MEDIA RELEASE

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HCU Network America and HCU Network Australia today announced the first recipient of their CBS deficiency global grants program – awarding a research grant to the University of Colorado School of Medicine in Denver to explore a potential treatment for homocystinuria due to cystathionine beta-synthase (CBS) deficiency. The research, led by Professor Kenneth N. Maclean aims to investigate the potential usage of different metabolic strategies designed to increase the efficacy of betaine to treat CBS deficient homocystinuria (HCU). Dr. Maclean, is a professor of pediatrics at the University of Colorado School of Medicine, and has had a long-standing interest and involvement in homocystinuria research.

HCU is a rare autosomal recessive metabolic genetic disorder. The disorder is caused by a faulty CBS enzyme leading to high levels of homocysteine and methionine. The severity of HCU varies and depends on whether the faulty CBS enzyme is completely inactive or can still metabolize some homocysteine. Left untreated, HCU can lead to a range of health problems over time, affecting the eyes, skeleton, brain and blood vessels. Common consequences of untreated and undiagnosed individuals are lens dislocation, blood clots and strokes, and varying degrees of cognitive impairment.

There are two forms of HCU; a 'milder' form that responds to vitamin B6 (pyridoxine) supplements and a more 'severe' vitamin B6 non-responsive form. About 40% of individuals with CBS deficient homocystinuria are vitamin B6 responsive. People who do not respond adequately to vitamin B6 need to be on a special diet that is low in protein and consequently low in methionine, as well as administration of a medication called betaine to help metabolize homocysteine. Medical formula is also given to provide amino acids for those on a low protein diet. While effective, compliance with a low protein diet and medical formula is extremely difficult and is very often poor, especially in late diagnosed patients. If effective, these new metabolic strategies could reduce the need for a low protein diet and formula.

Based on previous data in mouse models, Dr. Maclean will investigate the administration of different metabolic compounds combined with betaine in mice that are bred to carry the genetic defect that causes HCU, to determine whether adequate lowering of homocysteine occurs and what dosage levels may be needed. Dr. Maclean will also explore the potential mechanism by which these compounds achieve this effect.

"A number of lines of evidence have led us to hypothesize that improving our understanding of the regulation of the betaine metabolic pathway in HCU may hold the key to improving treatment in all forms of homocystinuria with a view towards reducing dependence upon methionine restriction and improving clinical outcome", said Dr. Maclean. "Preliminary work in our laboratory using an animal model of HCU, has indicated that this approach has the potential to deliver near normal levels of homocysteine in the presence of a normal protein diet which would represent a highly significant advance in treatment for this condition". A lot more work is required to capitalize upon these promising early findings and the grant from HCU Network America and HCU Network Australia constitutes an essential first step in that process. We are very grateful for this support as we work towards our ultimate goal of improved clinical outcome in this disease."

While the exact incidence is unknown and varies globally, it is estimated that CBS deficient homocystinuria impacts at least 1 in 200,000 people worldwide. It has been given the classification of a rare disease by the U.S. Office of Rare Diseases Research and is included as part of the newborn screening panel in many countries.

HCU Network America and HCU Network Australia launched the global grant program in 2017 as a joint initiative supported by a Scientific Advisory Board led by Dr. Viktor Kozich, Professor of Medical Genetics at Charles University in Prague. The grant call invited proposals for projects dedicated to assessing potential new therapies to treat HCU and for technologies to improve newborn screening.

"It is exciting to award our first grant and to explore this potential new mechanism, and we look forward to expanding our grants program to help improve the diagnosis and treatment of this challenging disease", said Margie McGlynn, President of HCU Network America.

"We are excited to be providing support to this research project which offers the potential to develop a new treatment approach for the disorder" said Tara Morrison, Director of the HCU Network Australia. "A treatment approach that could potentially relax or remove the need for a protein restricted diet is much-needed in this community and would ease the burden on the affected individual and the people who care for them."

Funding from the William R. Hummel Homocystinuria Research Fund, established in honor of Will Hummel, a teenage boy in Pennsylvania with HCU, is also being utilized by Dr. Maclean to supplement this grant. The funding from HCU Network America is through the Hempling Foundation for Homocystinuria Research, established in memory of Judy and Susie Hempling, two young girls from Buffalo, NY whose lives were cut short by HCU in the 1970s. HCU Network Australia thanks their community of supporters whose contributions made this grant possible.

About HCU Network America:

HCU Network America is a 501c(3) non-profit organization founded in 2016 dedicated to helping patients and their families affected by Homocystinuria (HCU) and related disorders. The mission of the organization is to inform and provide resources for patients and families, create connections, influence state and federal policy, and support advancement of diagnosis and treatment for HCU and related disorders.

About HCU Network Australia:

HCU Network Australia is an Australian health promotion charity established in 2014 with the vision: “to be a driving force in the journey to a cure, improving quality of life along the way”. The aim of the organization is to improve the outcomes of people impacted by homocystinuria through education, research and support.

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