Researchers report success in treating autism spectrum disorder

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Using a mouse model of autism, researchers at the University of Cincinnati (UC) and Cincinnati Children's Hospital Medical Center have successfully treated an autism spectrum disorder characterized by severe cognitive impairment.

The research team, led by Joe Clark, PhD, a professor of neurology at UC, reports its findings online July 2, 2012, in the Journal of Clinical Investigation, a publication of the American Society for Clinical Investigation.

The disorder, creatine transporter deficiency (CTD) is caused by a mutation in the creatine transporter protein that results in deficient energy metabolism in the brain. Linked to the X chromosome, CTD affects boys most severely; women are carriers and pass it on to their sons.

The brains of boys with CTD do not function normally, resulting in severe speech deficits, developmental delay, seizures and profound mental retardation. CTD is estimated to currently affect about 50,000 boys in the United States and is the second-most common cause of X-linked mental retardation after Fragile X syndrome.

Following CTD's discovery at UC in 2000, researchers at UC and Cincinnati Children's led by Clark discovered a method to treat it with cyclocreatine—also known as CincY, and pronounced cinci-why—a creatine analogue originally developed as an adjunct to cancer treatment.

They then treated genetically engineered mice as an animal model of the human disease.

"CincY successfully entered the brain and reversed the mental retardation-like symptoms in the mice, with benefits seen in nine weeks of treatment," says Clark, adding that no harmful effects to the mice were observed in the study. "Treated mice exhibited a profound improvement in cognitive abilities, including recognition of novel objects, spatial learning and memory."

As a repurposed drug (originally developed for another therapy), CincY has already been through part of the U.S. Food and Drug Administration (FDA) approval process. It is taken orally as a pill or powder.

UC's Office of Entrepreneurial Affairs and Technology Commercialization has reached agreement with Lumos Pharma, a privately held Austin, Texas, startup company based on UC technology, to develop and commercialize CincY. Lumos Pharma was created with technology licensed from UC's Office of Entrepreneurial Affairs and Technology Commercialization. Its CEO is Rick Hawkins, a 30-year biotech industry veteran. Jon Saxe is its chairman.

"It has taken many years to get here and I am happy that our efforts have led to this translational effort to make a therapy available to those afflicted with CTD," says Clark. "We look forward with commitment and hope to the day when those patients will benefit from our work."

The collaboration gained momentum when Lumos Pharma submitted a proposal based on Clark's technology to the National Institutes of Health and was selected as a drug development project partner by the National Center for Advancing Translational Sciences' Therapeutics for Rare and Neglected Diseases (TRND) program. Under TRND's collaborative operational model, project partners form joint project teams with TRND

and receive in-kind support from TRND drug development scientists, laboratory and contract resources.

Lumos Pharma plans to initiate a TRND-supported preclinical development plan, with TRND support continuing through the filing of an Investigational New Drug (IND) application with the FDA prior to beginning a clinical trial. Such a trial would be about three years away, Clark says.

More information: In addition to Clark, study team members are Yuko Kurosawa, PhD; Ton de Grauw, MD, PhD; Diana Lindquist, PhD; Victor Blanco, PhD; Gail Pyne-Geithman, DPhil; Takiko Daikoku, PhD; James Chambers, PhD; and Stephen Benoit, PhD. The research by Clark's team was supported by funding from the National Institutes of Health. The study authors report no conflicts of interest.

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