THE ALS FORUM

Discovering a Common Goal, Discovering a Cure

ALS Forum e-Newsletter Volume 94 **October 11, 2013**

Be sure to check out our newly redesigned ALS Forum website. We hope you like what you see and we would love to know what you think. Please email jgoodman@prize4life.org with any feedback you may have.

Visit the ALS Forum website to read the complete stories featured in this e-newsletter. Please forward this e-newsletter to friends and colleagues who may be interested in learning more about ALS.

Resources:

Visit the PRO-ACT Database at www.ALSDatabase.org

NEALS Biofluid Repository Available to Researchers

NINDS Fibroblast Repository

VABBB Tissue Request Information Site

Funding News:

MNDA Calls for Project Grant Applications. The summary application deadline is November 1, 2013.

Upcoming Meetings:

October 13-15, 2013: New Orleans, LA: American Neurological Association's 2013 Annual Meeting

October 14-15, 2013: Tel Aviv, Israel: BrainTech Israel 2013

October 29-30, 2013:

Research News

Lou Gehrig's RNA Interference Success in Mice, Monkeys

A recent article in *Molecular Therapy* is garnering attention for some impressive survival benefits observed in both SOD1 G93A and SOD1 G37R mice following treatment with an shRNA directed against SOD1. This research was led by first author, Dr. Kevin Foust of Ohio State University in Columbus, Ohio, and senior authors, Dr. Brian Kaspar of The Research Institute at Nationwide Children's Hospital in Columbus and Dr. Don Cleveland of the Ludwig Institute at the University of California, San Diego. High copy SOD1 G93A mice receiving AAV9-SOD1-shRNA at P1 showed a survival benefit of over 50 days, a 39% increase in lifespan. The effect was still pretty impressive when the mice were treated at day 85; the mice survived 30 days (23% increase in lifespan). Although these results are encouraging, the number of animals treated was fairly low (six female mice at P1 and five female mice at P85). The high copy SOD1 G93A mice are well-known to display significant heterogeneity in lifespan and also to show gender-specific effects on lifespan, which can confound study results (particularly those studies with small numbers). In addition, these animals are notorious for spontaneous copy loss (for further information see Scott et al. and the "Working with ALS Mice" manual), and the paper provided no quantitative evidence of transgene expression levels. These caveats aside, the finding that this AAV-shRNA approach also generated significant reductions in SOD1 expression in primate models ensures that we will be hearing more about translating this methodology to the clinic in the future, so stay tuned. Click here to read Dr. Amber Dance's coverage of the full story.

Can Algae Cause ALS?

Some researchers have long believed in an association between a neurotoxic amino acid called β-methylamino-L-alanine (BMAA) and neurodegenerative disorders, particularly ALS. This theory largely originated from the finding that the indigenous people of Guam, the Chamorros, consumed high levels of BMAA in their diet and had an

Boston, MA: SciBX Summit on Innovation in Drug Discovery and Development 2013

November 3-5, 2013: New York, NY: FasterCures: Partnering For Cures

November 7-8, 2013: San Diego, CA: 8th Annual Brain Research Conference: RNA Metabolism in Neurological Disease

November 7-8, 2013: San Diego, CA: Workshop, Introduction to Stereology for Neuroscientists

November 8, 2013: San Diego, CA: NINDS Workshop, Mechanisms of Misfolded Protein Propagation in Neurodegenerative Diseases

November 9-13, 2013: San Diego, CA: Society for Neuroscience Annual Meeting: Neuroscience 2013

December 4-5, 2013: Milan, Italy: 21st Annual Meeting of the International Alliance of ALS/MND Associations

December 6-8, 2013: Milan, Italy: 24th International Symposium on ALS/MND

February 2-4, 2014: Miami, FL: ADDF's 8th Annual Drug Discovery for Neurodegeneration Conference

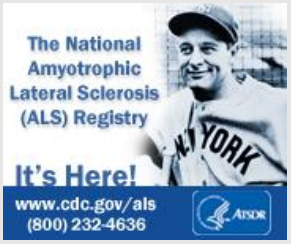
incidence of ALS nearly 100 times that seen in any other population. Blue-green algae blooms produce BMAA, and accumulating evidence suggeststhat people who live near these blooms, or consume shellfish that were isolated from water with these blooms, have a higher incidence of ALS. But what is the molecular link between BMAA and ALS? We may now know the answer. A group of scientists from Australia and the United States recently reported in *PLOS ONE* that BMAA can be incorporated into proteins in place of serine, leading to protein misfolding, aggregation, and ultimately cell death. Although the protein misfolding and aggregation evidence is certainly intriguing (especially considering the recent interest in SOD1 and TDP-43 aggregation and spreading), more work needs to be done to elucidate and quantify the proposed role of BMAA in ALS. Clickhere to read more on this provocative topic.

Ultra-Sounding out ALS

Much of the research on ALS tends to focus on treatment; but in order to treat ALS it first needs to be diagnosed -- and the earlier the better so that patients can get into clinical trials as soon as possible. The ALS Therapy Development Institute's blog recently highlighted the potential for neuromuscular ultrasound (NMUS) to one day noninvasively diagnose ALS. With the advent of higher resolution NMUS, scientists could be able to detect key muscle changes in people with ALS. NMUS needs to be standardized and clinically confirmed, but potentially it could be used to aid diagnosis along with more invasive electrophysiological methods like EMG, which is also under development to enable earlier diagnosis. For more on current research into the potential of NMUS see the recent blog post here. But NMUS may not be the only potential ALS diagnostic on the horizon. In 2011, Prize4Life awarded The $1M ALS Biomarker Prize to Dr. Seward Rutkove for his development of a potential ALS biomarker technology called electrical impedance myography (EIM). EIM sensitively measures the flow of a small electrical current through muscle tissue. By comparing the size and speed of the electrical current between normal tissue and tissue affected by ALS, EIM can accurately measure the progression of the disease (a key need for clinical trials), and hopefully one day soon be used as an ALS diagnostic. In fact, EIM is currently being tested in an ongoing trial of 100 patients to see how it performs in disease mimics and in another smaller study to "study its reliability and ability to differentiate ALS patients from healthy controls." The larger study will also compare the performance of EIM to ultrasound so hopefully we will have a definitive answer soon!

We Want You! The VA is Looking for ALS Researchers

The **Department of Veterans Affairs (VA) Biorepository Brain Bank (VABBB)** is seeking Veterans with amyotrophic lateral sclerosis (ALS)who would like to participate in research about conditions such as ALS that affect Veterans and researchers interested in conducting research relating to Veterans with ALS. Researchers interested in obtaining precious central nervous system tissue and associated clinical data to conduct ALS research are encouraged to apply to the VABBB to receive tissue and data. All applications for access to tissue will be reviewed monthly by a panel of subject matter experts and the VABBB Executive Committee. Final decisions about access will be made on the basis of qualifications of the investigator, scientific merit of the proposed research utilizing the tissue, quantities of tissue requested, statistical



Download your free copy:

SUPPORT THE ALS FORUM

Send the ALS Forum e-Newsletters to your colleagues!

Forward to a Friend

issues and availability of tissue. Researchers who are interested in applying for tissue from the VABBB are encouraged to visit the VABBB tissue request information site.

Drug News

Neuraltus Pharmaceuticals Appoints New President and CEO
Neuraltus Pharmaceuticals just announced that they have appointed a new President and Chief Executive Officer, Richard L. Casey. Casey will replace John Walker, who has been acting as Neuraltus' interim CEO since September 2012. Late last year Neuraltus announced the results from their Phase II clinical trial of NP001 in people with ALS. Although the results of the study did not reach statistical significance, the study hinted at an effect in a subset of patients. Casey is dedicated to advancing NP001 as a potential treatment for ALS patients. Casey said "Neuraltus' focus will be on conducting additional clinical research to demonstrate how the activity of NP001 can translate into a clear benefit for patients." Hopefully under Casey's leadership Neuraltus will be able to move NP001 forward.

A One-Man Startup for Better ALS Diagnosis
As discussed in the "Ultra-Sounding out ALS" article above, correct and early diagnosis of ALS is essential in order to gain earlier access to clinical trials and the only FDA approved drug for ALS, riluzole. However, early diagnosis is difficult and involves ruling out many other diseases first. Dr. Robert Bowser, professor and chairman of neurobiology at Barrow Neurological Institute in Arizona and sole founder of Iron Horse Diagnostics (named for "The Iron Horse," Lou Gehrig), hopes to change that. Iron Horse Diagnostics has developed two diagnostic tests, acerebrospinal fluid-based test and a blood test, based on ALS protein biomarkers that Dr. Bowser and colleagues had previously identified, pNfH(phosphorylated axonal neurofilament subunit H) and complement c3. These tests could enable earlier diagnosis of ALS. The company has already evaluated these diagnostic tests on multiple human biosamples where they showed 93% accuracy. Iron Horse Diagnostics has recently secured a pharmaceutical partner to test the diagnostic accuracy of these two tests in a prospective study involving 300 people. Click here for more about this story and stay tuned to the ALS Forum e-Newsletter for updates.

Research Continues for Stem Cell Treatment of ALS
The government may be in the midst of a shutdown, but thankfully clinical trials at universities continue to move forward, including the Neuralstem Phase II trial that is currently in progress at the University of Michigan in Ann Arbor, Michigan and at Emory University in Atlanta, Georgia. After positive Phase I trial results, Neuralstem was granted permission to move to a Phase II dose escalation and safety trial, which includes 15 patients who can be treated with up "to 40 injections and up to 400,000 cells per injection." Dr. Eva Feldman, principal investigator for the Phase II trial at the University of Michigan, recently presented the results of the Phase I trial and gave an update about the Phase II trial, in which a third patient has just been treated. The therapy has been shown to be effective in rat models of ALS, and seemed to show promise as a potential ALS treatment in four of the fifteen patients treated in the

Phase I. Click here to read more about the study.

BrainStorm Teams-Up with Dana Farber for Multi-Center ALS Trial
Following the successful completion of a Phase I/II trial at the Hadassah Medical Center in Jerusalem, Israel, BrainStorm Cell Therapeutics is on track to launch a Phase IIa multi-center ALS trial in the United States (US). BrainStorm just announced that they are completing the final step necessary to submit an Investigational New Drug (IND) application to the Food and Drug Administration (FDA) for approval. This step, involving transfer of intellectual property rights for BrainStorm's NurOwn™ technology to Dana Farber Cancer Institute (DFCI), is an important milestone, as The Connell and O'Reilly Cell Manipulation Core Facility at DFCI will provide NurOwn to the University of Massachusetts and Massachusetts General Hospital trial sites. The third trial site, the Mayo Clinic, will produce its own supply of NurOwn. For more information you can check out BrainStorm's site.

The ALS Forum was developed by Prize4Life, Inc.
P.O. Box 425783 Cambridge, MA 02142
www.prize4life.org

Identified content provided through a partnership with the Alzheimer Research Forum.