



Inside the Institute

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July 2013

Rett Syndrome Research Trust Awards \$2.2 million to CIDD Investigators

Congratulations to Drs. Ben Philpot, Bryan Roth, and Terry Magnusson, who were awarded \$2.2 million by the Rett Syndrome Research Trust (RSRT) to attempt reversing the course of Rett syndrome by a gene unsilencing approach. Rett syndrome, which predominately affects girls, is the most physically disabling of the autism spectrum disorders.

Rett syndrome is caused by random mutations in the gene *MECP2* on the X chromosome. All females have two X chromosomes and each active mutated gene rests beside a healthy but silenced twin. Drs. Philpot, Roth, and Magnusson's bold project is a screening initiative to identify compounds able to reactivate the silenced but healthy *MECP2* gene on the inactive X chromosome. RSRT has championed this approach since the game-changing discovery in 2007 that severe Rett-like symptoms in mice models can be reversed, even in late stages of the disease.

"If a drug could be identified to efficiently and effectively activate *MECP2*, we would be attacking Rett at its very root, with the potential of reversing the disorder," explains Dr. Philpot. "Our entire team is excited about the possibilities and we're ramping up the project as fast as possible."

Continued on page 6



The Rett Syndrome Research Trust has funded a team of UNC researchers to develop therapeutics for Rett syndrome. Front: Terry Magnusson, Noah Sciaky. Around table from left Megumi Aita, Hyeong-Min Lee, Portia Kunz, Ben Philpot, Bryan Roth, Bram Kuijer, Srikanth Kodali

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The CIDD Community Talk Series resumes on September 11th with "Parenting Across the Autism Spectrum" presented by Ann Palmer and Maureen Morrell

Save these dates for upcoming Talks: October 9, November 13, December 11

Sessions are held from 7PM to 8:30PM at the CIDD

FREE and all are welcome!

Dr. Anne Taylor Awarded Prestigious Sloan Fellowship

Biomedical engineer and CIDD investigator, Dr. Anne Marion Taylor, is among the 126 scientists and scholars in the United States and Canada to receive 2013 Sloan Research Fellowships from the Alfred P. Sloan Foundation.

Sloan fellowships are intended to enhance the careers of early career researchers, whose achievements and potential identify them as rising stars among the next generation of scientific leaders in eight fields: chemistry, computer science, economics, mathematics, evolutionary and computational molecular biology, neuroscience, ocean sciences and physics. Dr. Taylor will receive a two-year, \$50,000 grant to further her research.

Taylor's research explores the intersection of neurobiology, neurotechnology and biomedical engineering to study the cellular mechanisms critical in learning and memory. Her work seeks to develop microfluidic devices to improve the organization and access to neurons and neuronal circuits. One such device directs the growth of axons, enabling investigations in axonal and synaptic cell biology.

"The use of Anne's devices and methods has catalyzed a paradigm shift in the current understanding of synapse development," says Nancy Allbritton, chair of the joint department of biomedical engineering between UNC and North Carolina State University. "Her simple, robust tools are so successful and have had such a significant impact that the devices are now commercially available – a tremendous achievement for such a young investigator."

Sloan Research Fellowships have been awarded since 1995. Since then, 39 Sloan fellows have gone on to win the Nobel Prize in their fields and 16 have received the Fields Medal, the top honor in mathematics.



Spencer Smith Receives Klingenstein Fellowship Award in the Neurosciences

The Klingenstein Fellowship Awards provide early support to young investigators engaged in basic or clinical research that may lead to a better understanding of neurological and psychiatric disorders. Ten fellowships were awarded in May of this year. Among the recipients is CIDD investigator, Spencer Smith, Ph.D.

This grant supports highly challenging and ambitious research into how neurons integrate their synaptic inputs in vivo. This process can be quite complex and involve multiple layers of neuronal computations even within single cells. It is through Dr. Smith's innovations in direct electrical recordings from small neuronal compartments that we can begin to explore this process in vivo.



Last year, Dr. Smith also received a Career Development Award from the Human Frontier Science Program, an international organization funded by the governments of the G7 nations. This grant is supporting the development of a new type of two-photon microscope, one with an unprecedented wide field of view enabling the imaging of single neurons in multiple cortical areas simultaneously.

One of the fundamental unsolved questions in neuroscience is: How is the same cortical circuitry used for different behaviors? The neocortex is organized into functionally distinct areas. During behavior, these cortical areas exhibit changes in spiking activity and connectivity. Dr. Smith's ultimate goal is to better understand the cellular and synaptic neurophysiological mechanisms that underlie different functional areas working in concert to drive behavior.

North Carolina PSE Capacity-Building Summit: Leading the Way

The Carolina Institute for Developmental Disabilities, with support from the College Access Challenge Grant, presented the second annual capacity building summit for postsecondary education (PSE) for students with intellectual and developmental disabilities (I/DD).

The two-day event was hosted by the North Carolina Postsecondary Education Alliance (PSEA), founded in 2009 to expand opportunities for students with I/DD to continue their education past high school in inclusive programs at universities and community colleges. To that end, the PSEA mission to increase awareness and affect systems change while supporting program development has led to increased opportunities for students. From one program in 2009, North Carolina now has ten programs and others in the planning stages.

The Summit, entitled "Leading the Way," featured keynote addresses from Stephan-Hamlin Smith, Executive Director of the Association on Higher Education and Disability (AHEAD), and Cate Weir, Project Coordinator for Think College at the Institute for Community Inclusion at U-Mass, Boston. A special award was presented to N.C. Representative Verla Insko for her commitment to higher education for all citizens in the state.

Two hundred participants attended "how-to" sessions and engaged in a facilitated strategic regional planning workshop. A student panel shared their college experiences and career goals. Representatives from all NC programs set up displays to provide information and an opportunity for networking within the state.

Evaluation feedback was 100% favorable and in support of continuation of this model to meet the needs of a growing population and demand for appropriate transition programs, so that all students have the opportunity to continue their education and improve their quality of life.



CIDD Postsecondary Education Team: Back – Donna Yerby, Deb Zuver, Chris Cordeiro, Keith Erickson. Front — Kerry Hagner, Adrienne Villagomez, Robin Dorton

Jason Wolff Receives Young Investigator Award

Congratulations to Dr. Jason Wolff who received the Young Investigator Award this summer at the International Meeting for Autism Research (IMFAR) in Donostia / San Sebastián, Spain. IMFAR is the Annual Meeting of the International Society for Autism Research (INSAR).



Young Investigator Awards are given for the best biological and clinical empirical research papers published or in press in 2012 by an investigator who has been awarded their Ph.D. or M.D. in the past seven years. Up to two Young Investigator Awards are made. Each of these awards involves a stipend of \$1,500.

Dr. Wolff was recognized for 'best clinical empirical research paper' for his paper, Differences in white matter fiber tract development present from 6 to 24 months in infants with autism, which was published in the *American Journal of Psychiatry* (June 2012).

New NIH Funded Fragile X Study

The CIDD in conjunction with Stanford University would like to inform you of an exciting new research project involving families with a child diagnosed with fragile X. This innovative NIH funded research project received funding in the fall of 2012 and the study is now underway.

The multi-center study involves the collaboration of two sites: University of North Carolina at Chapel Hill and Stanford University in Palo Alto, CA. At UNC, the lead investigator is CIDD Director, Joe Piven, MD. Dr. Piven is an expert on autism, neuroimaging, genetics, mental retardation, and developmental disorders including but not limited to fragile X syndrome. His research interests include structural MRI, as well as diffusion tensor imaging of the developing brain in autism and fragile X particularly as it relates to development and function.

At Stanford, Allan Reiss, MD, is the lead investigator. Dr. Reiss has worked extensively with individuals affected by a variety of neurogenetic disorders including fragile X syndrome, Turner syndrome, Williams syndrome and velocardiofacial syndrome. He studies how genetic and environmental factors affect brain structure and function, and how this ultimately impacts the development and function of persons with these disorders.

The current project is a continuation of an initial study of preschoolers with fragile x syndrome (FXS) which looked at patterns of early brain growth in fragile x and observed generalized brain overgrowth in children with FXS as compared to controls evident at age 2 and maintained across ages 4 to 5. The new study will follow up with the children from the initial study as well as enrolling a small number of new participants with FXS between 4 and 13 years of age.

Families enrolled in the study will travel either to Chapel Hill, NC, or Palo Alto, CA, for a comprehensive series of non-invasive developmental assessments completed on the child with fragile X. Also, during this trip, the child will receive an MRI scan either during natural sleep or with the use of sedation depending on parents' preference and the child's capabilities. Participants will make a total of 2 trips to the respective study site approximately 2 years apart (e.g. visits at 4 and 6 years of age). There is no cost for participation as all travel and lodging costs are reimbursed by the study, and all services the study provides are at no charge to the family. In addition, families will receive feedback on the assessments and each MRI scan.

For more information on this project, please contact heidi.bryant@cidd.unc.edu.



United States Congressman David Price Visits the CIDD

U.S. Congressman David Price visited the CIDD this past month. He met with leaders from the CIDD for an informational session and tour of the facility. He also attended a "town hall meeting" that included all CIDD faculty and staff.

A+KIDS, a Web-Based Antipsychotic Registry for North Carolina Youths

The rise in use of antipsychotics among U.S. children is well documented and has been a particular concern to patients, families, pediatric health care prescribers, public and private payers, and policy makers. Multiple guidelines exist regarding safety monitoring for antipsychotics, yet rates of adherence to these guidelines are known to be poor.

In response, a novel Web-based registry was designed and implemented for medical providers serving child and adolescent North Carolina Medicaid recipients. This effort, A+KIDS (Antipsychotics - Keeping It Documented for Safety (A+KIDS)), is jointly funded by the North Carolina Division of Medical Assistance and Community Care Networks of North Carolina (CCNC), a statewide physician driven, managed care collaborative. The initial objectives of the project were to successfully establish a Web-based safety registry and to obtain and evaluate clinical information derived from the registry.

Dr. Robert Christian has been at the forefront in assisting with the development, improvement, statewide outreach, and formal evaluation of components of this effort. He is lead author of the study, "[A+KIDS, a Web-Based Antipsychotic Registry for North Carolina Youths: An Alternative to Prior Authorization](#)" published in *Psychiatric Services in Advance* (June 3, 2013).



Dr. Robert Christian

In April 2011, A+KIDS began asking prescribers of antipsychotics for children age 17 and under to respond to a set of questions regarding dose, indication, usage history, height, weight, and laboratory data such as blood glucose levels and lipid levels. Antipsychotic registrations were examined by linking North Carolina Medicaid prescription claims to registry entries. Prescribers were classified into different types, and the number of patients and registrations per prescriber were examined.

Top diagnosis groups for registry patients were unspecified mood disorders, autism spectrum disorders, and disruptive behavior disorders. Top target symptoms were aggression (48%), irritability (19%), and impulsivity (11%). Psychosis accounted for 5% of the target symptoms. Approximately 20% of NC Medicaid children with the primary diagnosis of ASD/DD were receiving antipsychotics.

"Depending on how you slice the data, NC Medicaid children with ASD/DD are the 2nd or 3rd most likely group to be receiving antipsychotics. This high ranking might be because children with developmental disabilities are disproportionately represented in the NC Medicaid population, but either way, a lot of the children in the state getting antipsychotics are kids with developmental disabilities," Dr. Christian explained. "It's not that these medicines are inherently bad. In fact they have helped many families. We just want to help get them to the kids that need them. It's very likely that many kids receiving antipsychotics, often in combination with other drugs, could be doing just as well or better with less medication."

Dr. Christian has a particular interest in the usage of antipsychotics and other psychotropic medications among those with developmental disabilities. In the coming months and years, he and his colleagues at Community Care of North Carolina, plan to evaluate to what extent NC Medicaid youths with ASD/DD might be at increased risk for antipsychotic prescribing, psychiatric polypharmacy, and psychiatric medication related side effects. Among the most important side effects of concern to doctors and their families are sedation, movement problems, weight gain, and other metabolic problems such as hyperglycemia, and hyperlipidemia.

Atypical Brain Circuits May Cause Slower Gaze Shifting in Infants Who Later Develop Autism

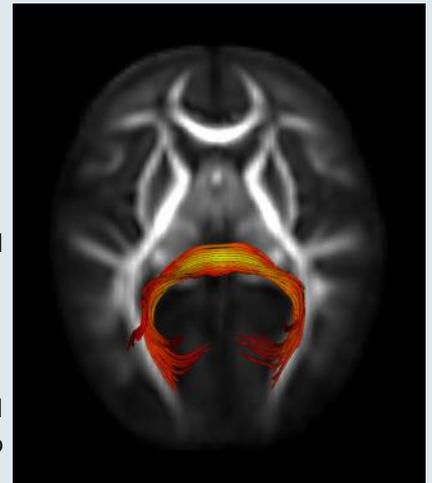
Recent research from CIDD investigators, published in the *American Journal of Psychiatry*, offers evidence that 7 month-olds later classified with an autism spectrum disorder (ASD) take more time to shift their gaze and attention from one object to another when compared to similar aged infants who do not develop ASD. The research also implicates a specific neural circuit, which may not be functioning optimally during this critical developmental period.

"It is important for 6 and 7-month-olds to be capable of efficiently shifting their gaze and visual attention toward and between important aspects of their environment in order to set the stage for more complex development around 9-12 months," says Dr. Jed Elison. Slight delays in this processing ability could initiate negative cascading effects on the development of social cognitive abilities, especially those that are cardinal features of ASD such as joint attention. When coupled with research published last year by CIDD investigators indicating blunted or slowed developmental growth in a number of circuits in the brain that rapidly transmit/carry information between distant brain regions, the current findings from CIDD investigators and their collaborators elucidates early brain and behavioral markers that predict later ASD symptoms.

The study included 97 infants who were recruited and assessed as part of the Infant Brain Imaging Study (IBIS), an international network of researchers and clinicians coordinated by Principle Investigator and CIDD director Joseph Piven. The IBIS Network consists of research sites at UNC, Children's Hospital of Philadelphia, Washington University in St. Louis, the University of Washington in Seattle, the University of Utah in Salt Lake City, the Montreal Neurological Institute at McGill University, and the University of Alberta and is currently recruiting younger siblings of children with autism and their families for ongoing research.

As part of the behavioral assessment around 6 months of age, the infants in this study looked at pictures on a computer screen while sitting on their mother's lap. Sophisticated eye tracking equipment recorded where the infants looked on the screen. The infants also napped during a brain scanning session where the researchers used safe and sophisticated brain imaging equipment to take pictures of the infant's brain. The families then returned for visits at 12 months and 24 months of age. At 24 months, the toddlers take part in a diagnostic evaluation to determine whether they are showing ASD symptoms. This test was used to classify groups of infants who showed ASD symptoms and infants who did not show ASD symptoms. One of the primary findings of the current research suggests that a specific neural circuit, the splenium of the corpus callosum, may not be supporting visual orienting in the same way for infants later classified with ASD as it is in low-risk typically developing infants.

"Our hope is that this finding may enhance early detection efforts, which should directly inform early interventions that could improve outcomes for individuals with ASD and their families" said Dr. Piven.



*Splenium of the Corpus Callosum:
Image credit to Jason Wolff Ph.D.,
UNC-CIDD*

Rett Syndrome Research Trust Award *continued*

A [recent paper](#) by Philpot and his colleagues published in the journal *Nature* describes successful reactivation of the silenced gene in Angelman syndrome, demonstrating that gene unsilencing is possible. Joining Philpot and Roth in this effort is Terry Magnusson, a world-renowned leader in X-inactivation.

RSRT is a nonprofit organization exclusively devoted to global research on Rett syndrome and related *MECP2* disorders. Their goal is to heal children and adults who will otherwise suffer the effects of these disorders for the rest of their lives. To learn more about the Trust, visit <http://www.rsrt.org/>.

The RSRT award will fund a team of three full-time post-docs and two technicians.

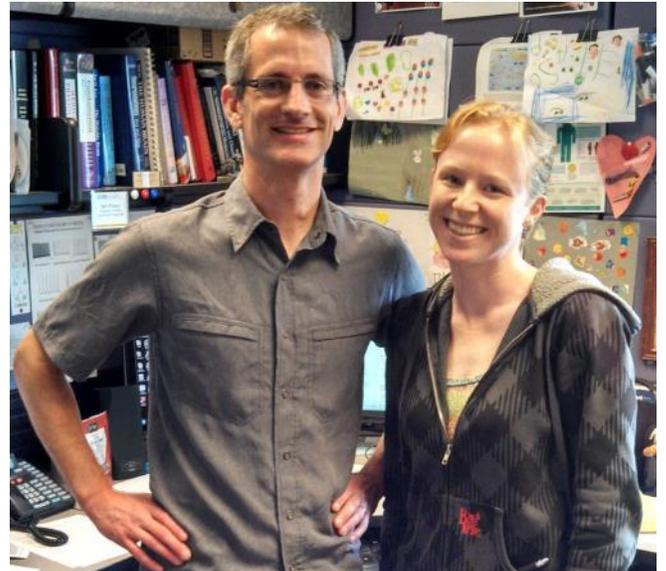
NMDAR Signaling: Insights into NMDAR Dysfunction that Occurs in DD

NMDA receptors (NMDARs) play a crucial role in normal human brain function and their dysfunction has been implicated in schizophrenia, epilepsy, depression, and other neurodevelopmental disorders.

NMDARs are located both presynaptically and postsynaptically where they are critical for memory formation, neuronal synaptic responses, and proper development of the nervous system. However, the mechanisms underlying presynaptic NMDAR function have remained unclear.

Research performed in Ben Philpot's Lab has elucidated the downstream signaling pathways utilized by presynaptic NMDARs during cortical development and further highlight their importance for proper synapse function.

Given the association of NMDARs with neurological disorders, this work may thus contribute to the understanding of synaptic dysfunction that may underlie these disorders. The study "Presynaptic NMDA Receptor Mechanisms for Enhancing Spontaneous Neurotransmitter Release" was recently published in the *Journal of Neuroscience*.



Drs. Ben Philpot and Portia Kunz (McCoy)

New Grants Funded by Autism Speaks Includes CIDD Research Projects

Autism Speaks, the world's leading autism science and advocacy organization, has awarded \$4.8 million in funding for 14 new research projects, including two CIDD research projects.

CIDD investigator, Laura Klinger, Ph.D., will conduct a landmark 40-year follow-up study of individuals served by the TEACCH Autism Program. This represents a unique opportunity to study outcomes in older adults with ASD. The results have the potential to influence legislative and community service decisions that affect adults with ASD.

Joe Piven, M.D. and colleagues will collect brain electroencephalographic (EEG) information on infants to determine whether EEG can be used to predict the early detection of autism. This targeted research project will complement the team's ongoing Infant Brain Imaging Study (IBIS) study of the brain and behavior development of infants at high risk of developing autism.

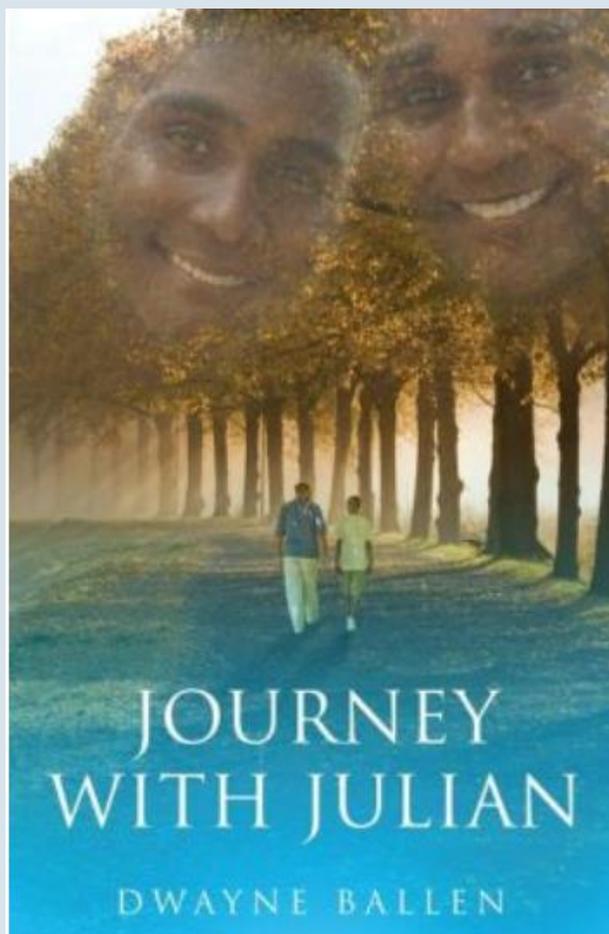
IBIS is supported through the NIH Autism Center of Excellence Network. Researchers also hope to gain a fuller understanding of brain-behavior relationships during the critically important period of infant brain development.

Dwayne Ballen on Katie Couric Show

Dwayne Ballen, a key community supporter of the CIDD, was recently interviewed on the Katie Couric Show about his new book, "Journey with Julian." Mr. Ballen is an award winning journalist and television sportscaster. He is also the father of a son with autism.

Mr. Ballen joined Katie Couric for a special television appearance with his son Julian. He was interviewed about his book and shared his inspiring story about the challenges and triumphs of raising a child with autism.

The show featured kids living with autism and accomplishing what no one thought was possible. It also highlighted parents who are every day heroes. To learn more visit <http://ktie.tv/1950UzS>



CIDD Postdoc & Trainee Accomplishments and News



Sarah Schipul (Psychiatry) presented a poster on Atypical ERP Effects during Auditory Processing in Children with Autism Spectrum Disorder at the *International Meeting for Autism Research*, San Sebastian, Spain. She also presented findings on Distinct ERP Responses during Auditory Processing in Young Children with Autism at the *Gatlinburg Conference on Research and Theory in Intellectual and Developmental Disabilities*, San Antonio, TX. Sarah's mentors are Ayse Belger and Grace Baranek.



Neeraja Ravindran (Clinical Psychology) presented selected results from her dissertation data at the Society for Research in Child Development biennial meeting in April. The topic of her poster was Parent and Professional Perspectives about Autism in South India: A Focus on Parent-Professional Relationships. Neeraja's primary post-doc supervisor is Lauren Turner Brown.



Graduate student **Megan Kovac** (School Psychology) has received a 2013-2014 UNC Dissertation Completion Fellowships for her dissertation addressing affective modulation of the postauricular reflex in children with autism. Megan is advised by Gabriel Dichter.



Anna Sabatino (Developmental Psychology) successfully defended her dissertation which investigated visual attention to social and nonsocial stimuli in children with autism. Anna is jointly advised by Gabriel Dichter and Steve Reznick.



Graduate student **Cara Damiano** (Clinical Psychology) has received a 2013-2014 UNC Dissertation Completion Fellowship for her dissertation addressing neural mechanisms of reward uncertainty in children with autism. Cara is advised by Gabriel Dichter.



Emily Furgang (Occupational Science/Occupational Therapy) successfully defended her dissertation, Engagement of Students with Intellectual and Developmental Disabilities in Postsecondary Education. Emily is advised by Ruth Humphry and mentored by Angela Rosenberg.



Dillon Cockrell (Psychology) received highest honors for his honors project on fMRI of reward loss in children with autism. Dillon is advised by Gabriel Dichter.

Newly Funded Grants in the IDDRC

Heather Hazlett, Ph.D.

NIMH

Through 1/31/2017

fcMRI in Infants at High Risk for Autism

Laura Klinger, Ph.D.

Autism Speaks

Through 1/31/2016

ASD in Mid-Adulthood: A 40 Year Follow-Up of Individuals Served by the TEACCH Autism Program

Sam Odom, Ph.D.

IES

Through 6/30/2017

Center for Secondary Education for Students with Autism Spectrum Disorder (CESA)

Ben Philpot, Ph.D.

NIMH

Through 11/30/2016

Epigenetic Regulation of Ube3a as a Treatment for Angelman Syndrome

Joseph Piven, M.D.

NIMH

Through 6/30/2017

Longitudinal MRI Study of Brain Development in Fragile X

Joseph Piven, M.D.

NICHHD

Through 5/31/2017

A Longitudinal MRI Study of Infants at Risk for Autism (ACE Network)

Sarah Short, Ph.D.

NIMH

Through 11/30/2016

White Matter and Working Memory Development in Typical and High-Risk Children

Linmarie Sikich, M.D.

NICHHD

Through 5/31/2017

Autism Center of Excellence SOARS Network – Study of Oxytocin in Autism to improve Reciprocal Social Behaviors

Bill Snider, M.D.

NINDS

Through 3/31/2017

Reversible cell type specific disruption of ERK signaling in developing cortex

Garret Stuber, Ph.D.

NIDA

Through 12/31/2016

Midbrain Neural Circuit Elements That Underlie Cue-Reward Associations

Kathy Sulik, Ph.D.

NIAAA

Through 11/30/2017

Structural and Functional Central Nervous System Pathology in an FASD Mouse Model

Kathy Sulik, Ph.D.

NIAAA

Through 5/31/2017

Craniofacial and CNS Pathology in a Mouse FASD Model

Anne Wheeler, Ph.D.

NICHHD

Through 9/22/2017

Decisional Capacity and Informed Consent in Fragile X Syndrome

Xiao Xiao, Ph.D.

NINDS

Through 3/31/2017

Gene delivery for fukutin-related protein deficiencies

Mark Zylka, Ph.D.

NIMH

Through 11/30/2016

Epigenetic regulation of Ube3a as a treatment for Angelman syndrome

Your Support

For more than 40 years, the programs of the Carolina Institute for Developmental Disabilities have provided innovative, high-quality clinical, research, and training activities supporting individuals with developmental disabilities.

Now, more than ever, we need well-trained practitioners, teachers, and researchers. State funds pay only part of the costs to recruit and retain the best faculty and support the unique training and programs that are the hallmarks of the Carolina Institute for Developmental Disabilities experience. It is private funds that sustain and enhance these extraordinary opportunities for students, patients, families, and faculty. We can't do it without you!

A gift to the Carolina Institute for Developmental Disabilities is an investment in the lives of thousands and in the future of our communities. Join us by giving today.

To make a donation by credit card, please visit the Medical Foundation of North Carolina's gifting page and choose "Carolina Institute for Developmental Disabilities:" [Click Here.](#)

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Send us your comments or sign up to receive the newsletter:
info@cidd.unc.edu.

A text only version of the newsletter in Word is available.



CIDD celebrates 2nd annual ice cream social with TEACCH