



NTSAD Funded Research Progress Updates

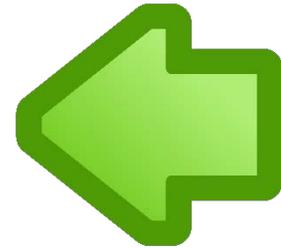
Lectin-assisted transnasal delivery of corrective enzyme for GM1 gangliosidosis (Final Report)

Grantee: BioStrategies

Investigators: David N. Radin, PhD; Carole L Cramer, PhD; Alessandra d'Azzo, PhD

- The focus of this study was to evaluate trans-nasal delivery of a RTB-fusion protein with β -galactosidase as an enzyme replacement therapy strategy for GM1 gangliosidosis. The RTB lectin, a sugar binding protein, could help facilitate transport of β -gal across mucosal surfaces. RTB lectin (β -gal:RTB) were produced in a plant-based protein production system.
- Several transnasal trials were carried out in GM1 (β -gal^{-/-}) mice by delivering β -gal:RTB to each nostril from 5 to 9 weeks of age and quantifying β -gal activity in various organs one hour later. While some β -gal activity was present in the cerebellum and brainstem (back portion of the brain), it was not detected in the olfactory bulb, midbrain or frontal brain (front portions of brain). These results did not support the original hypothesis that the drug would be mobilized to the brain via the olfactory nerves with the major site of accumulation being the olfactory bulb.
- In contrast, significant β -gal activity was detected in the liver of these animals following trans-nasal administration suggesting that β -gal:RTB may have first entered the circulatory system and subsequently traveled to the brain by crossing the BBB.
- NIH funding was then obtained to evaluate intravenous (IV) delivery of β -gal:RTB. β -gal:RTB was delivered IV twice weekly for 2, 4, or 6 weeks and fully normalized the low levels of GM1 ganglioside storage that accumulate in visceral organs (e.g., liver, spleen, kidney). There was also reduction in GM1 levels in the brain (cortex, cerebellum, and brain stem) indicating that IV-administered β -gal:RTB delivers corrective β -galactosidase to key CNS regions of pathological GM1 accumulation/storage.
- Future plans include studies to assess impacts of β -gal:RTB treatment at younger ages, to directly analyze impacts of treatment on cellular pathology and inflammation within brains of treated animals, and to expand cohort sizes. β -gal:RTB dosage, frequency, and treatment duration and other preclinical studies need to be completed to move these discoveries to clinical application.

UPDATE: We received a note from David Radin, PhD along with the news of the NIH SBIR bridge grant of \$2.5 million to further their research.



"Your support, however, has meant much more than monetary for BioStrategies as it has bridged our NIH SBIR funding over a period of several crucial years of our GM1 therapy development program and provided us the opportunity for the first time to become part of the wider community of GM1 stakeholders, especially patients and their families. Carole and I and, through us, the rest of our BioStrategies team, will always treasure the opportunity, encouragement, and friendship that you, your staff, and the patients and affected families that NTSAD encompasses have offered to us. You have inspired us to push on with our goal to bring our technology to fruition in treating GM1 patients."

NTSAD's \$160,000 Research Grant to BioStrategies has been leveraged as BioStrategies has recently received a two year NIH SBIR* Phase II award for \$2,438,483 and will focus on developing a therapeutic drug to treat GM-1 based on the company's proprietary innovative technology for delivering enzyme drugs to the brain and other hard-to-treat organs. Great news for GM-1!

** The Small Business Innovation Research (or **SBIR**) program is a United States **Government program**, coordinated by the Small Business Administration, intended to help certain small businesses conduct research and development (R&D). Funding takes the form of contracts or grants.*

Late Onset Tay-Sachs Registry & Repository

Grantee: Massachusetts General Hospital

Investigator: Florian Eichler, MD

Generously funded by the Katie & Allie Buryk Research Fund of NTSAD

- The investigators have completed a comparative review of literature reports and patient surveys for natural history data and outcome measures. An inventory of biological samples will supplement this review.
- This study aims to determine optimal outcome measures in LOTS patients. Outcome measures will be judged based on variability of data, change over a 6-month period, and patient ranking of importance. To date seven patients have completed baseline assessments and 5 more patients are planned for baseline assessments by November, 2017. All 12

Defining the Natural History of Canavan Disease through development of an International Registry.

Grantee: New York University

Investigators: Heather Lau, MD; Paola Leone, PhD

Co-funded with the Canavan Foundation

- A patient recruitment flyer was completed and approved by IRB.
- Nine patients consented to the natural history study.
- The NeuroBank database became active in March of 2017.
- The researchers continue to finalize their protocol and recruit patients to the study. They have

patients will then complete a 6-month follow up.

- The determined outcome measures will be incorporated into electronic case report forms (CRFs) to allow several centers to participate in future trials using NeuroBANK™. New measures will be added to the already established CRFs including neuropsychological scales, sleep scales, and video oculography. Once completed, electronic CRFs will then be implemented at 3 other institutions that see LOTS patients across the US and Europe. In addition, the investigators are working to create a common institutional review board (IRB) language across sites.
- After completion of the 6-month follow up, patient samples including blood and cerebrospinal fluid will be analyzed for biomarkers including quantification of GM2 ganglioside and other lipids. Biomarkers help track disease progression and are important to serve as outcome measures of therapeutic efficacy in clinical trials.

asked NTSAD to help with outreach to the Canavan families.



There is an ongoing Canavan Natural History Study being conducted by several researchers. You do not have to travel to participate in this study.

Please contact NTSAD if you're interested in contributing to the study and furthering the knowledge and data needed to pursue clinical trials.

You can read more about the study [here](#).

NTSAD is in communication with IntraBio regarding their research and planning for clinical trials with a compound called IB1000.

"IntraBio is now planning multi-national randomized, controlled pivotal clinical trials to evaluate the safety and efficacy of IB1000 as a therapeutic intervention in patients with TS, NPC and specific CA diseases. IntraBio hopes to commence enrollment in one or more of these pivotal trials in the EU in early 2018 to be followed by recruitment in North America." It is important to note that conducting clinical trials in a controlled manner is a key step in getting a drug approved for use.

We believe that results from the Late Onset assessments at the NTSAD conferences and natural history studies we've been involved in will have value as Intra-Bio plans future clinical trials.

Read the full press release from IntraBio [here](#) .



Lysosomal Disease Symposium
Wednesday, October 11, 2017
held as a part of the
Individualizing Medicine
Conference
October 9-10, 2017
Mayo Clinic, Rochester, MN

Attend the conference and bring attention to rare genetic diseases such as Lysosomal Storage Disorders and Tay-Sachs. Expert speakers will

Sunday, October 29, 2017
12:00 p.m.
Our Heritage and Our Health -
Ashkenazi Jewish Genetic
Diseases and the Founder Effect

Learning about your heritage is a beginning. All around the world distinct ethnic groups have been

explain the integrated resources available for the diagnosis, management, and research relating to people with these disorders.

Register today [HERE](#) and save \$100 with discount code: CIM

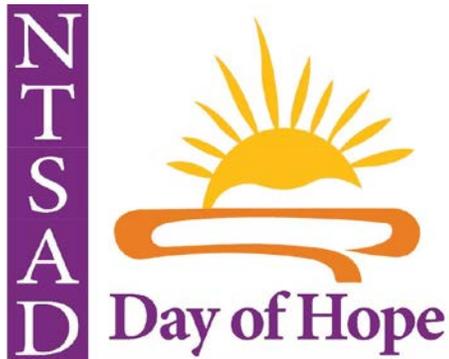
identified as having increased risks for particular genetic diseases. In the Ashkenazi Jewish population, several such inherited diseases are known. These include Gaucher disease, cystic fibrosis, Canavan disease, Bloom syndrome and others. Gaucher disease is the most common Jewish genetic disorder and among Ashkenazi Jews, 1 person in 15 is a carrier for this disease, and ~1/850 has Gaucher disease. To learn more about genetic diseases among persons of Ashkenazi Jewish descent, please attend this complimentary presentation. Visit the event's Facebook page [here](#).

Location:

Temple Emanuel
7 Haggetts Pond Road
Andover MA

Guest Speaker

Gary S. Frohlich, MS, CGC
Senior Patient Education Liaison
Sanofi Genzyme



2017 Day of Hope Results

The NTSAD community came together in full force and have raised funds for research via custom t-shirt sales, raffles, motorcycle runs, scavenger hunts, and other community based events. The results are still coming in but to date over \$25,000



**Thursday, October 5, 2017
Wine Taste for Brooke Chase**

**Somm Time Wine Bar
959 2nd Avenue
New York, New York**

has come in for research and we expect to reach our goal of \$60,000 in honor of NTSAD's 60th Anniversary!

Thank you to the many families and individuals who have had events, and to those who are having them!!!

The event will be an open wine bar and craft beer fundraiser (hors d'oeuvres, too) with all proceeds benefiting the organization. Somm Time will be serving four types of wine, in addition to having twelve craft beers on draft.

Buy tickets [here](#) for the evening and be sure to invite your friends that are in NYC!

Susan Kahn, Executive Director
Blyth Lord, President, NTSAD Board
Staci Kallish, DO, Vice President, NTSAD Board
Allison Bradbury, Chair, Research Initiative Committee
Fran Platt, PhD, Chair, Scientific Advisory Committee

2001 Beacon Street
Suite 204
Boston, MA 02135
(617) 277-4463 | info@ntsad.org
www.NTSAD.org



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