Mount Sinai School of Medicine

**Division of Medical Genetics**
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**September 1, 2015**

**To: National Niemann Pick Disease Foundation**
**Re: Edward Schuchman Research Fellowship Progress Report**
**Period: October 1st 2015 – April 1st 2016**

## Lay Summary

We are pleased to have been awarded the National Niemann-Pick Disease Foundation's Edward Schuchman Research Fellowship, which provides financial support for Mount Sinai's Niemann Pick A/B Natural History Study. Our project provides comprehensive evaluations for families affected with types A and B Niemann Pick disease. Study participants undergo multisystemic examinations to help define their individual disease status, and to provide data to the researchers about ASMD. This study has elucidated many important phenotypic aspects of ASMD, which has led to greater diagnostic and prognostic capabilities. Since our last progress report, we saw three participants. Over the next four months, we have twelve Niemann Pick B patients scheduled to come for evaluation. We will continue to collect and analyze data about bone disease, radiographic phenotype, ophthalmologic findings, hematologic abnormalities, liver disease, and neurological findings. Future goals include the analysis of the relationship between genetic information and clinical course. We would also like to identify and validate biomarkers that could be used to predict disease burden and response to treatment.

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**17SEP2015**

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**Re: Edward Schuchman Research Fellowship Progress Report**
**Period: October 1st 2015 – April 1st 2016**

We applied to the National Niemann-Pick Disease Foundation's Edward Schuchman Research Fellowship to fund a natural history clinical research study. Our goal was to not use the grant funds for salary support but to apply the funding to support patient care including MRIs, cardiology evaluations and laboratory testing. We estimated that we could evaluate 18 (both adult and pediatric) patients with Niemann Pick type A or B disease each year of funding.

The overarching goal of our clinical research study is to fully characterize the natural history of Niemann Pick types A and B disease. As new treatments for NPD are being developed, timely acquisition of this information is critical. It will be used to help determine clinical endpoints, identify potential safety concerns, and evaluate the efficacy of new treatments at improving clinical outcome in comparison to untreated patients. Thus, the specific aims of this study are:

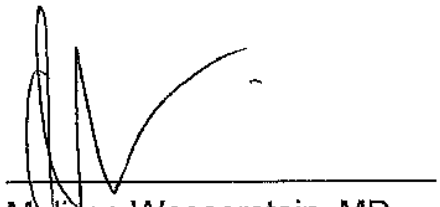
(1) to determine the range of the phenotype in this patient population
(2) to delineate the natural history of the disease and its impact on the quality of life
(3) to permit an analysis to determine correlations of phenotype with genotype
(4) to characterize the spectrum of pediatric disease from presymptomatic infants and children with enzymatic and/or genotypic diagnosis of NPD identified through newborn screening

Since our last Progress Report, we have evaluated another 3 subjects. This was a short-term reduction due to staff turnover, which has been addressed with the recruitment of a new study coordinator/Co-investigator, Misha Rashkin, MS, LGC. Since Misha's arrival, we have scheduled twelve more NP-B patients for evaluation within the next five months.

Subjects and their parents were able to speak with Niemann-Pick specialists for education, support and guidance. We have also spoken to patient's local physicians, nurses and family members to help coordinate care and to give medical advice. In some cases, we were able to complete genetic testing in our clinical lab which allowed us to give the genetic results directly to patients and/or parents. This allows subjects to use this information for family planning purposes or to share with other family members. We currently have twelve more patients scheduled for evaluation in the upcoming months and we are expecting to meet our recruitment goals.

Currently, we are focused on collecting data through subject medical evaluations. In addition, we also obtained SMPD1 and chitotriosidase genotype and enzyme analysis. We hope to collect this information from more patients to 1) describe the genotype/phenotype correlation and 2) determine if chitotriosidase enzyme activity could be used for a biomarker of disease burden.

Future goals include collecting complement levels in Niemann Pick patients. We also are working with a genetic counseling student to collect medical records in order to examine the earliest symptoms of Niemann Pick Disease and further examine genotype/phenotype analysis.



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