

Having trouble viewing this email? [Click here](#)



National Tay-Sachs & Allied  
Diseases Association, Inc.

Friday, JANUARY 16, 2015  
NTSAD Monthly Research Review

## TAY-SACHS GENE THERAPY CONSORTIUM Progress Report Summary for Milestone II

Previous **AAV vectors** encoding **Hexosaminidase (Hex)** showed toxicity in non-human primates (NHPs) without showing toxicity in other animal models. Our hypothesis is that exceptionally high expression levels were the direct cause of the unexpected toxicity. Therefore our goal was to find an optimal design that would be both non-toxic and effective.



Multiple new vectors were constructed and tested in mice. Three new vector designs based on safety parameters and level of enzyme over-expression were selected to test in monkeys.

The behavior of all six AAV-injected non-human primates remained normal throughout the 90-day study. Brain MRIs were carried out monthly. Detailed analysis of brain tissue revealed that group 1 expressed the highest enzyme activity at the injection site (87-fold above normal). In addition these animals had some evidence of toxicity, and in one injection site it resembled in the original observations with significant loss of neurons. The brains in groups 2 and 3 displayed only minimal to mild changes and total Hex activity was 9 times normal. The neuropathology findings in all groups agree with brain MRIs data as an abnormal signal in one injection site corresponded to a region with significant loss of neurons.

The formulation tested in group 1 was compared to the original AAV vector for its ability to reduce GM2 **ganglioside** content in the brain of **Sandhoff** (SD) mice. We showed that the two formulations are equally potent in reducing GM2 content in brain. However, because of the considerable neuropathology documented at one injection site with formulation 1, we decided to test the efficacy of a second vector design (tested in group 2 non-human primates) in reducing GM2 content in the brain of GM2 mice. The brain of these AAV-injected GM2 mice is being analyzed currently.

The outcome of the biochemical efficacy experiment in SD mice will determine the last stage of the studies in the non-human

## NTSAD's SAC Subcommittee on Therapies

The goal of the Subcommittee is to evaluate clinical trials or other proposed therapies for Tay-Sachs and related diseases to educate families regarding clinical trials and how to assess a proposed new or untested therapy. The next paper for NTSAD families will be about stem cells.

### Paper #1 Substrate Reduction Therapy

NTSAD Scientific Advisory Committee Chair, Fran Platt, PhD, put together this review paper about **substrate reduction therapies** for lysosomal storage diseases (LSDs).



Read the full paper [here](#).

## NTSAD Request for Proposals

### Next Steps in the Process

We received 25 pre-applications that are currently being reviewed by 15 scientists in NTSAD's network. Full proposals will be requested from those applications that are approved. Notifications will be made at the end of January.

primates, which will include toxicity and analysis of vector distribution in different organs. The final design of this study in NHPs will be discussed with the FDA to ensure its suitability before proceeding with the third and final phase of the vector selection research.

---

## MILLION DOLLAR BIKE RIDE (MDBR) GRANT AWARDED TO STUDY CANAVAN STUDY Canavan Natural History Study to Begin

Dr. Annette Bley, a pediatrician in Germany, was awarded a grant from the MDBR to study the natural history of **Canavan disease (CD)**. Dr. Bley previously worked with Dr. Florian Eichler in studying the natural history of infantile and juvenile GM2 gangliosidosis. She attended the 2010 NTSAD conference in Florida to discuss this work. Drs. Bley and Eichler will collaborate on this project as well. Dr. Bley currently cares for patients with CD at the University Hospital Hamburg Eppendorf in Germany.



Dr. Bley has developed a questionnaire to gather information about CD and has used this to gather information on a small number of patients. This led to the development of a database to gather information and learn about CD.

Using the MDBR grant, she hopes to add information from approximately 50 additional patients to this database. This will include family-reported information and information obtained from medical records.

This work will allow Dr. Bley and others to learn more about the natural course of CD and to develop quantifiable measures of the disease. This may include a CD-specific clinical scoring system to clarify the natural history of CD. She also hopes to correlate an MRI scoring scale to clinical symptoms in patients.

This type of work is essential for future clinical trials. It is necessary to understand the natural history of a disease in order to detect changes in outcomes through new treatments. The development of quantitative methods of understanding diseases enables researchers to show that a new treatment is beneficial to patients.

Sue Kahn will be meet with Drs. Bley and Eichler at the end of January to discuss how NTSAD can help with recruitment for the study.

**Our thanks to NTSAD's  
Million Dollar Bike Ride team  
that made this grant possible!**

## Sandhoff, Ketogenic Diet, and Miglustat

**Paper published in European Journal of Medical Genetics**

This paper, focusing on a study of *just one patient*, was published in December 2014. It reviews the responses of one child affected by Sandhoff disease after treatment with miglustat (Zavesca) and a ketogenic diet. **Read the full paper here.**



**Advisory  
Panel  
on Rare  
Diseases**

The **Patient Centered Outcomes Research Institute (PCORI)** is seeking to bringing voices from across the healthcare community into their research work. PCORI will consider all applications submitted before February 6, 2015 at 5:00 PM EST for these openings. **Click here to submit an application.**



**Make a Gift to  
Research Today.**



The 2015 Ride is  
on May 9th, 2015.

Visit the **MDBR** website to  
watch for updates regarding  
this year's ride!

Are you on Facebook  
and Twitter?



Like **NTSAD's Facebook page**  
and follow **@susanrkahn** for  
new developments in therapies,  
science, genetic testing, patient  
advocacy, and more.

### national tay-sachs & allied diseases association

susan kahn, executive director ([skahn@ntsad.org](mailto:skahn@ntsad.org))  
joan lawrence, development director ([joan@ntsad.org](mailto:joan@ntsad.org))  
diana pangonis, communications manager ([diana@ntsad.org](mailto:diana@ntsad.org))  
ingrid miller, office manager ([ingrid@ntsad.org](mailto:ingrid@ntsad.org))

2001 beacon street, suite 204  
boston, ma 02135  
(617) 277-4463  
[www.NTSAD.org](http://www.NTSAD.org)

Copyright © 20XX. All Rights Reserved.

[Forward this email](#)



This email was sent to [diana@ntsad.org](mailto:diana@ntsad.org) by [skahn@ntsad.org](mailto:skahn@ntsad.org) |  
[Update Profile/Email Address](#) | Rapid removal with [SafeUnsubscribe™](#) | [Privacy Policy](#).



National Tay-Sachs & Allied Diseases Association | 2001 Beacon Street, #204 | Boston | MA | 02135