



National Tay-Sachs & Allied
Diseases Association, Inc.

Friday, JUNE 10, 2016

NTSAD Monthly Research Review

NTSAD's 2016 RESEARCH INITIATIVES GRANT AWARDS

We are proud to announce the **2016 Research Initiative** grant awards, after **Scientific Advisory Committee** and **Corporate Advisory Council** members participated in the evaluation and consideration of 20 grant applications.

NTSAD has now awarded over 50 grants exceeding \$3.5 million since the inception of the Research Initiative. The fields of lysosomal storage disease and leukodystrophy research are busy with innovation, industry and hope. Especially in light of the recent news of gene therapy clinical trials starting for other lysosomal storage disorders, we are hopeful that one day we will announce the same news. Four new grants were awarded this year. There are six other NTSAD-funded projects in process. Stay tuned for progress reports in future NTSAD *Research Reviews*.

Rapid Identification of New Biomarkers for the Classification of GM1 and GM2 Gangliosidoses: A HNMR-linked Metabolomics Strategy

Principal Investigator: Martin Grootveld, PhD
Leicester School of Pharmacy
De Montfort University, UK

Co-Principal Investigator: Cynthia Tiff, MD, PhD

The objective of this study is to identify biomarkers of GM1 and GM2 in plasma, CSF (cerebrospinal fluid), and/or urine that have been sampled repeatedly from affected individuals over time. This will contribute to an overall goal of a greater understanding of disease pathogenesis as well as identification of potential drug targets.

The study will use nuclear magnetic resonance (NMR)-linked **metabolomics** to screen for biomarkers in

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Identifying GM1 and GM2 Biomarkers

Sandhoff Gene/Cell Therapy Studies

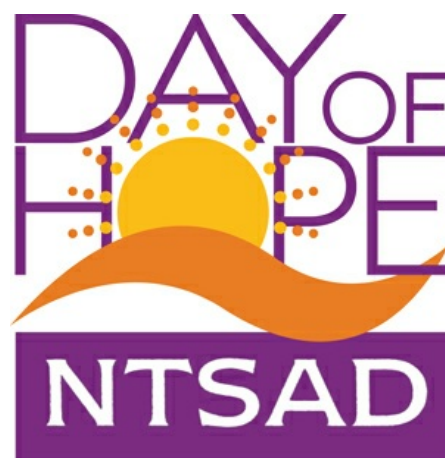
Late Onset Wearable Technology

Novel GM2 Therapies

Research: Recorded

A Hopeful Herd

Save the Date!
September 17, 2016



Stay tuned for more information about the day and its focus on research. There will be swag and energy. Most importantly, there will be **hope for a future** filled with treatments!

**Recorded Conference
Research**

samples from GM1 and GM2 patients and used advanced multidimensional datasets to extract detailed information. The study will further identify and validate potential NMR targets by liquid chromatography-mass spectrometry (LC-MS), a technique that has a higher level of sensitivity.

Novel combined gene/cell therapy strategies to provide full rescue of the Sandhoff pathological phenotype

Principal Investigator: Angela Gritti, PhD
San Raffaele Scientific Institute
San Raffaele Telethon Institute for Gene Therapy (Italy)

This study will evaluate gene and cell therapy approaches in the mouse model of Sandhoff disease. Specifically, this study will compare three therapeutic methods: 1) direct intracranial **lentiviral** gene therapy, 2) neural stem cell transplantation (with or without gene correction of cells), 3) and bone marrow transplantation. These therapies will initially be tested individually and subsequently in combination. A combination of these therapies has demonstrated a synergistic effect and extension of lifespan in a mouse model of a similar disease providing the rationale to assess these therapies for Sandhoff and Tay-Sachs diseases.

Clinically Relevant Outcome Measures for Patients with Late Onset Tay-Sachs disease Ascertained Real-Time Through Patient Wearable Technology

Principal Investigator: Cynthia Tift, MD, PhD
National Human Genome Research Institute
National Institutes of Health
(Funded by Katie & Allie Buryk Research Fund of NTSAD)

This study is a next step in identifying relevant outcome measures for clinical trials. This six month exploratory study will use 5-8 ambulatory or partially ambulatory adult patients with late onset Tay-Sachs or Sandhoff disease to collect patient data on ambulation, falls, wake/sleep cycles, and other patient input that can be tested as potential clinically relevant outcome measures for future clinical trials. Data is collected through a wearable device and transmitted through a mobile app to Dr. Tift for analysis. The data collected will be compared to clinical testing including gait lab metrics to be conducted at the NIH Clinical Center at the time of initial evaluation and at the six month endpoint.

Presentations on NTSAD's YouTube



NTSAD Research Update Session



GM-1 Research Meeting

A HERD OF HOPE.

The Jacob Sheep are unique. The fact that they have Tay-Sachs makes them invaluable to researchers like the Tay-Sachs Gene Therapy Consortium group. However, while we need them, they need us to help feed them and care for their needs!



To support caring for the herd, follow them on their [Facebook page here](#). Help them like they have helped us.

Are you on Facebook and Twitter?

Identifying Novel Therapeutics for Treating GM2 Gangliosidosis

(Co-funded with the Katie & Allie Buryk Research Fund and the Vera Pesotchinsky Research Fund of NTSAD)

Principal Investigator: Beverly Davidson, PhD
Children's Hospital of Philadelphia

Co-Principal Investigator: Fran Platt, PhD
Oxford University (UK)



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Substrate reduction therapy (SRT) has the potential to be broadly applicable to several lysosomal storage diseases, including the gangliosidoses. However, the SRT drug Miglustat (approved for Gaucher disease in 2002) does not cross the blood-brain barrier to an extent that could mediate benefit in patients with Tay-Sachs disease.

This study will analyze Miglustat and the closely related drug Lucerastat using human macrophages (a type of white blood cell that digests cellular debris and foreign objects). This comparison will allow identification of common pathways affected by both Miglustat and Lucerastat and determination of other drugs that act in a similar manner. Drugs that share common features, but have improved central nervous system penetrance for treating the gangliosidoses (including GM-1), will then be tested for their ability to reduce stored substrate levels when applied to patient-derived cells. As Miglustat has additional anti-inflammatory properties relative to Lucerastat, this analysis may also shed light on the inflammatory pathways targeted by Miglustat.

national tay-sachs & allied diseases association

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