



National Tay-Sachs & Allied  
Diseases Association, Inc.

Tuesday, NOVEMBER 17, 2015

## NTSAD Monthly Research Review

### What is GM-1?

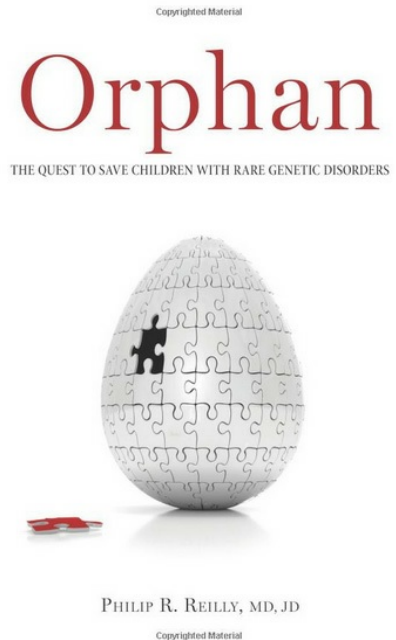
Gangliosidosis-1 (GM-1) is caused by a mutation in the gene responsible for a vital enzyme called beta-galactosidase ( $\beta$ -gal). The role of  $\beta$ -gal is to degrade a fatty substance or lipid called GM-1 ganglioside. In the absence of  $\beta$ -gal, GM-1 accumulates abnormally in cells, especially in the nerve cells, or neurons, of the brain. This ongoing accumulation, or "storage", of GM-1 causes progressive damage and eventually death of the cells.

Clinically, GM-1 presents as infantile, juvenile, or late-onset forms. The age of onset and the severity of symptoms are dependent on the amount of  $\beta$ -gal activity that is present. Symptoms of infantile GM-1 typically emerge in the first 6 months of life and are very progressive due to the least amount of  $\beta$ -gal activity. Juvenile and late-onset GM-1 have more variable age of onset and disease progression due to a range in  $\beta$ -gal activity.

### What is the latest with GM-1 Research?

**NTSAD-funded Research Initiative project - "Lectin-assisted transnasal delivery of corrective enzyme for GM-1 gangliosidosis"** *David Radin, PhD, Carole Cramer, PhD, and Alessandra d'Azzo, PhD*

We first reported on the initial progress from Drs. Radin and Cramer in May. They are working on replacing absent beta-galactosidase ( $\beta$ -gal) in mice with GM1 delivered through the nose in their two-year research project. These are the



We are pleased to share the link to this recently published book by our 2013 Imagine & Believe honoree and NTSAD's good friend, Phil Reilly, MD, JD.

*It is more than a book about disease and research - it gives voice to thousands of people who, all too often, have endured terrible illnesses, bravely faced arduous clinical trials, and (sometimes) known victories, almost always in silence.*

Order on Amazon and be sure to use [smile.amazon.com](http://smile.amazon.com) and

highlights from their one-year progress report:

\* Drs. Radin and Cramer created a  $\beta$ -gal fusion protein using a sugar-binding lectin called RTB ( $\beta$ -gal:RTB) with hopes that the lectin may help carry  $\beta$ -gal from the nose directly to the brain. They also plan to compare intranasal delivery of  $\beta$ -gal:RTB to more traditional intravenous (IV) administration of the same compound.

\* GM-1 mice were treated with  $\beta$ -gal:RTB delivered to each nostril and  $\beta$ -gal activity in the brain was measured.

\* Increased  $\beta$ -gal activity levels were consistently observed in the cerebellum of treated mice (in all 3 mice studied) and in the brain stem and midbrain of 2 out of 3 treated mice.

\* Detection of  $\beta$ -gal activity in these more distal regions (the cerebellum and brain stem are further from the nose) may suggest transport via either nerves or blood vessels in the brain.

\* Drs. Radin and Cramer will continue this work by studying correction of GM-1 disease in the brain of the mice and comparing nasal delivery to IV delivery.

Download an executive summary of the 12-month progress report from the NTSAD library [here](#).

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## GM-1 Gene Therapy Research at Auburn University

*Doug Martin, PhD, Auburn University (AL)*

GM-1 gangliosidosis is naturally occurring in cats, and a breeding colony has been maintained for over 40 years in order to study the disease and assess therapies. GM-1 affected cats were treated by gene therapy using a non-harmful adeno-associated virus (AAV) as a delivery vehicle. AAV was directly injected into the brain of GM-1 affected cats using 4 injection tracts in a single surgery lasting ~ 2 hours.

\* The average survival for GM-1 cats treated by AAV gene therapy is currently 6 times longer than untreated cats.

\* Untreated GM-1 cats live for 8 months, while treated cats now range from 4.7 - 6.0 years old.

\* Almost half of all treated GM-1 cats remain alive

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## BDSRA Opens RLOI for 2016 Funding Cycle

COLUMBUS, Ohio, November 16, 2015 -- The Batten Disease Support and Research Association (BDSRA) has issued a request for letters of intent (RLOI) for the 2016 research grant cycle. BDSRA supports scientific investigations through an annual merit review process, awarding grants to researchers throughout the world. To learn more, visit their website [here](#).

## Gene Therapy for Batten Disease

NIH issued a press release relating to gene therapy for Batten Disease, a lysosomal storage disease, and the new way of delivering replacement genes that may be effective in slowing the progression of the disease.

Click [here](#) to read the full NIH news release.

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## Natural History Studies

### National Institutes of Health (NIH)

National Human Genome  
Research Institute  
Bethesda, Maryland

*GM-1 or GM-2 gangliosidosis  
(Infantile, Juvenile, Late Onset)*

**Mass General Hospital (MGH)**

and in good health, with subtle or no clinical signs of disease.

\*  $\beta$ -gal enzyme activity was restored throughout most of the brain and spinal cord at normal or above normal levels. However, enzyme activity remained low in a few small areas.

\* Half of treated cats developed seizures - a part of the natural disease course in untreated cats - which suggests that small areas of the brain were not treated completely. The seizures are well-controlled by medication.

\* Untreated GM-1 cats have never been able to reproduce since they were first reported over 40 years ago. AAV-treated GM-1 cats have produced many litters of kittens.

\* All treated cats are able to see and hear normally.

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### Article highlight: Canadian doctors "break" blood brain barrier in experimental treatment

Recently, an article was published by several outlets with a hopeful headline, which was then shared by many on Facebook. The article focused on an experimental cancer treatment used to treat a brain tumor in one patient in Canada. We asked a couple of our Scientific Advisory Committee members to offer their insight:

\* The patient was given chemotherapy by IV and then an experimental procedure was used to inject tiny bubbles (microbubbles) into the bloodstream. A high-intensity ultrasound was then focused on the brain tumor, causing these microbubbles to vibrate, tearing the proteins of the blood brain barrier at the site of the tumor. The researchers hope that this allowed the chemotherapy to leave the blood and enter the brain at the site of the tumor.

\* A clinical trial is planned to include 9 additional patients and study the safety and efficacy of this procedure. A second study is planned to study treatment of another type of brain tumor.

\* While exciting, it is not yet clear if this procedure will be helpful in treating brain tumors. It is also not clear if this will apply to diseases that affect the whole brain, like Tay-Sachs, Sandhoff, GM1, and Canavan, or if this will only be helpful for treating small regions of the brain like tumors.

\* Also the risks of disrupting the protective blood brain

Boston, Massachusetts  
*Late Onset Tay-Sachs, Late Onset Sandhoff or Late Onset GM-1*

### University of Minnesota (UMN)

Clinical and Translational  
Science Institute

Minneapolis, Minnesota

*Infantile/Juvenile/Late Onset Tay-Sachs or Sandhoff diseases*

For more information about these studies, contact Diana, Director of Family Services, [here](#).

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## Are you on Facebook and Twitter?



Like **NTSAD's Facebook page** and follow [@susankahn](#) for new developments in therapies, science, genetic testing, patient advocacy, and more.

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## What Questions Do You Have about Research?

We want to hear from you and address any topics or answer any questions you may have about research. Our Research Initiative Committee is a group of knowledgeable experts who are ready to tackle the tough questions and address the topics that are meaningful to you.

Send Diana an email [here](#) with

barrier for up to 12 hours needs to be assessed.

\* We look forward to seeing the published results of these studies, learning more about this procedure, and determining if this may be useful in treating widespread brain diseases.

your ideas for next month's issue  
for December 18, 2015.

Read this and other articles about this here:

<http://www.inquisitr.com/2552192/canadian-doctor-first-to-break-blood-brain-barrier/> and

<http://www.ctvnews.ca/health/canadian-researchers-break-blood-brain-barrier-with-new-ultrasound-treatment-1.2648878>.

*Stay tuned for an upcoming update from Lysogene about their collaboration with University of Massachusetts Medical School and Auburn University.*

*Our thoughts are with them as France and the world heals from the violence of this past Friday.*

## **national tay-sachs & allied diseases association**

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