Civitan International Research Center

Fall 2017

UAB CIVITAN INTERNATIONAL RESEARCH CENTER
Empowering Minds Through Science℠

UPCOMING EVENTS
B'ham Sci Café –
John's Diner – 6:00 p.m.

September 19
Saving Sea Turtles

October 15
Chemistry of Immortality

November 21
Brain Science Podcast

THIS EDITION

DIRECTORS
Alan Percy, MD
Interim Director

Lucas Pozzo-Miller, PhD
Scientific Co-director

Vicki Hixon, BS
Managing Director

Center of Excellence Award

By Bob Shepard
UAB's Civitan Rett Syndrome Clinic has been named a Center of Excellence by rettsyndrome.org, one of the nation's leading advocacy groups.

Alan Percy, M.D., (right), a leading clinician and researcher in Rett Syndrome receives the Center of Clinical Excellence Award along with members of the clinic team, and Rett Syndrome.org.

The University of Alabama at Birmingham Civitan Rett Syndrome Clinic has received the Center of Excellence award from Rettsyndrome.org, a leading advocacy organization for patients and families affected by Rett syndrome.

The award will be presented at a reception Friday, Sept. 8, at 4 p.m. at the Children's of Alabama Performance Area on the second floor of the Benjamin Russell Hospital for Children, 1600 Seventh Ave. South.

Rett syndrome is a neurological disorder seen almost exclusively in females, affecting one in every 10,000-23,000 individuals. It is found in all racial and ethnic groups worldwide.

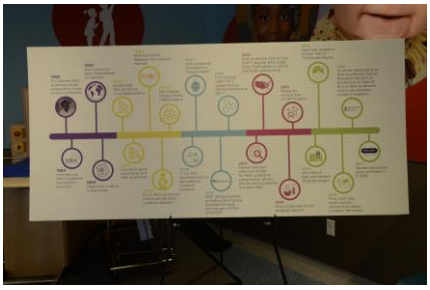
Alan Percy, M.D., director of the UAB Civitan Rett Syndrome Clinic, is an internationally renowned researcher and clinician in Rett syndrome. When at Baylor College of Medicine in the 1980s, Percy was one of the first physicians in the United States to identify the condition.

In 1999, a decade long search for the genetic basis for Rett syndrome succeeded in identifying mutations in the MECP2 gene in girls fulfilling the criteria for the syndrome. This discovery allowed confirmation of clinical diagnoses and the development of genotype-phenotype correlations. Research at UAB is now examining the molecular genetics of children who do not meet all diagnostic criteria for RS, but who are near the border zones of clinical involvement.

Patients with Rett syndrome tend to have small hands and feet and a deceleration of the rate of head growth. Repetitive stereotyped hand movements, such as wringing and/or repeatedly putting hands into the mouth, are common. Gastrointestinal disorders and seizures are also frequently seen. Patients typically have no verbal skills, and about 50 percent of affected individuals do not walk.

Survival into adulthood is now expected barring other illnesses or serious physical complications. Girls and women with Rett syndrome can be expected to demonstrate a full range of emotions and enjoy satisfying social, recreational and educational experiences at home and in the community.

Rettsyndrome.org is a national organization working to accelerate research to cure Rett syndrome and empower families with information, knowledge and connectivity. Since 1998, Rettsyndrome.org has invested more than $41 million in Rett syndrome research.



Mike Warren, CEO, Children's of Alabama
Alan Percy, M.D., Sarah Katherine Bateh Endowed Professor

RESEARCH UPDATE

Drug improves brain performance in Rett syndrome mice

By Jeff Hansen

Improvements in motor function and memory suggest human neurodevelopmental disorders may be amenable to treatment, even after onset of symptoms. According to a researcher, neurodevelopmental disorders with intellectual disability and autism may not need to last a lifetime.

Lucas Pozzo-Miller, Ph.D.

After learning that a small-molecule drug improves breathing in a mouse model of the neurodevelopmental disorder Rett syndrome, University of Alabama at Birmingham researcher Lucas Pozzo-Miller, Ph.D., wondered if he could test it on other brain functions.

Pozzo-Miller has now found that the brain penetrant drug — a small-molecule mimetic of BDNF, or brain derived neurotrophic factor — is able to improve brain performance in Rett syndrome mice — specifically synaptic plasticity in the hippocampus and object location memory. The hippocampus is involved in learning and memory.

This finding, in collaboration with Frank Longo, M.D., of Stanford University, who had shown the drug's improvement of breathing deficits in Rett mice in collaboration with David Katz, Ph.D., of Case Western Reserve University, adds to the growing realization that neurodevelopmental disorders that affect early brain development may be amenable to treatment, even after the onset of symptoms, says Pozzo-Miller, a professor of neurobiology in the UAB School of Medicine.

"Neurodevelopmental disorders with intellectual disability and autism may not need to last a lifetime," Pozzo-Miller said. This offers hope to many patients and their families and caregivers.

In mouse experiments by Longo collaborating with other laboratories around the country, the drug LM22A-4 has also been shown to promote motor recovery after hypoxic-ischemic strokes, improve motor impairment in Huntington's disease and enhance recovery of limb function after spinal cord injury in mice.

Rett syndrome affects about one of every 10,000 females worldwide. Infants develop typically until 6-18 months of age, when symptoms of intellectual disability, autistic features, deficits in motor control and sensory perception, breathing irregularities, and epilepsy start to appear. Most Rett syndrome individuals have a loss-of-function mutation in the gene for a transcriptional regulator, MeCP2.

This mutation reduces BDNF in the brains of Rett syndrome individuals and the brains of Rett-model mice. LM22A-4 is a mimetic of the BDNF loop domain, and it is a partial agonist of the BDNF receptor TrkB.

"Neurodevelopmental disorders with intellectual disability and autism may not need to last a lifetime."

Pozzo-Miller, Longo and colleagues found that a four-week systemic treatment of female mice that have one mutant MeCP2 gene improved their ability to note that an object had been moved in the hippocampal-dependent, object location memory test and restored long-term potentiation in the hippocampus — a phenomenon underlying the plasticity of brain synapses. It also increased the distance mice traveled in an open field test, a measure of general locomotor activity, to normal levels.

The researchers dug deep into brain neurobiology to show that LM22A-4 improves spatial memory by subduing excitatory synaptic transmission and network activity in the hippocampus to levels that allow induction of synaptic plasticity and behavioral learning and memory.

Co-authors of the paper, "A small-molecule TrkB ligand restores hippocampal synaptic plasticity and object location memory in Rett syndrome mice," published in Disease Models & Mechanisms, are Wei Li, Alba Bellot-Saez and Mary L. Phillips, UAB Department of Neurobiology and the UAB School of Medicine Civitan International Research Center; and Tao Yang, Stanford University School of Medicine Department of Neurology and Neurological Sciences.

Funding came from the Rett Syndrome Research Trust, Rettsyndrome.org, and National Institutes of Health grants NS-065027 and HD-074418.

Civitan International Research Center
Neurodevelopmental Bioinformatics Initiative

Bioinformatics Specialist Dr. Lara Ianov joins staff

The Civitan International Research Center (CIRC) at UAB welcomes Bioinformatics Specialist Dr. Lara Ianov to our Neurodevelopmental Bioinformatics Initiative. Lara obtained a Ph.D. in Genetics and Genomics from the University of Florida in 2017, working with Dr. Thomas Foster. Lara has considerable formal training in genetics, neuroscience, DNA sequencing approaches, and bioinformatics analyses. As part of the CIRC, Lara will provide assistance to researchers in the UAB neuroscience community in design, execution, and analysis of high-throughput, whole-genome sequencing approaches.

The mission of the CIRC is to improve the well-being and quality of life for individuals and families affected by neurodevelopmental disabilities; to provide interdisciplinary clinical and research training in neurodevelopmental disabilities; to utilize this knowledge to develop and provide high quality exemplary services and programs; and to exchange information in a timely way with consumers, practitioners, scientists, and society. As part of these efforts, the CIRC established the Neurodevelopmental Bioinformatics Initiative (NBI) in 2016. The mission of the NBI is to improve utilization of whole-genome sequencing technologies to enhance our understanding of typical and atypical brain development, autism spectrum disorders, intellectual disabilities (e.g. Down, Fragile X, Rett syndromes), developmental disabilities, impaired cognitive development, and the effects of environmental toxins on the development of the human brain.

Information and Contact:
To find out more about the NBI and follow our progress, please visit our homepage here and follow us on Twitter. If you are interested in collaborating with the initiative, contact Dr. Lara Ianov at lianov@uab.edu.

Megan Rich chosen as an Alabama Bright Light

Megan Rich, a graduate research assistant at the Civitan International Research Center was featured in Alabama Bright Lights which focuses on interesting stories within Alabama. Megan's research focuses on finding treatments for common brain disorders

http://alabamanewscenter.com/2017/06/02/megan-rich-and-her-ground-breaking-brain-research-make-her-an-alabama-bright-light/

TOURS

To schedule a tour of the
Civitan International Research Center

Contact:
Vicki Hixon
vhixon@uab.edu