Friday, January 20, 2017

2016 Million Dollar Bike Ride Grant Recipient for NTSAD

Chris Stephen, MD, CHB, Massachusetts General Hospital

"Quantitative oculomotor assessment in Late Onset Tay-Sachs"

This grant opportunity was made possible by Team NTSAD in last year's Million Dollar Bike Ride. The Penn Orphan Disease Center in coordination with reviewers provided by NTSAD selected the proposal submitted by Christopher D. Stephen, MB, CHB, neurologist, Movement Disorders, Dystonia Clinic and Ataxia Unit, Massachusetts General Hospital. Below is a summary of his work.

There are several potentially disease-modifying therapies and symptomatic treatments on the horizon for LOTS. However, for such trials, sensitive measures of disease (biomarkers) are urgently needed to both identify early signs of disease and to monitor subtle disease progression. Eye movements are abnormal and a discriminating feature in LOTS but have been little studied and are very common in the related cerebellar ataxias, often occurring before the onset of troublesome symptoms and have been suggested in studies as a potential clinical biomarker. We therefore plan to precisely measure eye movements in a lab setting, assess cognitive functioning and psychiatric symptoms, as well as perform a first study of subjective sleep quality in LOTS. In this study, we will recruit patients with LOTS at different disease stages as part of an ongoing natural history study as well as individuals without the disease. The study will enable us to see whether detailed assessment of eye movements can detect early signs of disease better than neurological examination, and whether eye movement testing can serve as an accurate measure of disease severity in

LOTS and therefore be useful for upcoming clinical

MILLION DOLLAR BIKE RIDE
RAISING MONEY FOR RARE DISEASE RESEARCH

4th Annual Million Dollar Bike Ride for Research

LOTS and therefore be useful for upcoming clinical trials.

Read full summary of grant **here**.

Bike Ride for Research

Saturday, May 20, 2017

Highline Park

Philadelphia, PA

Research Progress Update for Late Onset Study

Florian Eichler, MD, Massachusetts General Hospital

Late Onset GM2 Gangliosidoses Registry and Repository

Since initiating this project, the team at MGH has made progress on all aims. They have done a comparative review of literature on Late Onset Tay-Sachs (LOTS) disease and natural history collected through patient surveys. They have begun bringing Late Onset patients to Massachusetts General Hospital (MGH) for participation in a pilot project to determine optimal outcome measures and assess longitudinal biomarkers. They are currently working with data managers at NeuroBANK(TM) to build case report forms (CRF) for Late Onset. They have also collected biological samples with the goal of assessing longitudinal biomarkers in Late Onset patients.

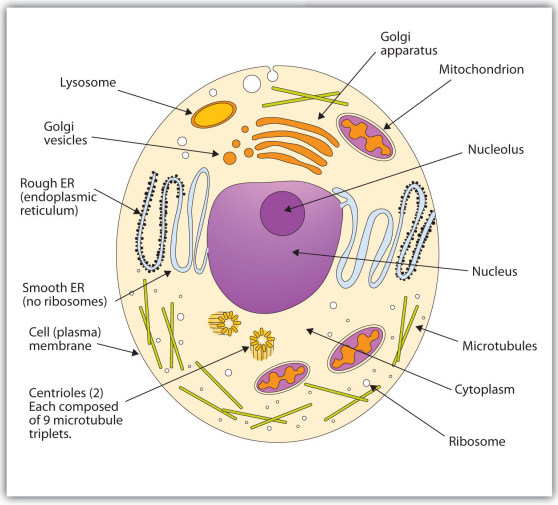
This important project was funded with a generous grant from the Katie & Allie Buryk Research Fund of NTSAD.

Final Report: Lipodomics Study

Doug Martin, PhD, Auburn University

Lipid Biomarkers of Tay-Sachs Disease

Identifying optimal biomarkers of Tay-Sachs disease (TSD) is an important precursor to clinical trials. The study identified four lipid molecules elevated in the cerebrospinal fluid (CSF) of untreated TSD sheep: GM2 (18:0), GM2 (20:0), ceramide (18:0), and monohexosylceramide (16:0). Among them, both species of GM2 were highly elevated in TSD sheep and decreased substantially after treatment. Therefore GM2 ganglioside has the most potential to be an informative biomarker for clinical trials.



Impact: Biomarkers are unbiased indicators of disease progression. In this work, investigators set out to uncover informative biomarkers of TSD in cerebrospinal fluid (CSF) from TSD sheep using a method called 'targeted lipidomics.' Lipidomics is the large-scale study of cellular lipids in biological systems. Research usually involves the identification and quantification of the thousands of cellular lipid molecular species and their interactions with other

WHAT ARE LIPID MOLECULES?

Lipids [like GM2 gangliosides] are fundamental building

lipids, proteins, and other metabolites.

It is known that the primary storage product of Tay-Sachs disease is GM2 ganglioside, a lipid. Using lipidomics, researchers tested the hypothesis of whether GM2 could be a biomarker for TSD and obtained positive results.

In addition, scientists assessed whether lipidomic biomarkers can be used to chart disease progression after gene therapy treatment. It was found that GM2 ganglioside remained above normal in the treated sheep, reflecting incomplete treatment. The finding was in agreement with other evidence.

blocks of all cells and play many important and varied roles. They are key components of the plasma membrane and other cellular compartments, including the nuclear membrane, the endoplasmic reticulum, the Golgi apparatus, and trafficking vesicles such as endosomes and lysosomes.*

*https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4055261/

RESEARCH INITIATIVE: 2017 Request for Proposals Update

Sixteen pre-applications were received on January 4th. A group of reviewers will select and invite those with promising proposals to submit a full application by February 22, 2017. Grant recipients will be announced in the June issue of NTSAD's Research Review.

Read about past grants awarded over the last 14 years here.

NTSAD is please to promote the **Canavan Disease Patient Insight Network (PIN)**. It's purpose is to understand and share the health experiences of people with Canavan Disease. More than a traditional registry, a PIN helps us build an engaged Canavan Disease community, where patients are at the center. Privacy is protected using our partner, PatientCrossroad's proven platform, so participants can share de-identified data if they choose. Participants may also choose to receive notice of clinical trial recruitment and the latest research news.

Register today here.

www.NTSAD.org

Susan Kahn, Executive Director 2001 Beacon Street, Suite 204

Brian Manning, President, NTSAD Board Boston, MA 02135

Fran Platt, PhD, Chair, Scientific Advisory Committee (617) 277-4463 | info@ntsad.org

Veronica Huang, Science Communications Intern www.NTSAD.org