to the family.”

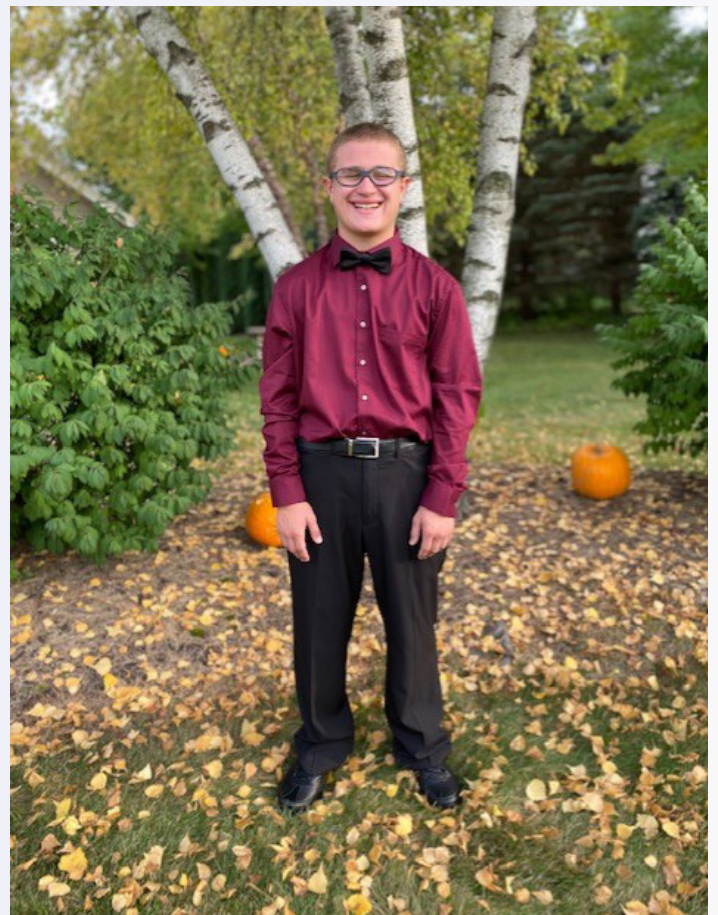
**Emily Lorang, MS, CCC-SLP**, a speech-language pathologist and doctoral student under Sterling, has also spent a decent amount of time working with the Manlick family as an examiner in several of Sterling’s studies. The Manlicks were actually the first family Lorang tested. “I remember being so nervous even

though I had practiced and prepared,” Lorang said. “They were just the best family to be the first ones. They were so kind and flexible and it was a really great experience.” Since then Lorang has worked with the Manlicks several more times and is always thrilled by their willingness to do or try anything. Sterling is equally as impressed as she knows that participating in research studies can be demanding.

“James has always been so willing even though it can be hard because we ask a lot. But he’s always been

a joy,” Sterling said. “He’s a hilarious person, loves being around people, and is willing to do the tasks and work hard. So, it’s not just his parents that are so willing and awesome, but it’s James too.”

Both Sterling and Lorang are inspired by the Manlick family, not just for their unwavering commitment to



*James Manlick, dressed for Homecoming*





***“They were just the best family to be the first ones. They were so kind and flexible and it was a really great experience.”***

Emily Lorang

furthering research but also because of their ceaseless optimism and perpetual positivity. “They are such a joy and positive presence. Especially now, having people who have this level of optimism is such a breath of fresh air. It is so meaningful for everyone around them,” Sterling said.

In 2020, the Manlick family was awarded the Family Volunteer Award by the Friends of the Waisman Center. The award seeks to recognize a family that, “has made exceptional volunteer efforts on behalf of the Waisman Center.” While honored and pleased to win the award, Sharon says that the award is simply a pleasant byproduct as recognition was never their intention.

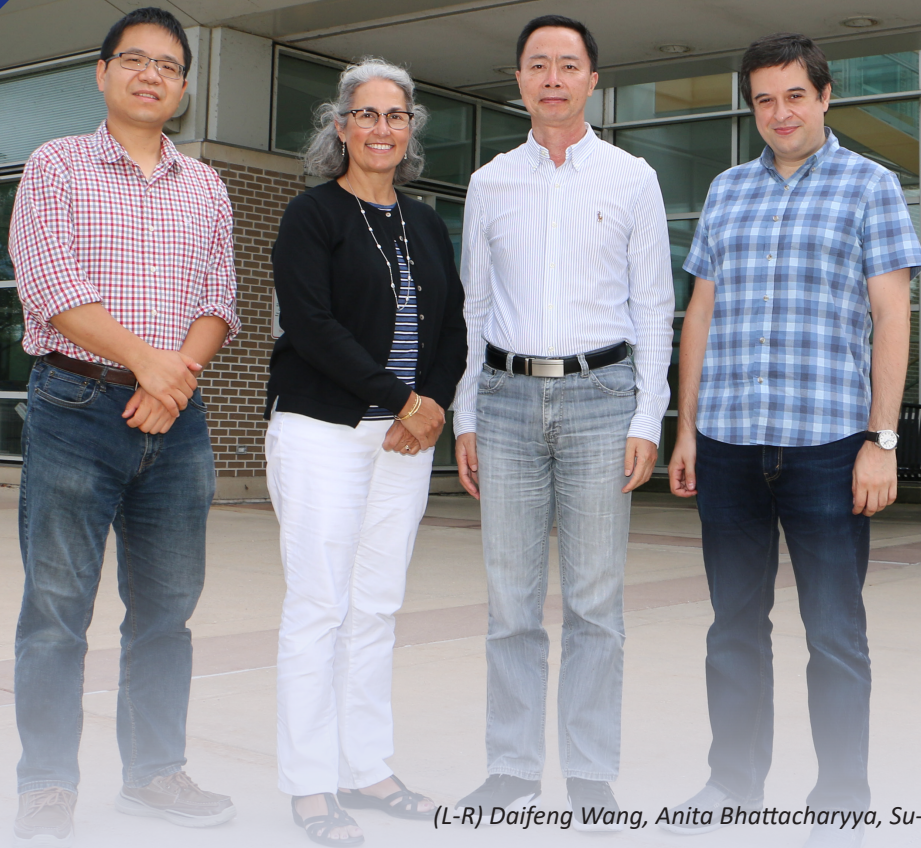
“We never had the thought of we’re going to do this to try and win an award or get some kind of acknowledgement. It’s always been just what can we do, how can we help and how can we have an impact,” Sharon said. For the Manlicks, this is their way to contribute and they are going to continue doing it for as long as they can. But for James, the next big milestone is homecoming.

He decided on black slacks, a maroon long-sleeve button-up, and a spiffy black bowtie to wear to the event. He was also a part of the homecoming parade with an organization called Best Buddies, which helps establish friendships between people with intellectual and developmental disabilities and those without. Despite FXS’s impact on many aspects of James’ life, it had no bearing on the simple pleasure of attending a school dance. And as James transitions into adulthood, the Manlick family will continue to do what they can to support fragile X syndrome research to help families nationwide.

“We love visiting the Waisman Center so, whenever they like us to come, we will be there,” Sharon said. “It really is all about how we can do our part as best as we can.”



*The Manlick Family*



(L-R) Daifeng Wang, Anita Bhattacharyya, Su-Chun Zhang & André Sousa

## New \$11 million award to study intellectual disability in Down syndrome

**W**aisman investigators **Anita Bhattacharyya, PhD**, an assistant professor of cell and regenerative biology and **Su-Chun Zhang, MD, PhD**, professor of neuroscience and neurology at the School of Medicine and Public Health at UW-Madison, were awarded an \$11 million Transformative Research grant by the National Institute of Child Health and Human Development (NICHD) of the National Institutes of Health (NIH) to study developmental brain changes that lead to intellectual disability in Down syndrome. Part of the High-Risk, High-Reward Research program, the NIH Director's Transformative Research Award supports exceptionally innovative or unconventional research projects with the potential to create or overturn fundamental paradigms.

Down syndrome, also known as trisomy 21 (T21) due to the triplication of chromosome 21, is the most common genetic cause of intellectual disability, affecting approximately 6 million people worldwide. Bhattacharyya, Zhang, and two other Waisman researchers are combining efforts to develop models that will allow for the study of disruptions in brain

development that result in cognitive dysfunction in Down syndrome. The study may reveal how brain development in individuals with Down syndrome differs from typically developing individuals, identify features that will help understand intellectual disability in Down syndrome, and identify potential targets for therapy.

"One of the things that I was really acutely aware of is that, although Down syndrome is quite prevalent and we know a lot about individuals with Down syndrome—their characteristics, their features, we even know that they will develop Alzheimer's disease—what we don't have a good understanding of is how brain development in Down syndrome is different. We have surprisingly little information about this," says Bhattacharyya.

Current animal models used to study the syndrome, Bhattacharyya says, fail to mimic the disorder well. Bhattacharyya's proposed model will be based on human induced pluripotent stem cells (iPSCs), a type of stem cell derived from adult skin or blood cells that can be reprogrammed to become other



functional cell types, such as neurons, a type of brain cells. Using iPSCs derived from individuals with Down syndrome and transforming them into neurons from the cerebral cortex –a part of the brain that makes humans, humans, Bhattacharyya explains – they can accurately study which neuronal pathways are affected by T21 during development.

In order to have a reference that validates their stem cell-based model, they plan to build an atlas of the prenatal cortex in Down syndrome. For this atlas, they will identify the specific types of neurons, synapses and molecular pathways that are altered in Down syndrome, particularly during prenatal-to-early postnatal stages. “The atlas will give us a roadmap of what happens in prenatal brain development in Down syndrome,” says Bhattacharyya.

After determining these changes, they will use the iPSCs derived from individuals with Down syndrome to figure out if the stem cells mimic those differences observed in the prenatal brain. “The model is only good if it recapitulates or mimics what’s really happening,” says Bhattacharyya.

In addition, Zhang’s lab will decipher the functional differences in T21 neurons. Previous data from Zhang and Bhattacharyya indicate that human T21 neurons are not as active as their control counterparts. This study will extend these findings by digging deep into the causes of this reduced activity.

The causes of intellectual disabilities in Down syndrome are prenatal, which creates a challenge because of the limited access to prenatal brains. Bhattacharyya hopes that by directly comparing their stem cells to prenatal tissue, they will be able to validate the stem cells and confidently move forward with them as a model.

So far, their results show that these iPSC-derived cells recapitulate some of the changes, such as missing neuron types, observed in adult brains of individuals with Down syndrome. These results give them confidence that their model will present more of these features.

“This is my dream project,” says Bhattacharyya, “and it took 15 years to get it together because several things had to happen. One is, we had to assemble the right people to do this kind of project.”

The work will be done in collaboration with new Waisman Center investigators **Daifeng Wang, PhD**, assistant professor of biostatistics and medical informatics, and computer science, and **André Sousa, PhD**, assistant professor of neuroscience.

“We have assembled this amazing team that all happen to be at Waisman Center,” says Bhattacharyya. “Zhang, who is known for using human stem cells to study neurodevelopment and neurodegenerative disorders, my lab that is focused on Down syndrome modeling, Sousa, who has expertise in single-cell sequencing in human brain development, and Wang, who is going to take all that data and apply his computational skills.”

This five-year grant, which also includes collaborators at the University of Washington-Seattle and Seattle Children’s Hospital, will allow the team to explore an understudied yet needed area of Down syndrome research, which they hope will help inform more research on Down syndrome in the future, for their lab and others.

*This research was supported by a grant from the National Institute for Child Health and Human Development 1R01HD106197-01.*



***“This is my dream project, and it took 15 years to get it together. We have assembled this amazing team that all happen to be at Waisman Center.”***

Anita Bhattacharyya



*Julie Poehlmann-Tynan & Doug Dean*

## Landmark study on impacts of substance abuse and stress in child brain development

**T**he University of Wisconsin-Madison will be one of 25 sites to study early brain and behavior development and the impact of early exposure to substances – such as opioids – and social stressors in infants and young children. The new initiative, **HEALthy Brain and Child Development (HBCD) Study**, is led by the National Institute on Drug Abuse and funded by 10 institutes and offices at the National Institutes of Health and the Helping to End Addiction Long-term<sup>SM</sup> Initiative of the National Institutes of Health (NIH HEAL Initiative<sup>SM</sup>). The Wisconsin site will be led by **Douglas Dean III, PhD**, assistant professor of pediatrics and medical physics, and a Waisman investigator, and Julie Poehlmann-Tynan, PhD, Dorothy O’Brien Professor of Human Ecology.

Much is still unknown about how a child’s developing brain is impacted by the influence of adverse environments. The HBCD Study will establish a large cohort of pregnant people and follow them

and their children for at least 10 years. Findings from this cohort will provide a template of typical neurodevelopment in order to assess how prenatal and perinatal exposures to substances and environments may alter developmental trajectories. This research infrastructure can also be leveraged for urgent health needs, such as the current impact of the COVID-19 pandemic on development, or future health and environmental crises.

“It’s a landmark study for furthering what we know about infant brain development and behavioral development, especially in the context of risk,” says Poehlmann-Tynan.

The longitudinal study will collect data on pregnancy; infant and early childhood structural and functional brain imaging; body measurements; medical history; family history; biospecimens; and social, emotional and cognitive development. Knowledge gained from this research will help identify factors that confer



risk or resilience for known developmental effects of prenatal and postnatal exposure to certain drugs and environmental exposures, including risk for future substance use, mental disorders, and other behavioral and developmental problems.

Dean's work at UW-Madison focuses on brain imaging using magnetic resonance imaging (MRI) techniques to study early brain development. Meanwhile, Poehlmann-Tynan studies early childhood development in a family context, especially under conditions of risk. "It's super exciting to combine our expertise in infants and young children and families, and also the brain development piece," says Poehlmann-Tynan. Both investigators were part of the planning stage of the project that was a cross-campus collaborative effort that included **Andy Alexander, PhD**, professor of medical physics and psychiatry, Pilar Ossorio, PhD, professor of law and bioethics, **Elizabeth Planalp, PhD**, assistant scientist at Waisman Center, **Viji Easwar, PhD**, assistant professor of communication sciences and disorders, Ellen Goldstein, PhD, assistant scientist in the Department of Family Medicine and Community Health, **Steve Kecskemeti, PhD**, scientist at Waisman Center, Ryan McDonald, MD, assistant professor of obstetrics and gynecology, and Florence Hilliard, study manager in the Department of Family Medicine and Community Health.

This award is part of the Phase II HBCD Study, in which a fully integrated, collaborative infrastructure will support the collection of a large dataset that will enable researchers to analyze brain development in opioid-exposed and non-drug-exposed infants and children across a variety of regions and demographics.

Studies in early childhood development, says Dean, have been limited by the small sample size. The nature of this project – big sample size and participation of multiple sites – "is going to generate a lot of new knowledge about early brain and behavior development," says Dean.

Upon collection, the data will become publicly available, which will allow for new projects examining important questions about brain and behavior development, says Dean.

This information, in addition to providing a reference on brain development for researchers and clinicians, may also provide insight into ways to reduce the impact of opioids and other substance use on development.

Longitudinally, HBCD also aims to understand the impact of growing up in the presence of adverse environmental exposures, such as drugs, stress, or COVID-19. The knowledge produced by HBCD may help inform policy formation and guide the development of interventions to reduce the neurodevelopmental effects of adverse environments.

During the COVID-19 pandemic, there has been an increased use of opioids, methamphetamines, alcohol, and THC in the general population. Additionally, many people who are pregnant or have young children have been stressed and isolated, says Poehlmann-Tynan. "It's also a really important study that's looking at the interaction of different kinds of exposures along with a child's emerging social and emotional development. It is also looking at their brain development and understanding those pieces at this time when we're still in the middle of a worldwide pandemic. It's extremely timely."

The Wisconsin study will be a collaborative effort and include the Department of Pediatrics, School of Human Ecology, the Office of the Vice Chancellor for Research and Graduate Education, the Morgridge Institute for Research, and the Waisman Center, which will provide the facilities and instrumentation for data collection. "The project would be very difficult to do without the kind of the infrastructure that we have at Waisman," says Dean. "Having the research core and imaging facilities all under one roof, I think it's going to make it a really nice way to bring families in [to participate in the study]."



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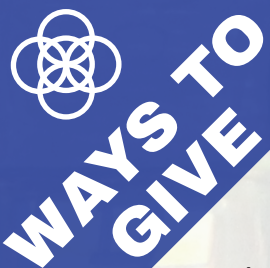
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- Underwrite a scientific talk
- Sponsor a Waisman event
- Support a postdoctoral student
- Participate in a Friends of the Waisman Center fundraising event

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# Waisman Center Leadership

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Professor, Medical Physics & Psychiatry

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