MEDIA RELEASE FOR RELEASE: January 15, 2025

HCU Network America announces the recipient of its fifth research grant, awarded to the University of Fribourg in Switzerland. The funding will support the development of new therapies to treat classical homocystinuria. The research, led by Dr. Tomas Majtan, aims to develop a cell-based assay to assess CBS protein stability as a screen for pharmacological chaperones. Dr. Majtan is a senior researcher in the Department of Pharmacology at the University of Fribourg in Switzerland.

Classical Homocystinuria (HCU) is a rare genetic metabolic genetic disorder. The disorder is caused by a faulty cystathionine 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 a medication called betaine to help metabolize homocysteine. A 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 challenging and is very 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. Tomas Majtan, “Mutations in the cystathionine beta-synthase (CBS) gene cause the CBS proteins to malfunction. These mutation-impaired CBS proteins don’t fold correctly, are unstable, and break down quickly. When CBS doesn’t work properly, a substance called homocysteine builds up in the body, leading to a condition called homocystinuria (HCU). In this project, we aim to create a new method to monitor how CBS proteins fold inside cells and use this method to find new drugs that can fix the misfolding and instability of these proteins. If successful, this project could lead to new treatments for HCU.

HCU Network America Board President, Margie McGlynn said, “This project will help advance an

important screening tool and identify potential chaperone therapies that could stabilize a defective CBS enzyme and lower homocysteine levels in many patients, which would be expected to have a very beneficial effect on their clinical status and quality of life."

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

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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.