ALS Forum e-Newsletter Volume 133 **August 7, 2015**

The ALS Ice Bucket Challenge is back! To learn more visit www.alsicebucketchallenge.org. To support the ALS Forum click here. Your contributions will help enrich this resource!

Visit the ALS Forum website to read the complete stories featured in this e-newsletter. Please let your friends and colleagues know about the ALS Forum. It is easy to sign up for the newsletter here.

Resources:

ALS Drugs in Development Database

The ALSGene tool: www.ALSGene.org

The PRO-ACT Database: www.ALSDatabase.org

NEALS Biofluid Repository Available to Researchers

VABBB ALS CNS Tissue Request Information Site

Funding Opportunities:

ALS Association Clinical Management Grants. Letter of Intent due September 14, 2015.

Clinical and Translational Science Award (CTSA U54). Applications due Sept 25, 2015.

ALS Therapy Alliance (ATA) RFP. Applications due Oct 15, 2015.

California Stem Cell Agency (CIRM) 2.0

Research News

One Year Later - Assessing the Impact of the Ice Bucket Challenge

Last summer, the ALS Ice Bucket Challenge (IBC) went viral, with millions of people dumping ice water on their heads and donating to ALS charities. In addition to raising awareness of the rare disease, the IBC raised over $220 million for ALS organizations around the world (see Sep 2014 news). One year later - how have these funds be spent? While aiming to balance long-term goals with urgent needs, charities have committed their new funds to a spectrum of causes, from patient care to scientific research. On the research front, the funds raised by the IBC have helped accelerate large scale sequencing projects, stem cell research, and initiation of new clinical trials. The impact of last year's phenomenon has been tremendous, and its initiators plan to bring the IBC back every August until there is a cure! To read Amber Dance's 2-part report on the impact of the IBC funds, click here (Part I) and here (Part II).

Transcriptome Data Uncovers Differences between C9ORF72 and Sporadic ALS

Brain transcriptome data from C9ORF72 ALS and sporadic ALS patients are now publicly available, courtesy of researchers from the Mayo Clinic. Senior authors Leonard Petrucelli of the Mayo Clinic in Jacksonville, Florida and Hu Li of the clinic in Rochester, Minnesota, and colleagues examined RNA expression, alternative splicing, and 3' UTR lengths in two areas of the brain, the frontal cortex and the cerebellum. According to the publication in the July

Awards. Due last business day of each month.

Upcoming Meetings:

Call for Papers - deadline Sept 24, 2015! See AMIA 2016 Joint Summits on Translational Science and listing below.

September 2015

Sept 3-6, 2015: Prague, Czech Republic: 2nd World Congress on Neurotherapeutics

Sept 9-11, 2015: Philadephia, PA: CNS Diseases World Summit

Sept 19-20, 2015: Montreal, Canada: 10th Annual Symposium of the Fondation Andre-Delambre

Sept 27-29, 2015: Chicago, IL: American Neurological Association Annual Meeting

Sept 24-25, 2015: Ottawa, Canada: Ottawa International Conference on Neuromuscular Biology, Disease and Therapy

Sept 27-29, 2015: Chicago, IL: American Neurological Association Annual Meeting

Sept 30 - Oct 4, 2015: Brighton, UK: 20th International World Muscle Society Congress

October 2015

Oct 15-16, 2015: Chicago, Illinois: 10th Brain Research Conference RNA Metabolism in Health and Disease.

Oct 17-21, 2015: Chicago, Illinois: The Society for

20 *Nature Neuroscience,* computational analysis of the transcriptome data revealed potential differences in the mechanisms underlying C9ORF72 ALS and sporadic cases: in the C9ORF72 patients, dysregulated RNAs were primarily involved in vesicle transport and the unfolded protein response, while in the sporadic cases, the altered RNAs were involved in synaptic transmission and cellular defense. These findings suggest that different therapeutic approaches may be needed for these two patient subgroups.

Mutant SOD1 Impairs Autophagy by Early Disruption of Retrograde Transport

New findings link the SOD1 mutation and early deficits in motor neuron retrograde transport that lead to impaired autophagy. As reported in the 15 July *Neuron*, Zu-Hang Sheng and colleagues at the National Institute of Neurological Disorders and Stroke in Bethesda, Maryland, found that binding of mutant SOD1 to dynein rendered the motor protein incapable of attaching to its normal cargo and transporting it to the cell body for degradation. This resulted in decreased axonal transport of mitochondria-containing endosomes, ultimately impairing lysosome-mediated autophagy of damaged mitochondria in motor neurons. When a dynein-adaptor protein, snapin, was overexpressed in the spinal cord of mutant SOD1 mice, mitochondrial function and motor neuron survival improved. The authors next plan to investigate how defects in transport of other organelles may also be involved in motor neuron degeneration.

Scientists Decipher Motor Neuron Activity Patterns in ALS Patients

Brain-controlled prosthetic devices hold potential to substantially improve quality of life for people with ALS or spinal cord injury. However, advances in technology are constrained by our limited understanding of the complex neuronal signals that control human movement. An exciting development was published in the June 23*eLife* by a team of researchers led by Jaimie Henderson and Krishna Shenoy of Stanford University. Using multi-electrode arrays implanted into the motor cortex of two ALS patients, the researchers were able to record neuronal activity from close to 100 neurons, while simultaneously recording subtle hand movements with sensitive sensors. Intriguingly, the team discovered that voluntary movement in humans is controlled by similar dynamic neuronal activity as they had previously identified in non-human primate studies. These results can help researchers develop improved algorithms for translating neural activity into electric signals that can move robotic arms or computer cursors, as recently demonstrated by Shenoy's team in preclinical studies (see press release).

Neuroscience Annual Meeting.

Oct 31-Nov 5, 2015: Santiago, Chile. World Congress of Neurology

November 2015

Nov 14-18, 2015: San Francisco, CA: American Medical Informatics Association (AMIA) Annual Symposium

December 2015

Dec 11-13, 2015: Orlando, FL: International Symposium on ALS/MND.

2016

January 2016

Jan 24-27, 2016: Santa Fe, New Mexico: Keystone Symposium on Molecular and Cellular Biology: Axons: From Cell Biology to Pathology.

March 2016

March 21-22, 2016: San Francisco, CA: AMIA Joint Summits on Translational Science

April 2016

Apr 2-6, 2016: Solden, Austria: 18th International Neuroscience Winter Conference.

April 16-23, 2016: Vancouver, Canada:American Academy of Neurology (AAN) Annual Meeting.

July 2016

July 2-6, 2016: Copenhagen, Denmark:10th FENS Forum of Neuroscience

Modified Two-Photon Technique Allows Imaging through Skull
An optical upgrade to the two-photon microscope enables researchers to examine cells in the brain directly through the rodent skull. According to the paper in the July 13 *Proceedings of the National Academy of Sciences,* scientists led by Meng Cui at the Howard Hughes Medical Institute in Ashburn, Virginia adjusted the two-photon microscope by adding a micro-electromechanical system (MEMS)-based mirror that can correct for distortions caused by light scattered by the thick skull. The researchers were then able to visualize dendritic spines and microglia in action through the rodent skull. Read about it here.

Drug and Device News

Study Suggests Diaphragm Pacing May be Detrimental in ALS
Diaphragm Pacing Systems (DPS) deliver electrical impulses to the diaphragm to stimulate muscle contraction and improve respiratory function. In 2011, the NeuRX DPS gained Humanitarian Device Exemption approval by the United States FDA to treat respiratory failure in ALS patients, and has since been widely introduced in ALS clinics (see May 2012 news). According to the report in the July 30 *Lancet Neurology*, the first randomized, controlled clinical trial to evaluate efficacy of DPS with non-invasive ventilation (NIV) as compared to NIV alone has yielded disappointing results. The multi-center clinical trial in the UK, called DiPALS, found that survival was on average 11 months shorter in the group of patients using DPS. These findings suggest that diaphragm pacing is not generally beneficial in ALS patients, and merit further analysis of the reasons for the discrepant findings with prior studies.

Google and Ancestry.com Partner to Decipher Human Longevity
Calico, the Google-backed research and development company focused on longevity and development of interventions to increase human lifespan, has announced a partnership with AncestryDNA to study the genetics of the human lifespan. Ancestry is a subsidiary of Ancestry.com that has amassed a database of over one million genetic records through direct-to-consumer DNA testing kits. Calico will gain access to the anonymized genetic data as well as family trees and supporting information, and will mine the data to identify pathways shaping heritability of longevity. This partnership is part of a growing trend toward genetic data-driven drug discovery, similar to the recent partnership between 23andMe and Genentech surrounding Parkinson's disease research (see Jan 2015 news). We look forward to seeing ALS research join this trend with projects such as ProjectMine (see Oct 2014 news).

New Remote-Controlled Probe Can Manipulate Brain Function

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Scientists have combined the powers of nanotechnology, optogenetics, and gene therapy to create a remote-controlled, wireless brain implant that can release drugs, viruses, or shine light with just the click of a button. According to the report in the July 14 *Cell*, senior authors John Rogers from University of Illinois, Urbana-Champaign and Michael R. Bruchas at Washington University School of Medicine in St. Louis, and colleagues implanted a microscopic probe into defined brain areas of freely moving mice. Using their programmable probe, they could stimulate animal movement, label neuronal circuits, and change reward-related behavior. In the future, these optofluidic devices could potentially combat disease by using light-activated release of pharmaceuticals. In the publication, the authors provide the blueprints for the implant, allowing other scientists to create their own and develop novel applications.

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