



ALS Forum e-Newsletter Volume 137

October 9, 2015

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](#)

Webinars:

ALSA Webinar: [Developing Therapy Based on the Root Cause of ALS](#). Oct 13, 2015. 1:00PM PST.

Alzforum Webinar: [Fluid Business: Could "Liquid" Protein Herald Neurodegeneration?](#) Oct 30, 11am EST.

Funding Opportunities:

[MDA Venture Philanthropy](#). LOI due Dec 1, 2015.

[California Stem Cell Agency \(CIRM\) 2.0](#)

[Prize4Life and the ALS Association Launch the ALS Assistive Technology Challenge!](#)

The ALS Association and Prize4Life are happy to announce the launch of [The ALS Assistive Technology Challenge](#). The challenge aims to support the development of diverse technologies for communication by ALS patients at different disease stages. The [call for abstracts](#) closes on November 9th!

Research News

[Fly Model Suggests Dipeptides, not RNA, are at Fault](#)

A hexanucleotide expansion of GGGGCC repeats in the C9ORF72 gene are a major genetic cause of ALS and frontotemporal dementia (FTD). Researchers have begun to unravel how these repeats lead to neurotoxicity (see [Aug 2015 news](#)), but it has remained unclear whether the repetitive RNAs are to blame, or rather the dipeptide repeat proteins (DPRs) translated from these RNA transcripts. As reported in the September 23 *Neuron*, Fen-Biao Gao from University of Massachusetts Medical School in Worcester, MA, and colleagues created a *Drosophila* model that expressed 160 copies of the GGGGCC repeats flanked by the human sequences requires for splicing out the RNA repeats into the nucleus. Despite forming RNA aggregates in the nuclei, the RNA was not detrimental to the cells. Placing the flies in a warmer environment increased DPR production, and only then was a toxic effect observed. Do these findings translate directly to humans? Click [here](#) to read more.

[Antivirals as a Future Therapy for ALS?](#)

[Awards](#). Due last business day of each month.

Upcoming Meetings:

October 2015

Oct 17-21, 2015: Chicago, Illinois: [The Society for Neuroscience Annual Meeting](#).

Oct 31-Nov 5, 2015: Santiago, Chile. [World Congress of Neurology](#)

November 2015

Nov 1-3, 2015: New York, NY. [Partnering for Cures](#).

Nov 4-6, 2015: Clearwater, FL: [Annual NEALS Meeting](#).

Nov 6-7, 2015: Barcelona, Spain: [International Spinal Cord Repair](#).

Nov 11-13, 2015: Geneva, Switzerland: [World Orphan Drug Congress](#).

Annual Nov 13, 2015: Boston, MA: [ALS TDI Leadership Summit](#).

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

Nov 18-20, 2015: Gold Coast, Australia: [International Conference on Neurology and Epidemiology](#).

Nov 29-Dec 4, 2015: Cambridge, UK: [Molecular Neurodegeneration](#).

December 2015

Dec 10-12, 2015: Atlanta, GA: [World Stem Cell Summit](#).

A subset of AIDS patients exhibit ALS-like symptoms that subside with anti-retroviral therapy. New findings by HIV-researcher Avindra Nath and colleagues from the National Institute of Neurological Disorders and Stroke in Bethesda, Maryland, reveal an intriguing link between endogenous retroviruses and sporadic ALS (sALS). The researchers found that in human endogenous retrovirus (HERV)-K is activated in cortical and spinal neurons of a subset of people with sALS (see also [Dec 2010 news](#)). According to the report in the September 30 *Science Translational Medicine*, expression of the HERV-K viral envelope protein in mice is sufficient to cause upper and lower motor neuron degeneration and motor impairments. Interestingly, the ALS-associated protein TDP-43 regulates HERV-K expression. Read more [here](#).

[ER Stress Links SMA and ALS](#)

Spinal muscular atrophy (SMA), the most common fatal genetic disease of young children, is caused by mutations in the survival of motor neuron 1, telomeric (SMN1) gene. Although the underlying genetic mutation is known, the causes of selective motor neuron (MN) vulnerability in SMA are not well understood. A team of researchers led by Lee Rubin at the Harvard Stem Cell Institute in Cambridge, MA, performed RNA sequencing on purified MNs derived from induced pluripotent stem cells (iPSCs) from SMA patients and health controls. As reported in the Aug 27 of *Cell Stem Cell* online, reduced SMN expression led to hyperactivation of the ER stress response. MN survival was ameliorated by administering ER stress inhibitors to a mouse model of SMA. This study identifies ER stress as a common pathway implicated in selective MN death in both SMA and ALS (See [Jan 2015 news](#)), and suggests that drugs targeting the ER stress pathway could potentially benefit both disease groups.

[Lysosomal Dysfunction is Common Theme in FTD](#)

Researchers led by Adrian Issacs and colleagues at the University College London have identified a pathological phenomenon shared between familial cases of frontotemporal dementia (FTD) and lysosomal storage diseases, pointing once again to dysfunction of the lysosomal degradation pathway as a contributing factor in FTD (see [Aug 2012 news](#)). Reporting in the September 10 *Acta Neuropathologica* online, the researchers observed large autofluorescent aggregates in the brains of mice expressing a mutant version of charged multi-vesicular body protein 2B (CHMP2B), a cause of familial FTD. Using immunogold labeling, the researchers were able to confirm that these aggregates were of endosomal-lysosomal origins. These aggregates were also visible in the postmortem brains of FTD patients, but not in healthy controls. The researchers next plan to characterize the composition of

Dec 11-13, 2015: Orlando, FL: [International Symposium on ALS/MND](#).

2016

January 2016

Jan 12-16, 2016: Hokkaido, Japan: [The Society of Neuromuscular Sciences Inc., 10th Annual Scientific Meeting](#).

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

February 2016

Feb 25-26, 2016: Manchester, UK: [11th Annual Biomarkers Congress](#).

March 2016

March 6-8, 2015: Miami, FL: [Annual Drug Discovery for Neurodegeneration Conference](#).

April 2016

Apr 2-6, 2016: Sölden, 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](#)

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these aggregates to further unravel their source and their possible role in neurodegeneration.

[Over 2500 Whole Human Genome Sequences Now Available](#)

In the October 1 *Nature*, a consortium of researchers reported the complete results of the 1000 Genomes Project, a seven-year long, international collaboration in which 2,504 whole human genomes from 26 populations were sequenced (see [Nov 2012 news](#)). The data revealed nearly 90 million variants in the human genome, most of which are attributed to SNPs, while others are structural variants, such as insertions and deletions. The scientists also found 240 genes to be potentially "dispensable", as these genes were completely absent from many of the genomes. In addition to being able to freely access the sequences on the [1000 Genomes website](#), researchers can also purchase immortalized cell lines that have been generated from a subset of the genome donors. The interim datasets published in 2012 have already been used as reference datasets for genetic association studies in ALS (see [ALSGene](#)).

Drug News

[Postmortem ALS Genome Sequencing Project Fosters New Insights](#)

A new, collaborative whole-genome sequencing (WGS) effort has been launched with the goal of fostering new insights into ALS by linking genetic, clinical and pathological data from ALS patients. Human tissue samples from deceased ALS patients will be provided through the Target ALS [Postmortem Tissue Core](#), a multi-center tissue bank located at several universities throughout the United States. The sequencing will be conducted at the New York Genome Center (NYGC), and the genetic data will be linked to patients' clinical information and tissue samples, thus providing a wealth of new information that integrates genetics, clinical data, and tissue pathology. In addition, the ALS Association and TargetALS [have announced](#) an expansion of the TargetALS tissue core to include biofluids from people with ALS, which will also be incorporated into the genetic analysis efforts at the NYGC. Click [here](#) to read more.

[Improved Neural Implant Speeds Typing for ALS Patients](#)

The latest iteration of the [BrainGate2](#) Neural Interface System (NIS) has enabled two paralyzed participants with ALS to type words on a computer screen simply by imagining their finger moving. The patients received microelectrode arrays implants into their motor cortex (see [Aug 2015 news](#)), which decoded neural signals produced by the patients to move a computer cursor. By imagining their fingers selecting letters on the screen, the users were able to type out words with unprecedented

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accuracy. As reported by Jaimie Henderson and colleagues in the September 28 Nature Medicine, one participant was able to type at a speed of 6 words per minute, a dramatic improvement upon earlier versions of the NIS. The team is now aiming at even further improving this technology.

[Biotech Startup Receives \\$30.6 Million to Study Candidate AD and FTD Drug](#)

Though only three-years old, the small Swiss biotech, [Asceneuron](#), has raised \$30.6 million to help fund studies for a new candidate drug for Alzheimer's disease (AD). Asceneuron's focus is on small-molecule drug discovery for tauopathies and neurodegenerative disease, such as AD and frontotemporal dementia (FTD). The drug currently at the forefront of their repertoire is ASN-561, an inhibitor of O-GlcNAase (OGA), which based on preclinical data can decrease amyloid plaque formation and cognitive decline in a transgenic mouse model of AD. As a second indication, ASN-561 is also under development as a candidate therapy for FTD.

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