



Happy New Year to everyone! We look forward to another year of providing you with cutting-edge ALS news coverage!

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:

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:

[EU Joint Programme-
Neurodegenerative
Disease Funding
Opportunity](#). Pre-proposals
due March 10, 2015.

[CDC Grant Opportunity:
Analyze and Evaluate
Potential Risk Factors for
ALS](#). Applications due
March 23, 2015

Upcoming Meetings:

January 2015

January 25-30, 2015: Taos,
New

Conference News

[SFN 2014 Part IV: ALS Mechanisms and Models](#)

At the Society for Neuroscience Meeting held November 15-19 in Washington, DC, over 30,000 neuroscientists came together to discuss cutting-edge research on development, genetics, molecular mechanisms, tools and therapeutics in all areas of neuroscience. In this report, we bring you highlights of the nanosymposium on "Motor Neuron Disease Mechanisms and Models", where researchers gathered to share their latest findings about mechanisms and models of ALS and other neuromuscular diseases. Click [here](#) to read the full report.

Research News

[New Mouse Model with SOD1 Mutation May Model Early ALS](#)

More than a dozen ALS mouse models have been developed carrying mutations in superoxide dismutase 1 (SOD1). Although these models have helped researchers unravel disease mechanisms of ALS, they have yielded limited results in translating candidate ALS therapies into humans. Now there is a new mouse model available to researchers, which unlike prior models, does not highly overexpress SOD1. Acevedo-Arozena of the Medical Research Council (MRC) in Harwell, U.K. and colleagues report in the December 2 *Human Molecular Genetics* that mice homozygous for D83G mutation in SOD1 exhibit motor neuron death, neuromuscular junction denervation and motor deficits reminiscent of early stage ALS. However, unlike prior models, the mice do not become fully paralyzed. The model may prove useful for modeling selective neuronal susceptibility in ALS, as well as for screening for effective therapies based on measures other than survival. Click [here](#) to read more detail about this new ALS mouse model.

[Arginine-rich Peptides Implicated in Toxicity of C9ORF72 Repeat Mutations](#)

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 15-20, 2015: San Francisco, CA: [Molecular Med Tri-Con 2015](#).

February 22-26, 2014:
Santa Fe, NM: [Keystone Symposia: Neuroepigenetics](#)

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](#).

Mutations in the C9ORF72 gene are the most common known genetic cause of ALS and frontotemporal dementia (FTD). However, how exactly this hexanucleotide repeat expansion in an intron causes disease is still a matter of debate (see [Aug 2014 news story](#); [Sept 2011 news story](#)). According to a paper in the December 17 *Neuron* by Davide Trotti and colleagues at the Thomas Jefferson University in Philadelphia, the arginine rich dipeptides that are translated from the repeat RNA transcripts are the primary culprit. In rodent primary cortical and motor neuronal cultures, as well as in induced pluripotent stem cells derived from C9ORF72 ALS patients, arginine-rich dipeptides localized to the nucleolus and induced rapid cell death. Does the repeat RNA also play a role in toxicity? Click [here](#) to find out more!

[Endoplasmic Reticulum Protein Regulates Selective Motor Neuron Vulnerability in ALS](#)

Certain subtypes of motor neurons of ALS patients exhibit remarkable resistance to neurodegeneration, yet the mechanisms of this selective neuronal vulnerability are not well understood. In a paper in the January 5 *Nature Neuroscience* online, researchers led by Smita Saxena at the University of Bern in Bern, Switzerland identify an endoplasmic reticulum (ER) protein that appears to be a key player in selectively protecting motor neurons (see also [March 2009 news story](#)). The protein, called Sil1, is a co-chaperone that helps another chaperone, binding immunoglobulin protein (BiP), sense ER stress and protect the neuron from an overblown stress response. Reducing levels of Sil1 in ALS mouse models overexpressing mutant SOD1 accelerates the course of disease, while selectively increasing Sil1 expression in the most vulnerable motor neurons delayed denervation and prolonged survival. Click [here](#) to read more about these intriguing findings!

[tRNA-derived G-quadruplexes Trigger Stress Granule Formation and Protect Neurons](#)

Familial ALS patients with mutations in the C9ORF72 gene carry hundreds or thousands of copies of hexanucleotide repeats in the gene's first intron, rather than up to a couple dozen copies of the repeat. The repeat RNA forms a 3-D structure called a G-quadruplex, which aggregates with RNA-binding proteins in RNA foci that are hypothesized to be toxic to cells (see [Nov 2014 news story](#); [Nov 2013 news story](#)). A study published November 17 in *Proceedings of the National Academy of Sciences* online identified endogenous G-quadruplexes formed under stress conditions from fragments of tRNA, called tRNA-derived, stress-induced RNAs (tiRNAs). The tiRNAs inhibit translation and promote formation of neuroprotective stress granules. Paul Anderson and colleagues at the Brigham and Women's Hospital in Boston developed a more stable quadruplex based on DNA, which they show penetrates motor neurons and triggers a neuroprotective response. Further research is needed to determine whether these structures interact with pathological RNA repeats and could have therapeutic potential for ALS patients with C9ORF72 mutations. Click [here](#) to read more.

Drug News

[Brainstorm Cell Therapeutics Announces Final Results of Phase IIa Study of NurOwn in ALS](#)

March 11-15, 2015:
Washington, DC: [MDA Scientific Conference](#).

March 18-20, 2015:
Newcastle upon Tyne,
UK: [8th Annual MRC Neuromuscular Translational Research Conference](#).

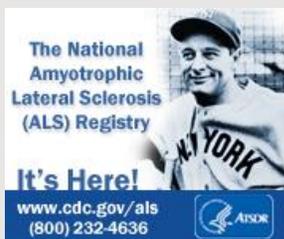
March 18-22, 2015: Nice,
France: [12th international Conference on Alzheimer's and Parkinson's Diseases](#).

April 2015

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](#).

April 18-25, 2015:
Washington, DC: [The American Academy of Neurology \(AAN\) Annual Meeting](#).



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[Brainstorm Cell Therapeutics announced](#) the final analysis of results of its Phase IIa clinical trial of NurOwn in ALS conducted at the Hadassah Medical Center in Jerusalem. The company's stem cell therapy technology consists of transplantation of autologous mesenchymal stem cells differentiated to secrete neurotrophic factors (MSC-NTF). The small-scale trial enrolled 14 early stage ALS patients, 12 of whom were followed for 3 months or more. The company reported promising outcomes, with 92% of patients experiencing a decline in rate of disease progression based on ALS Functional Rating Score-Revised or forced vital capacity, and some patients demonstrating improvements in function. NurOwn is currently being tested in a Phase II study in the United States (see [April 2014 news story](#)). Stay tuned for the results! Click [here](#) to read more.

[New Industry-Academia Consortium Focuses on Epigenetic Biomarkers in ALS](#)

A new governmentally-funded consortium in the UK will focus on testing and validating novel ALS epigenetic biomarkers. The consortium is funded by the UK government jointly with UK's innovation agency, Innovate UK, at a total amount of £1.26m (\$1.92m) and includes biotechnology company [Chronos Therapeutics](#), [Oxford BioDynamics](#) and the University of Oxford. The consortium brings together the expertise, data and samples of Chronos with a proprietary biomarker discovery platform developed by Oxford Biodynamic to rapidly and precisely identify epigenetic signatures in patient blood samples. Jointly, the parties will aim to identify novel epigenetic diagnostic and prognostic biomarkers for ALS. Click [here](#) to read more about this exciting new partnership.

[Genervon Announces Results of Testing GM6 in a Compassionate Use Patient](#)

Last October, [Genervon Biopharmaceuticals](#) announced promising results in its Phase IIa trial in ALS of GM6, a peptide-based drug that modulates multiple pathways involved in inflammation, apoptosis and hypoxia (see [Oct 2014 news story](#)). Now, the company is submitting additional data to the US Food and Drug Administration from a compassionate use trial of a single ALS patient in late stages of the disease. The patient, who was diagnosed with ALS 10 years ago, was given 6 doses of GM6 and followed for 12 weeks. The company reported small but significant improvement relative to baseline, including an increase in swallow volume and oral volume consumption. In addition, biomarker data on SOD1, Cystatin and total tau revealed changes toward the normal values. Although these data result from a single patient, they support further evaluation in larger cohorts of late-stage patients. Click [here](#) to read more.

[Hematopoietic Stem Cell Transplants May Slow Progression of Multiple Sclerosis](#)

Relapsing-remitting multiple sclerosis (RRMS) is the most common form of the autoimmune disease and is characterized by relapses of deteriorating neurological function. In a publication in the December 9 *JAMA Neurology* online, researchers from the [Immune Tolerance Network](#) reported interim results of a clinical trial of 24 patients treated with high-dose immunosuppressive therapy and autologous hematopoietic cell transplant (HDIT/HCT). Three years after treatment,

close to 80 percent of patients remained in remission and did not experience progression of their disease symptoms. An accompanying editorial suggests that this therapy may be particularly beneficial in patients who did not experience benefits with immunosuppressive treatment alone. These findings are of particular interest since similar approaches are currently being tested in small trials in ALS (see [drug news](#), this issue). Click [here](#) to read more.

The ALS Forum was developed by [Prize4Life, Inc.](#)

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