National Tay-Sachs & Allied Diseases Association, Inc.

Friday, JANUARY 15, 2016

NTSAD Monthly Research Review

A Brave New World.
Are there possibilities with CRISPR?

A magazine article was released on December 2nd, 2015 entitled "What can you actually do with your fancy gene-editing technology? Wading through the hype about CRISPR". (click **here** to read the full article.) This article specifically mentioned Tay-Sachs disease and caught the attention of some in our community.

What is Gene Editing?
Genome editing, or genome editing with engineered nucleases (GEEN) is a type of genetic engineering in which DNA is inserted, replaced, or removed from a genome using artificially engineered nucleases, or "molecular scissors."

What is CRISPR?
CRISPR, which stands for ' clustered, regularly interspaced, short palindromic repeats', is a technique used for gene editing."

- CRISPR uses a specific type of protein called a nuclease as a sort of scissor to cut DNA. At the cut site, gene editing systems can then introduce a specifically engineered DNA construct.
- The implication for disease treatment is that these mechanisms can modify genes by either introducing a desired trait (ex. Editing immune cells to recognize and attack cancer cells) or by removing a harmful trait (ex. Removing a disease causing mutation). This modification can be done in somatic cells, all of

NTSAD Request for Proposals for 2016 Update

NTSAD's Research Initiative issued its 2016 Request for Research Proposals in December 2015. Nineteen pre-applications were submitted covering a variety of topics including basic research, biomarkers, new methods of drug delivery, and small molecule therapies.

The next step will involve reviewing the pre-applications and inviting a select group to submit full applications. The reviewers are volunteers from NTSAD's scientific advisory groups, including members of Scientific Advisory Committee (SAC), the Corporate Advisory Council (CAC), and the Research Initiative Committee.

the cells of the body that can not be passed on to future generations, or germ line cells including sperm, egg, and early embryo in which genes are passed on through generations.

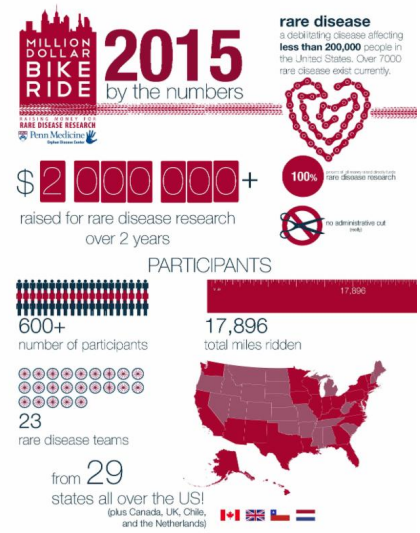
- Earlier in 2015 a Chinese scientist was the first reported to edit the genome of a human embryo and sparked great controversy. The researchers found that of 86 embryos treated with CRISPR, only 28 survived and were successfully cut and only a fraction of those contained the intended replacement DNA. The scientific community was in resounding agreement that the technology is too immature to do any further testing in human embryos. Read more about the study and the controversy **here.**

- In order to correct inherited disorders such as Tay-Sachs, GM-1, or Canavan disease, the germ line cells, meaning the egg or sperm of parents known to carry the trait or a very early embryo known to be affected, would have to be edited because once a child is born every cell in the body has a copy of the faulty gene. In the case that both parents are known carriers, in-vitro fertilization with pre-implantation genetic diagnosis is already readily available to screen embryos (statistically 25% will be normal, 50% will be carriers, and 25% will be affected) in order to implant only healthy embryos. PGD therefore negates the need to edit genes for these conditions.

The article mentioned above addresses this specific point:

"Consider the severe genetic disorders, like Tay-Sachs.....in recessive genetic diseases (where two faulty copies are needed), 75 percent will be normal. So most won't require any editing at all. Parents could opt for in-vitro fertilization (IVF), after which doctors could screen the resulting embryos for those that don't carry any copies of the risky genes. This technique, known as **pre-implantation genetic diagnosis (PGD)**, only fails when both parents carry the necessary variants, and all their embryos would be similarly affected. Those pairings, however, are very rare.

"If we really care about avoiding genetic diseases, germline



THIRD ANNUAL MILLION DOLLAR BIKE RIDE

Ride with Team NTSAD on Saturday, May 7, 2016

If we raise at least $20,000, these gifts will be matched up to $50,000 to fund a research grant focused on our group of rare genetic diseases.

If you're interested in riding with Team NTSAD in Philadelphia, contact Allison Bradbury **here**.

The 2015 Team NTSAD MDBR grant award went to Marlene Jacobson, PhD, of Temple U. for her project, "Patient-Derived Phenotypic Assay to Discover Treatments for Tay-Sachs Disease". The 2014 MDBR grant award went to Annette Bley, MD, University Hospital - Hamburg, for "Quantitative description of the clinical course of Canavan disease".

editing isn't the first, second, third or fourth thing that we should be thinking of," said Eric Lander from the Broad Institute. "Instead, it would do more good to make genetic diagnostic tests more widely available, so parents would know that they were carriers of risky genes, and could sign up for PGD."

To learn more about the mechanism of CRISPR watch this short animated video here.

Make a Gift to Support Research **here** today.

Traumatic Brain Injury: Is it reversible?

New research shows brain injury due to trauma may be reversible. A study published in July 2015 focuses on abnormal tau proteins in the brain that form after traumatic brain injury (TBI).

- Normal tau protein functions in the brain to provide a support system for neurons, helping them keep their shape, which is very important for normal brain function.
- Abnormal tau proteins have been associated with neurodegenerative diseases such as Alzheimer's disease and chronic traumatic encephalopathy (CTE). CTE occurs in individuals who have severe or repeated concussions or other brain injuries, such as military veterans exposed to blasts and football players.
- Tau proteins have also been detected in the brain of Sandhoff disease mice, suggesting that abnormal tau proteins play a role in this and possibly other inherited neurodegenerative diseases.
- In this study, researchers at Beth Israel Deaconess Medical Center used a mouse model to study the effects of TBI. By simulating TBI injuries in mice, they found that abnormal tau, called cis P-tau, forms soon after a mild TBI injury and resolves within weeks. More severe TBI injuries lead to larger production of cis P-tau. Cis P-tau is toxic to neurons

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

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patient advocacy, and more.

and can spread through the brain, leading to neuron death with eventual signs of neurodegenerative disease.

- The researchers developed an antibody which can neutralize the toxic cis P-tau and stop the damage it causes. When given after TBI injury, this antibody reduces the amount of cic P-tau in the brain and prevents the abnormal tau from spreading through the brain.
- This research is still in the early stages, but suggests there may be therapy available for preventing neuronal damage due to abnormal tau proteins.
- Read more **here**.

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susan kahn, executive director (**skahn@ntsad.org**)
joan lawrence, development director (**joan@ntsad.org**)
diana pangonis, family services director (**diana@ntsad.org**)
ingrid miller, office manager (**ingrid@ntsad.org**)
becky benson, conference coordinator (**becky@ntsad.org**)
alison perkus, development associate (**alison@ntsad.org**)

2001 beacon street
suite 204
boston, ma 02135
(617) 277-4463

www.NTSAD.org