



ALS Forum e-Newsletter Volume 138

October 23, 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:

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

Funding Opportunities:

[ALS Assistive Technology Challenge](#). Abstracts due Nov 9, 2015.

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

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

[The ALS Mobile Analyzer](#) is a Prize4Life initiative aimed at collecting objective, frequent and accurate measurements of disease progression in people with ALS (PALS) in order to improve patient care and clinical trial design. It is based on the ALS Functional Rating Scale (ALSFRS), the primary questionnaire being used today in ALS clinical settings, and could eventually replace it as a more objective tool. The mobile application [just went live](#), and we are seeking controls and PALS to enroll! To find out more and download the app, click [here](#).

Research News

[ALS Proteins Form Functional Liquid Droplets in Cells](#)

Two recently published studies have found that the ALS-linked, RNA-binding proteins, FUS and hnRNPA1, can condense into cytosolic liquid droplets on their way to forming cellular granules. In the September 24 *Cell*, co-senior authors Paul Taylor and Tanja Mittag at St. Jude Children's Research Hospital in Memphis, Tennessee, described how hnRNPA1 can form solid fibrils through a liquid intermediate state that forms distinct droplets in the cytosol. Mutant forms of the protein can solidify faster than wild-type forms and promote pathological fibril formation. Separately, in the October 15 *Molecular Cell*, senior author Nicolas Fawzi and colleagues at Brown University, provide further support for recent findings on FUS liquid droplets (see [Sept 2015 news](#)), using NMR to study the FUS low complexity domain. The authors report that FUS droplets interact with RNA polymerase II, suggesting that transcription may occur within the FUS liquid drop, an interesting and novel proposal. Find out more at this upcoming [Alzforum webinar](#).

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

Upcoming Meetings:

October 2015

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](#).

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

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[Neurons Derived Directly from Fibroblasts Act the Age of Their Donor](#)

Neurons generated directly from patient fibroblasts act older than those derived through an induced pluripotent stem cell (iPSC) intermediate, as reported in the October 8 *Cell Stem Cell*. Led by Fred Gage at the Salk Institute in La Jolla, California, scientists examined gene-expression profiles of fibroblasts and iPSCs generated from humans of a range of ages. The resulting iPSC-derived neurons did not exhibit the age-related changes seen in the original fibroblasts, but the induced neurons (iNs) did. Further experiments revealed that decreased expression of RanBP17, a regulator of nucleocytoplasmic compartmentalization (NCC), was associated with aging in fibroblasts and iNs, but not in iPSCs. First author Jerome Mertens' plans to examine aging signatures using iNs from people with Alzheimer's disease as compared to healthy aging adults. These findings suggest that iNs may provide cellular models particularly suited for neurodegenerative diseases, including ALS.

[Activated Astrocytes Can't Keep Up as ALS Progresses](#)

Astrocytes are known contributors to ALS pathology through non cell-autonomous mechanisms, but whether they act primarily through loss of supportive functions or secretion of toxic factors is still a matter of debate (see [Oct 2011 news](#), [Nov 2014 news](#), [Jul 2015 news](#)). A report in the October 15 *Frontiers in Cellular Neuroscience* provides evidence for the former. Researchers led by co-senior authors Janine Kirby and Pamela Shaw at the Sheffield Institute for Translational Neuroscience in the UK examined gene expression in isolated astrocytes from mutant SOD1 (mSOD1)-expressing mice at symptomatic and late stages of disease. As disease progressed, astrocytes shifted into an activated state and ramped up activity of lysosomal and phagocytic pathways, possibly to dispose of cellular waste from degenerating neurons. Late-stage astrocytes also exhibited disrupted expression of genes involved in cholesterol homeostasis, possible due to increased phagocytosis of neuronal debris. Now the researchers are aiming to identify interventions that can restore astrocyte function.

[Video Article Demonstrates Rapid Neurological Scoring Method in SOD1-G93A Mice](#)

A new video article published by researchers from the [ALS Therapy Development Institute](#) in Cambridge, Massachusetts, demonstrates a rapid and simple approach for phenotypic scoring of the SOD1-G93A mouse model of ALS. The mouse model recapitulates several key aspects of the human disease, including motor neuron loss, progressive muscle atrophy and paralysis. However, due to the inherent variability in these transgenic mice, large cohorts are needed in drug efficacy studies in order to reliably assess drug effects (see [Working with ALS](#)

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, 2016: 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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[Mice](#) and [Scott et. al., 2008](#)). It is therefore beneficial to have a rapid and objective approach to assess motor phenotype throughout the course of disease. In the September 8 *Journal of Visualized Experiments*, Theo Hatzipetros and colleagues present a video protocol and accompanying paper on the NeuroScore system to assess hindlimb function, and present representative results throughout disease progression. This can serve as a useful reference for ALS researchers conducting large scale studies in this model.

[Scientist Visualize Coordinated Spinal Motor Neuron Activity](#)

Understanding how circuitry that controls locomotor behavior is established during development can contribute to designing therapies aimed at restoring these functions if they are lost due to disease. As published in the Sep 2 *Neuron*, scientists led by Samuel Pfaff at the Salk Institute in La Jolla, California, developed a novel approach for real-time visualization of neuronal activity based on two-photon microscopy and the genetically-encoded fluorescent calcium sensor, GCaMP6f. Using this approach, first-author Christopher Hinckley and colleagues were able to visualize the characteristic synchronous firing of subgroups of lumbar spinal motor neurons (MNs) in response to activation of the locomotor central pattern generator (CPG), a network of neurons that ultimately drives rhythmic muscle activity for walking. By manipulating the genetic and spatial identity of subtypes of lumbar MNs, the researchers were able to identify which characteristics of the circuitry are genetically determined and which are established based on spatial cues. These findings reveal complex hierarchical rules that govern wiring of locomotor circuits in the spinal cord.

Drug News

[Barrow Neurological Institute and TGen to Identify Prognostic Biomarkers for ALS](#)

Two research institutes based in Phoenix, Arizona are co-recipients of a one-year NIH grant of over half a million dollars slated for identifying biomarkers for ALS. The Barrow Neurological Institute team, which is led by Robert Bowser, will partner with the non-profit research institute [Translational Genomics Research Institute \(TGen\)](#) to investigate blood and CSF samples from 30 ALS patients, and 30 controls - either healthy or with other neurological disorders. By employing genomic and proteomic techniques along with bioinformatics approaches, the collaborators hope to identify diagnostic biomarkers as well as biomarkers for tracking disease progression. Findings from this study could accelerate disease diagnosis, identification of pathways involved in the disease, and development of new ALS therapies.



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[BrainStorm Announces Completion of Treatments in Phase II Clinical Trial in ALS](#)

[BrainStorm Cell Therapeutics](#), a biotechnology company focused on developing stem cell therapies for neurodegenerative diseases, has completed treatment of all patients enrolled in its Phase II clinical trial of NurOwn in the US. NurOwn is an adult stem cell therapy that uses bone marrow-derived autologous mesenchymal stem cells (MSC), which secrete neurotrophic factors. The MSCs are administered into patients via intramuscular and intrathecal injections. The Phase II trial, which followed after a Phase IIa clinical trial in Israel (see [Jan 2015 news](#)), was a double-blind study of safety and efficacy of NurOwn treatment as compared to placebo in ALS patients.

[CurePSP Launches Program to Recruit Patients into Clinical Trials for Neurodegenerative Diseases](#)

CurePSP, a Maryland-based non-profit advocacy organization, has launched the [Patient Engagement Program \(PEP\)](#) to increase clinical trial recruitment and ultimately speed the development of treatments for neurodegenerative disorders. CurePSP is focused on "prime of life" neurodegenerative diseases, including progressive supranuclear palsy (PSP), a fatal, frontotemporal brain disorder. The key components of PEP, which will initially focus on PSP clinical trials, will be to link patients with clinical trials ongoing at companies and research institutions, and to work with clinicians and allied health professionals on clinical trial recruitment strategies. Agreements have already been made between the non-profit and the pharmaceutical companies [Bristol-Myers Squibb](#) (BMS) and [AbbVie](#). Both AbbVie and BMS have recently initiated Phase I clinical trials in PSP, testing C2N-8E12 and BMS-986168, respectively.

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