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HCU Network America announces the recipient of its seventh research grant, awarded to the University of Colorado, to develop new treatments for Classical Homocystinuria. The research, led by Dr. Ken Maclean, aims to lower homocysteine levels and improve cardiovascular complications in HCU patients with the combination of taurine and formate added to betaine treatment. Dr. Maclean is a Professor of Pediatrics at the University of Colorado School of Medicine.

Classical Homocystinuria (HCU) is a metabolic disorder that follows an autosomal recessive inheritance pattern. The disorder is caused by a faulty Cysteine-Beta-Synthase (CBS) enzyme, leading to high levels of homocysteine and methionine. The severity of Classical 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 experienced by untreated or uncontrolled individuals include lens dislocation, blood clots and strokes, and varying degrees of cognitive impairment.

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

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. The U.S. Office of Rare Diseases Research has classified it as a rare disease, and it is included as part of the newborn screening panel in many countries.

According to the principal investigator, Dr. Ken Maclean, "The regimen for the more severe form of HCU consists of a low protein diet combined with betaine treatment, and sticking to the low protein diet can be very challenging. The Maclean lab has been investigating a number of biochemical changes in HCU that appear to limit the ability of betaine to optimally lower homocysteine. Our goal was to understand those biochemical changes so that we might find a way to make betaine more effective and, if possible, reduce the need for the burdensome low-protein diet and medical foods that negatively impact the quality of life for individuals with HCU. In our mouse model of HCU, we found that if we combine betaine with the one-carbon molecule formate, a naturally occurring compound, we can achieve near-normal levels of homocysteine, even in the presence of a full-protein diet. This treatment is currently entering a phase 1 clinical trial in humans, and if successful, will represent a big step forward in treatment in HCU."

Dr. Maclean went on to say, “The new grant from HCU Network America is important because treatments that work in mice don't always work as well in humans. Consequently, while the human trial proceeds, we now want to see if combining the amino acid taurine with formate and betaine will bring additional benefits in terms of potentiating betaine treatment while augmenting the safety profile of our approach. We believe the successful completion of this project will shed new light on the pathogenic mechanisms

involved in HCU and potentially represent a highly significant step towards improved treatment for this rare condition."

HCU Network America Board President Margie McGlynn said: "This project is focused on assessing the impact of 2 new potential therapies, formate and taurine, that could be combined with betaine to lower homocysteine levels. This combined treatment could potentially have a very beneficial effect on the clinical status and quality of life of classical HCU patients."

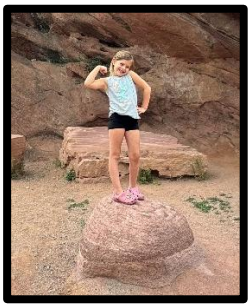
HCU Network America thanks the community of supporters whose contributions made this grant possible.

The Hummel Family

Margie McGlynn via the Hempling Foundation for HCU Research

In memory of her sisters Judy and Susie

Team Dayton



Ellie’s Entourage

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 organization's mission is to inform and provide resources for patients and families, create connections, influence state and federal policy, and support the advancement of diagnosis and treatment for HCU and related disorders.