THE ALS FORUM

*Discovering a Common Goal, Discovering a Cure*

**ALS Forum e-Newsletter Volume 118** **December 19th, 2014**

*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.*

*We will be taking a brief break and will return after the New Year. We wish you and all your loved ones happy and healthy Holidays and New Year!*

**Resources:**

The ALSGene tool: www.ALSGene.org

The PRO-ACT Database: www.ALSDatabase.org

NEALS Biofluid Repository Available to Researchers

NINDS Fibroblast Repository

VABBB Tissue Request Information Site

**Funding Opportunities:**

ALS ACT, ALSA, NEALS and the ALS Finding a Cure Foundation RFP: Phase II Clinical Development of Novel, High-Potential Treatments for People with ALS. Letter of Intent due January 9, 2015.

ALSA Investigator-initiated Research Grant Program. Abstracts due January 13th, 2015

**Webinar:**

ALSA/NEALS Expanded Access Webinar: Jan 8, 2014, 2:00-3:00 PM EST.

## Conference News

Brussels: 25th International Symposium on ALS/MND

The 25th International Symposium on ALS/MND took place in Brussels, Belgium from 5-7 December 2014. This is the largest medical and scientific conference in the ALS community, and this year boasted close to 900 attendees. The opening plenary talk was an inspiring presentation by Dr. Alfred Sandrock, M.D., Ph.D., Chief Medical Officer (CMO) of Biogen Idec (and member of Prize4Life's Scientific Advisory Board). Dr. Sandrock presented his expert opinion of the challenges in ALS drug development and potential solutions to accelerate development of an effective therapy. Click here to read Prize4Life's full coverage of Dr. Sandrock's presentation.

SfN 2014: Exosomes Emerge as Critical Vehicles for Cell-to-Cell Communication in the Brain

Exosomes are small vesicles with specialized functions that transmit materials between cells, and are emerging as an important mode of cell-to-cell communication in the nervous system. Signaling via exosomes has been implicated in ALS and other neurodegenerative diseases as a key method for propagation of misfolded proteins, including SOD1, between neighboring cells (see Dec 2012 news story). This year's Society for Neuroscience Annual Meeting, which took place Nov 15-19 in Washington, D.C., highlighted the cutting-edge research on exosomes in the nervous system, and their role in health and disease. Click here to read the latest from SfN on exosomes:
Part I: Exosomes: the Fedex of the Nervous System?
Part II: Exosomes: Purveyors of Neurodegenerative Disease?

## Research News

Targeting Pharmaco-resistance Pumps Improves Riluzole Efficacy in ALS Mice

The central nervous system is adept at protection from toxins, and utilizes specialized transporters in the endothelial cells of the blood-brain-barrier to pump them out. However, this mechanism also rids the

**Upcoming Meetings:**

**January 2015**

January 13-17, 2015: Hokkaido, Japan: Society for Neuromuscular Sciences 8th Annual Scientific Meeting

January 25-30, 2015: Taos, New Mexico:Neuroinflammation in Diseases of the Nervous System

**February 2015**

February 1-3, 2015: Cambridge, UK: Biomarkers for Brain Disorders: Challenges and Opportunities

February 10-12, 2015: Cardiff, UK: Digital Health Assembly Open Innovation Conference

February 17-19, 2015: Boston, MA: World CNS Summit 2015

February 22-26, 2014: Santa Fe, NM: Keystone Symposia: Neuroepigenetics

brain and spinal cord of potentially beneficial drugs, report researchers from the Thomas Jefferson University in Philadelphia, PA. In the November 20 *Annals of Clinical and Translational Neurology,* Piera Pasinelli, Davide Trotti and colleagues demonstrate in an ALS mouse model that inhibition of two drug efflux transporters with a drug called elacridar improves efficacy of riluzole, the only drug approved by the U.S. Food and Drug Administration (FDA) for treating ALS. Targeting the drug efflux transporters may also be a beneficial approach for improving the efficacy of other candidate therapies for ALS that are expelled by these pumps. Click here to read more about this promising proof-of-concept study.

Lessons Learned from Epidemic Spreading Shed Light on Neurodegenerative Disease

Propagation of protein pathology between molecules or even neurons has been demonstrated for several ALS-linked proteins, such as SOD1 and TDP-43 (see June 2013 news story, Dec 2012 news story). A new study published Nov 20 in *PLOS Computational Biology* applied models from human epidemic spreading, such as the H1N1 virus in 2009, to gain insight on "spreading", or propagation, of protein misfolding in the aging brain. Researchers from the Montreal Neurological Institute in Montreal, Canada applied epidemic spreading models (ESMs) to Positron Emission Tomography (PET) Amyloid β (Aβ) datasets from the Alzheimer's Disease Neuroimaging Initiative (ADNI), and found that these models precisely describe propagation and deposition of misfolded proteins in the AD brain. The researchers now plan to integrate the influence of other factors such as vascular dysregulation into ESMs of misfolded protein propagation. Click here to read more about this original work.

TDP-43 Protein Structure Reveals Distinct Nuclear and Cytoplasmic Conformations

Cytoplasmic aggregates of the RNA-binding protein TDP-43 are a pathological hallmark of ALS and some cases of frontotemporal dementia (FTD), but the causes of aggregation and its contribution to disease are not well understood (see Jan 2014 news story). A new study published December 12 online in *Proceedings of the National Academy of Sciences* sheds light on naturally occurring conformational changes in TDP-43 that can promote aggregation. The authors, led by Jianxing Song from the National University of Singapore, present the structure of the TDP-43 amino terminal domain, and reveal two conformations in equilibrium: a tightly folded nucleic acid-binding conformation and a loose, aggregation-prone structure. How do these structures contribute to TDP-43 function in the nucleus and potentially in the cytosol (see Feb 2014 news story)? Click here to find out more.

iPSCs Derived From Stored Blood Samples Open Doors for ALS Research

Techniques for generating neurons from stem cells derived from individual patients' cells (induced pluripotent stem cells, iPSCs) have opened the doors for modeling, drug screening and development of personalized therapeutics in many diseases, including ALS (seeconference news this issue, May 2014 news story, April 2014 news story). In the December *Stem Cells Translational Medicine*, researchers

February 23-24, 2015: Manchester, UK:

10th Annual Biomarkers Congress

February 25-26, 2015: La Jolla, CA: Biocom Global Life Sciences Partnering Conference

**March 2015**

March 1-3, 2015: San Diego, CA: 9th Annual Drug Discovery for Neurodegeneration Conference

March 1-6, 2015: Ventura, CA: Glial Biology, Functional Interactions Among Glia and Neurons: Glial Cells in Health and Disease.

March 1-6, 2015: Ventura, CA: Oxidative Stress and Disease: The Redox Biology of Age-Related Diseases.

March 11-15, 2015 Washington, DC: MDA Scientific Conference.

**April 2015**

led by Dhruv Sareen of Cedars-Sinai Medical Center in Los Angeles, California report on a new method for generating iPSCs from stored blood samples. This approach greatly expands the patient pool for studies in ALS and other rare diseases, as cell lines can be generated from deceased patients whose blood samples are stored in large biorepositories. Click here to read more.

## Drug News

MIT Professor and Former Onyx CEO Co-found Neurodegenerative Disease-focused Company

Tony Coles, the former CEO of Onyx Pharmaceuticals, and Professor Susan Lindquist of MIT's Whitehead Institute in Cambridge, Massachusetts have joined forces to found a new biotechnology company focused on neurodegenerative diseases. The company, called Yumanity Therapeutics, is based on approaches developed in Susan Lindquist's laboratory to screen compounds that inhibit protein misfolding in yeasts and induced pluripotent stem cells (iPSCs) derived from patients. The company has already identified a lead compound for Parkinson's disease, which is being tested in mouse models. Currently, the founders are funding the company themselves, but they are aiming to close a round of funding in early 2015. Click here to read more.

Annexon Biosciences Closes $34M Series A Funding for Neurodegenerative and Autoimmune Disease Therapy

Redwood City, California-based Annexon Biosciences has closed a $34M Series A financing round to develop their lead candidate, ANX005, for treating autoimmune and neurodegenerative diseases. The company was established in 2011 by Ben Barres of Stanford University School of Medicine and Arnon Rosenthal, co-founder of Alector and Rinat Neurosciences. ANX005 is a monoclonal antibody that inhibits the classical complement cascade, an important player not only in autoimmunity but also in the response of the aging brain to stress. Annexon will initially focus on rapidly advancing this candidate therapy for Huntington's disease. Click here to read more.

Brainscope's Handheld TBI Assessment Device Receives FDA Clearance

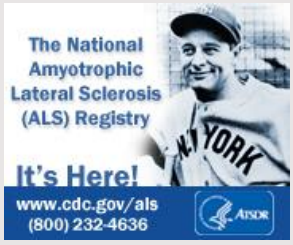
A new handheld device developed by the medical neurotechnology company Brainscope has obtained FDA clearance as an adjunctive technology to Computerized Tomography (CT) scans for assessment of traumatic brain injury (TBI). The compact device, called Ahead 100, records the electroencephalograph (EEG) of patients, and can rapidly and accurately determines the severity of a head injury and the need for further assessment of injury via CT scan. The device is particularly useful in urgent care settings, immediate assessment of sports injuries, and limited resource settings. The next generation of this device is an improved technology that is also adaptable for use with smartphone and tables. EEG-based technologies also hold promise for ALS (seeMay 2012 news story), and hopefully this device will be adapted to help ALS patients too. Click here to read more.

Otsuka Pharmaceutical to Acquire Avanir Pharmaceuticals

In late 2010, Avanir Pharmaceuticals obtained approval of the U.S. Food

April 7-11, 2015: Soelden, Austria: The 17th International Neuroscience Winter Conference.

April 7-8, 2015: San Francisco, CA: The 10th Annual Neurotech Investing and Partnering Conference.

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and Drug Administration (FDA) to market Nuedexta, the first drug for treating pseudobulbar effect, the uncontrollable bursts of laughing or crying that occurs in patients with ALS and several other neurological disorders (see Oct 2010 news story). Avanir has now been acquired by the US subsidiary of Otsuka Pharmaceuticals, Otsuka-America. The acquisition will not only give Otsuka marketing rights to Nuedexta, but also access to Avanir's expertise in drug discovery development for neurological diseases. Click here to read more.

The ALS Forum was developed by Prize4Life, Inc.

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