



National Tay-Sachs & Allied
Diseases Association, Inc.

Friday, APRIL 29, 2016

NTSAD Monthly Research Review

We are pleased to share the following progress reports for three of the seven NTSAD 2015 Research Initiative grants.

2015 NTSAD RESEARCH GRANT

Denis Lehotay, PhD, Queen's University, Ontario

Project: Development and validation of a rapid, MS/MS-based method to detect Hex A deficiency in Tay-Sachs disease

This project focuses on the development of newborn screening for Tay Sachs disease. Newborn screening is important for diagnosing the disease early in life, before symptoms begin. An important step in getting the project off the ground was making arrangements with the Provincial Newborn Screening Laboratory of the Province of Quebec to obtain blood spots from the areas of Quebec with a high incidence of Tay-Sachs disease, and obtaining approval from the relevant Research Ethics Review Boards.

They needed to obtain additional amounts of the synthetic substrate and internal standards used in analyzing hexosaminidase activity by mass spectrometry. These were made by custom synthesis by the Laboratory of Dr. Michael Gelb in Seattle.

The initial experiments to set up a mass spec-based method for Tay-Sachs disease have begun. They have demonstrated that in extracting hexosaminidase (the enzyme deficient in Tay-Sachs patients) from blood spots and using synthetic substrates and internal standards, they will need to do short incubations (30-60 minutes) instead of overnight incubations. Their experiments are continuing to work out the details and exact conditions of the enzyme assay before we embark on testing and validation of the method.

In the News...

NTSAD mom, Sherri Epstein, featured in **NEWSWEEK** article about Canavan gene therapy and the work of Guangping Gao, PhD and Dominic Gessler.

Read the full article [here](#).

AAV gene therapy clinical trial is underway for Batten CLN6 disease and has been in the news online. More information and details on the research and the trial is available [here](#).

Read the family story in the **People** article [here](#).

ALD NEWS! bluebird bio Reports Interim Clinical Data from Starbeam Study with pediatric patients affected by Cerebral adrenoleukodystrophy. Dr. Florian Eichler, NTSAD Scientific Advisory Committee member, presented the data at the American

2015 NTSAD RESEARCH GRANT

Eric Sjoberg, PhD, OrPhi Therapeutics

**Project: Generation of a Knock-in Mutant HexB Mouse Model
Funded by the Katie & Allie Buryk Research Fund of NTSAD**

Eric Sjoberg, PhD and his team have successfully introduced a point mutation into the mouse HEXB gene that should mimic a known disease (Sandhoff disease) causing mutation resulting in low but detectable levels of hexosaminidase activity. This will create a mouse model for late onset Tay Sachs and Sandhoff diseases to use in further research.

Pharmacological chaperones (PCs) are small molecules that selectively bind and stabilize certain mutant proteins, allowing them to pass the protein folding-related quality control system and to be transported and delivered to their final functional location (e.g., cell surface, lysosomes). This animal model is significant because it will allow PCs to be tested in vivo in this mouse, a key step towards translating research into a therapy. PC therapy is most effective with milder mutations, as are typically found in juvenile and late onset forms of disease. While the model is a Sandhoff disease model, the class of molecules they are working on for increasing HexB activity also increases the enzymatic activity involved in Tay Sachs disease, HexA. They are currently breeding animals to homozygosity (to generate a genetically pure mutant) and anticipate performing initial dosing studies within 3 months where they will monitor increases in both HexB and HexA enzymatic activity. As the animals age, they will be characterized for disease specific features, and if present, this animal model will be utilized for subsequent proof of concept efficacy studies with PCs that OrPhi Therapeutics is currently developing.

2015 NTSAD RESEARCH GRANT

The Hexosaminidase A Variants of Unknown Significance (HAVUS) Classification Project

Tricia Z. Page, MS, CGC, LGC, and Senior Director of JScreen, gave a presentation about this research project at the American College of Medical Genetics Conference (ACMG) in March. The goal of this project is to enable greater than 98% carrier detection rate on sequencing through classification of variants of unknown significance (VUS).

By completing enzyme analysis on individuals found to have VUSs in the HEXA gene, we can determine the meaning of these variants (as either causing Tay Sachs disease or as part of our normal variation). This will pave the way toward improving DNA testing methodologies for Tay-Sachs screening. The presentation is available [here](#).

This project was funded by NTSAD in partnership with the

Academy of Neurology (AAN)
Annual Meeting during the
Clinical Trials Plenary Session.

Read the press release [here](#)
from **bluebird bio**.

On a related note:

Next week is the **American Society of Cell & Gene Therapy Annual Meeting** in Washington DC.

NTSAD has been making introductions between people in our research, corporate, and investment networks so they can connect at this gene therapy conference. Hopefully these conversations will lead to next steps for getting treatment to patients.



If at least \$20,000 is raised,
these gifts will be matched up

Cameron & Hayden Lord Foundation, the Evan Lee Ungerleider Fund of NTSAD, Mathew Forbes Romer Foundation, and the New York Area Fund of NTSAD.

NTSAD's 2016 Research Initiative Grant Awards will be announced in May's Research Review.



It is spring and the Jacob Sheep herd has grown with the recent births of new lambs in the flock.

With a gift of \$1,000, you can name one of these unique lambs!

Tay-Sachs disease is present in the population of a rare breed of sheep called Jacob Sheep. The genetic makeup of these sheep is very similar to humans in the way that matters most for solving the mystery of Tay-Sachs disease.

The funds raised help care for the Jacob Sheep. It costs just \$125 to feed one sheep in the flock for one month. Our goal is to raise \$17,500 in 10 months to feed and care for them. These sheep are an important part of the Tay-Sachs Gene Therapy (TSGT) Consortium research project. The sheep are currently cared for at Auburn University where the research is being carried out. Follow the sheep on Facebook [here](#).

You can help care for these sheep or even adopt a sheep by mailing a donation form or [donate online here](#).

RARE Patient Advocacy Symposium
May 6, 2016, Philadelphia, PA

Register today to join **Global Genes and the UPenn's Orphan Disease Center** are collaborating for the first time on the **RARE Patient Advocacy Symposium**, a half-day patient advocate education program on May 6, 2016 in Philadelphia at the Sheraton Philadelphia University City Hotel.

Advocates will learn from compelling case studies delivered by

to \$50,000 to fund an NTSAD research grant focused on our group of rare genetic diseases.

Double the Impact! Make a gift to support TEAM NTSAD [here](#).



Make a Gift to Support Research [here](#) today.

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patient community and the biotech industry representatives about participating in drug development, keys to advancing research and directing research funding for their rare disease community, and nonprofit organizational growth and development.

Click [here](#) for more information and to register.

national tay-sachs & allied diseases association

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