Lay Summary

Background: Niemann Pick Disease (NPD) type A and B is a rare disease caused by a deficiency in the acid sphingomyelinase enzyme. The deficiency causes a buildup of a lipid (or fat) which affects organs in the body. It is a change (or mutation) in the gene, called *SMPD1*, which causes the enzyme deficiency. Type A NPD is a severe neuronopathic disorder which leads to death by three years of age. In contrast, patients with Type B NPD have little or no neurologic involvement and usually survive into late adolescence or adulthood. Currently, there is no FDA approved treatment for types A or B NPD.

Purpose: The purpose of this research study is to describe the natural history of NPD type A and B. Another goal of this research is to analyze the types of genetic mutations that cause NPD type A and B and determine how this affects disease course. In addition, we hope to characterize the spectrum of pediatric disease in presymptomatic infants with NPD type A and B identified through an NIH funded pilot newborn screen.

Preliminary Data: Our previous research has outlined the symptom variability among patients who are affected with NPD. We have published numerous papers describing the clinical features of NPD type B such as pediatric growth restriction, pulmonary symptoms, ocular findings, abnormal lipid profiles and calcification of the coronary arteries. We have also described the natural history of type A NPD. Ten patients were studied and revealed that the clinical course was very similar between patients as all patients presented with hepatosplenomegaly by 4 months and had neurologic deficits by 9 months. From this data we have been able to give newly diagnosed families information about prognosis and clinical course for both type A and type B disease.

However, more research is needed to identify individuals who are most at risk for certain clinical outcomes. For instance, in a recently published paper, we found that there was a significant death rate among the NPD type B in the pediatric population. It is important to identify patients who are most at risk of severe disease. However, currently, there is not an accepted marker or clinical test that could be used to identify this group of patients. We hope to obtain spleen volumes from more pediatric patients because it is thought the spleen size could correlate with disease severity.

Methods: The research will take place in the International Center for Types A and B Niemann-Pick Disease, at the Icahn School of Medicine at Mount Sinai. Dr. Melissa Wasserstein will be the principal investigator and medical director. Natalie Lippa is a certified genetic counselor who specializes in NPD type A and B and will be the co-investigator for this study.

This study is designed to collect serial data in patients with NPD. Patients will complete various study evaluations including: medical history, physical examination, ophthalmologic examination, cardiac assessment including electrocardiogram and echocardiogram, neurologic assessment, blood testing, genetic testing, urinalysis, magnetic resonance imaging scan of the abdomen, pulmonary function tests, chest X-ray, bone age in pediatric patients, high-resolution CT scan of the chest, bone density studies, coronary artery scoring, and questionnaires. In general, patients will be asked to return to Mount Sinai every 2 years. The clinical presentation of NPD is variable and therefore, PI may request that subjects return to Mount Sinai for more or less frequently. In addition, patients with Niemann Pick type A disease will also be asked to return to Mount Sinai more frequently if possible. The data will then be analyzed using standard statistical analysis and all evaluations will be completed at Mount Sinai which will ensure consistency and accuracy in results. Overall, we hope that this information will help design future clinical trials and provide patients and physicians important information about NPD.