BUILDING STRENGTH
changing lives

CONTACT:
Erin Coller, Director of Communications
erin@creatineinfo.org

FOR IMMEDIATE RELEASE

ACD FUNDS NEARLY $140,000 FOR RESEARCH FOCUSED ON CREATINE TRANSPORTER DEFICIENCY TREATMENT

Carlsbad, CA (March 27, 2024) - The Association for Creatine Deficiencies (ACD) has funded two creatine deficiency research projects, totaling nearly $140,000. These projects will focus on drug repurposing for Creatine Transporter Deficiency (CTD) and investigation into the ability of specific CTD variants to uptake creatine.

ACD has contracted to fund $77,800 of research in the lab of Dr. Sylvia Stockler, at the University of British Columbia (UBC), for drug repurposing to confirm the function of regulatory approved drugs to treat specific CTD variants by restoring functional activity of dysfunctional SLC6A8 transporters. Early findings indicating the usefulness of this project come from an ACD-funded fellowship awarded to Dr. Peter Axerio-Cilies in Stockler's lab. Axerio-Cilies' fellowship research identified compounds that exhibited a potential to successfully deliver creatine to cells in engineered cell lines. This research project will move those findings to the next phase of testing in patient-derived fibroblasts.

"It is very exciting for our community to see the progression of research funded by their donations," said ACD Executive Director Heidi Wallis. "It is a testament to our fellowship program's mission, to create a relationship with researchers who are as committed to finding a cure as we are and foster lifelong creatine deficiency researchers."

Axerio-Cilies, a postdoctoral fellow at UBC in the Djavad Mowafaghian Centre for Brain Health, through an ACD fellowship grant, generated a drug-repurposing pipeline in Stockler's lab at BC Children's Hospital Research Institute in Vancouver, British Columbia. This pipeline aimed to find treatments for CTD using already approved drugs. This has a huge advantage over developing new drugs, since many repurposable drugs have already been developed for use in humans for another disease indication. In this secondary use, there is limited need to conduct safety studies and identify the best route of delivery, so these drugs can potentially be brought to market for CTD faster. Axerio-Cilies and his team identified a small number of

drugs that appeared to restore creatine transporter functionality in cell lines engineered to express mutant SLC6A8. In this new phase of research, funded by ACD, Stockler and Axerio-Cilies plan to study if patient-derived fibroblasts obtained from the Coriell NIGMS Repository show increased levels of creatine in response to exposure to the drugs. If successful, this work could result in a potential clinical trial for CTD patients.

"Exploring how existing drugs can work as a therapeutic option for CTD patients will open doors for CTD patients and steer the course of future research projects," said Stockler. "Drug repurposing is the quickest path to a cure or treatment for CTD, so I am very grateful for ACD's support in funding this research and accelerating the pathway to a potential treatment."

A $60,036 research project will be conducted by Dr. Filippo Ingoglia at the Creatine Deficiency Research Center located at the University of Utah. Ingoglia, who serves as medical director of the Biochemical Genetic Laboratory at ARUP Laboratories, aims to develop an assay to assess CTD patient cells' ability to uptake creatine. His project may assist in diagnosis of CTD as well as understanding which SLC6A8 variants have partially functioning transport and are good candidates for creatine supplementation to improve outcomes for patients.

"As a parent, it's difficult to know what to expect when you receive a CTD diagnosis for your child.There is little known about CTD, especially related to your child's specific genetic variant," said ACD board member and CTD parent, Randy Allen. "There is real value for parents and researchers in understanding individual variants to make decisions regarding care and treatment."

Understanding the expression of the SLC6A8 gene and differences in creatine uptake between various mutations may open doors for patient-specific treatments and a better holistic understanding of the SLC6A8 gene and the range of phenotypic expression among patients. Overall, Ingoglia is inspired by his overarching goal in researching CTD which is "to bring hope and make a positive impact on the lives of CTD patients and their families."

Ingoglia is certified by the American Board of Medical Genetics and Genomics in Clinical Biochemical Genetics. At the Creatine Deficiency Research Center, Ingoglia is working under the mentorship of Dr. Nicola Longo, an experienced and published creatine deficiency researcher and clinician. Ingoglia has previously worked on determining the effectiveness of

therapeutic agents for the treatment of guanidinoacetate methyltransferase (GAMT) deficiency and focused on creatine metabolism in patients with urea cycle disorders. His pivot now to studying CTD will allow him to explore the development of a functional test to confirm CTD diagnosis. The creation of a CTD functional test will support definitive CTD diagnoses, classification of SLC6A8 gene variants of uncertain significance (VUS), and identification of CTD patients with residual transport activities.

About ACD: The Association for Creatine Deficiencies' mission is to eliminate the challenges of CCDS. ACD is committed to providing patient, family, and public education to advocate for early intervention through newborn screening, and to promote and fund medical research for treatments and cures for Cerebral Creatine Deficiency Syndromes. Because CCDS mimic symptoms of other medical conditions, patients are often first diagnosed with autism, cerebral palsy, epilepsy, and other disorders. Proper diagnosis and early intervention are critical to establishing interventions needed to improve life quality and longevity for the CCDS patient. ACD is dedicated to continuously supporting research and exploring new avenues to improve patient outcomes on the path to finding a cure for CCDS. For more information regarding ACD, please visit creatineinfo.org.

# # #