

## **University of Minnesota Researchers Study Effect of Antioxidant Therapy in Type 1 Gaucher Disease**

Gaucher disease (GD) (pronounced “Go-Shay”) is caused by mutations in the gene encoding the lysosomal enzyme, glucocerebrosidase (GBA), and can lead to enlarged spleen and liver, low blood cell counts, bleeding problems and bone disease. According to the National Organization for Rare Disorders (NORD), there are approximately 6,000 individuals with Gaucher disease in the United States. It was previously thought that Type 1 GD (GD1), the most common type of Gaucher disease, did not affect the brain. However, recent studies show that individuals with the GBA mutation have a higher risk of developing Parkinson’s disease. Additionally, several patients with GD1 report at least one neurological symptom.

“While current therapies significantly improve outcomes, patients continue to experience pain and fatigue,” said Reena Kartha, PhD, a research assistant professor with the University of Minnesota Center for Orphan Drug Research. Dr. Kartha will present these findings at the ‘NORD: Rare Diseases and Orphan Products Breakthrough Summit’, Oct. 16-17, 2017 in Washington, D.C. “Our hypothesis is that some symptoms, which persist in treated patients, may be due to an increase in oxidative stress and inflammation.”

In her study, Kartha and colleagues set out to characterize oxidative stress and inflammation in the blood and brain of individuals with GD1. They also will determine whether these factors can be altered with orally administered N-acetylcysteine (NAC), which is both an FDA-approved medication and over-the-counter dietary supplement with antioxidant and anti-inflammatory properties. To date, 10 healthy controls and four patients have completed the ongoing study (NCT02583672). All participants provide three blood samples over a 90-day period for analysis of oxidative stress and inflammation biomarkers in blood. Brain imaging using magnetic resonance spectroscopy is also conducted on patients before and following three months of NAC.

“Preliminary analysis of baseline data indicates alterations in brain bioenergetics and blood antioxidant and inflammatory biomarkers in patients,” said Kartha.

Kartha and colleagues say that their results may lead to a greater understanding of GD1 pathophysiology; identification of potential biomarkers for use in diagnosis; and improved monitoring of disease progression and therapy. The results of this study will also provide information needed to determine if phase III clinical trials of NAC or other antioxidants/anti-inflammatories are warranted; and can guide study design and sample size estimation.

Other University of Minnesota researchers involved in the study include James Joers, PhD; Marcia Terluk, PhD; Paul Tuite, MD; Usha Mishra, MS; Kyle Rudser, PhD; Gulin Oz, PhD; Jeanine R. Jarnes, PharmD; and James C. Cloyd, PharmD. Dr. Kartha is a Rare Diseases Clinical Research Network scholar and a Lysosomal Disease Network (LDN) fellow. The Lysosomal Disease Network (U54NS065768) is part of Rare Diseases Clinical Research Network (RDCRN), an initiative of the Office of Rare Diseases Research (ORDR), NCATS. The Lysosomal Disease Network is funded through collaboration between NCATS, the National Institute of Neurological Disorders and Stroke (NINDS), and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). This project is jointly funded by LDN, Sanofi Genzyme and Pfizer Inc.