



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](http://www.ALSGene.org)

The PRO-ACT Database:  
[www.ALSDatabase.org](http://www.ALSDatabase.org)

[NEALS Biofluid Repository Available to Researchers](#)

[NINDS Fibroblast Repository](#)

[VABBB Tissue Request Information Site](#)

**Funding Opportunities:**

[NCATS Small Business Contract Funding](#). Applications due November 5, 2014.

[EuroMOTOR Competitive Call for Novel Therapies for ALS](#)

**Upcoming Meetings:**

**October 2014**

October 22-24, 2014:  
Clearwater beach,  
FL: [NEALS Annual Meeting](#)

October 23-25, 2014:  
Vancouver, Canada: [The 9th International Conference on Frontotemporal Dementias](#)

**Research News**

**[The Mitochondrial Gene CHCHD10 is a Risk Factor for ALS and FTD](#)**

Four new publications confirm findings from earlier this year (see [June 2014 news story](#)) that the mitochondrial gene coiled-coil-helix-coiled-coil-helix domain containing 10 (CHCHD10) is a disease gene for ALS and FTD. These publications report a total of 11 families or cases of CHCHD10 mutations, which cause a spectrum of phenotypes including ALS, ALS with frontotemporal dementia (ALS-FTD), and mitochondrial myopathy. The most recent paper, published September 26 in *Brain* online by Bryan Traynor and colleagues from the National Institute of Aging in Bethesda, Maryland, was the result of the first whole genome sequencing (WGS) of familial ALS patients. The identification of these ALS-causing mutations provides additional supporting evidence for the role that mitochondrial defects play in ALS (see related story, this newsletter). Click [here](#) to read more about this new ALS risk gene.

**[Mitophagy Pathway Links ALS and Parkinson's Disease](#)**

A growing body of evidence points to malfunctioning mitochondria as central players in neurodegenerative diseases such as Alzheimer's, Parkinson's disease (PD) and ALS (see [Feb 2010 news story](#); [Nov 2011 news story](#); [Jan 2012 news story](#)). A new study published October 7 in *Proceedings from the National Academy of Sciences* reveals a common mitochondrial disposal pathway that is impaired in both ALS and PD. The investigators, led by Erika Holzbauer and colleagues at the Perelman School of Medicine at the University of Pennsylvania in Philadelphia, demonstrate that the ALS gene optineurin (see [May 2010 news story](#)) operates downstream of the PD genes parkin and PTEN-induced putative kinase 1 (Pink1) to regulate disposal of aging mitochondria via mitophagy. When mitophagy is impaired, aging mitochondria linger in the cells, eventually causing neuronal death. How do optineurin mutations cause ALS but not PD? Click [here](#) to find out more.

**[TDP-43 Forms Toxic Amyloid Oligomers in FTD](#)**

Cytoplasmic inclusions containing TDP-43 are a hallmark of ALS and frontotemporal dementia (FTD). These inclusions contain hyper-

## November 2014

November 7, 2014: Boston, MA: [10th Annual ALS TDI Leadership Summit](#)

November 13-14, 2014: Arlington, VA: [24th Neuropharmacology Conference](#)

November 13-14, 2014: Arlington, VA: [9th Brain Research Conference Neuroprotection: Basic mechanisms and translational potential](#)

November 14, 2014: Washington, DC: [Advances in ALS and FTD Genetics Workshop](#)

November 15-19, 2014: Washington, DC: [The Annual Society for Neuroscience Meeting](#)

November 16-18, 2014: New York, NY: [Partnering for Cures](#)

## December 2014

December 3-5, 2014: San Antonio, TX: [World Stem Cell Summit](#)

December 3-6, 2014: Cold Spring Harbor, NY: [Neurodegenerative Diseases: Biology & Therapeutics](#)

December 5-7, 2014: Brussels, Belgium: [International Conference on ALS/MND](#)

December 17-20, 2014: Hotel Vila Galé Coimbra, Portugal: [Mitochondria, Metabolism and Disease](#)

## January 2015

January 13-17, 2015: Hokkaido, Japan: [Society for Neuromuscular](#)

phosphorylated and polyubiquitinated TDP-43 in both full-length and cleaved forms, however, the contribution of each of these forms to ALS pathophysiology is not completely understood. A new paper published September 12 in *Nature Communications* by Yun-Ru (Ruby) Chen of Academia Sinica in Taipei, Taiwan and colleagues present the most comprehensive characterization to date of the full-length TDP-43 oligomers, and provide evidence that these oligomers can cross-seed amyloid- $\beta$  to oligomerize. Using a new antibody specifically targeting oligomeric TDP-43, the researchers demonstrate that this form of TDP-43 is also present in human FTD postmortem brain samples, suggesting that it may play a role in neurodegeneration. Click [here](#) to read more about these exciting findings.

### [SOD1 Aggregation Dynamics Correlate with ALS Clinical Phenotypes](#)

Over 100 mutations in the SOD1 protein have been linked to ALS, but how all these distinct mutations lead to the same disease is still a matter of debate. A new study published October 14 in *Proceedings of the National Academy of Sciences* applied sophisticated biophysical methods to examine how mutations in the SOD1 protein affect protein stability and aggregation dynamics. The researchers, led by Elizabeth Getzhoff and John Tainer at The Scripps Research Institute in La Jolla, California, together with colleagues from the Lawrence Berkeley National Laboratories in Berkeley, California and University of Georgia, found that in all SOD1 mutations examined, the mutation increased protein instability and reduced copper retention. Interestingly, SOD1 mutations that led to more rapid protein aggregation were also associated with faster progression of clinical symptoms. Click [here](#) to read more.

## Drug News

### [Fast-Track Designation Granted to NurOwn for Treating ALS](#)

The U.S. Food and Drug Administration (FDA) has granted Fast-Track designation to BrainStorm Cell Therapeutics' NurOwn for treating ALS. The company's stem cell therapy consists of autologous mesenchymal stem cells differentiated to secrete neurotrophic factors to support and repair damaged neurons. NurOwn is currently being tested for ALS in a Phase II clinical trial ongoing at three ALS medical centers in the US (see [April 2014 news story](#)). The Fast Track designation will provide BrainStorm Cell Therapeutics with more frequent meetings with the FDA and potentially earlier submission of the New Drug Application, which together will help accelerate the development of this therapy for this unmet need. Click [here](#) to read more.

### [Human Placental Cells Safe for Treating Multiple Sclerosis](#)

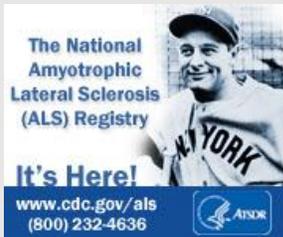
In a first-of-its-kind study, a stem cell therapy consisting of human placenta-derived stromal cells was shown to be safe in multiple sclerosis (MS) patients. The Phase 1b study of this cellular therapy, called PDA-001, was led by researchers from The Mount Sinai Hospital in New York jointly with Celgene Cellular Therapeutics, a subsidiary of Celgene Corporation. This approach could provide a new avenue for MS therapy development, as these cells are more abundant than bone marrow-derived mesenchymal stem cells (see [related news story](#)), and a single donor can supply sufficient cells for many patients. Although the study

[Sciences 8th Annual Scientific Meeting](#)

January 25-30, 2015: Taos, New Mexico: [Neuroinflammation in Diseases of the Nervous System](#)

**February 2015**

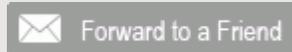
February 1-3, 2015: Cambridge, UK: [Biomarkers for Brain Disorders: Challenges and Opportunities](#)



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was geared toward safety testing, preliminary assessment suggests that PDA-001 may lead to repair of damaged tissue in this disease. Click [here](#) for more details about this groundbreaking study.

[New DoD Initiative Aims at Improving Success of Traumatic Brain Injury Clinical Trials](#)

Athletes who suffer repeated head injuries are at significantly higher risk of developing neurodegenerative diseases later in life than the general population (see [Aug 2010 news story](#); [Sept 2012 news story](#)), with a reported 3-fold risk of death from Alzheimer's disease or ALS. Yet according to the Center for Disease Control, no treatment for concussion or traumatic brain injury (TBI) has proven to be effective. A new \$17M award from the Department of Defense (DoD) to a multidisciplinary team led by Geoffrey Manley, Chief of Neurosurgery at the San Francisco General Hospital and Trauma Center, aims to improve TBI clinical trial success. The new initiative, called the TBI Endpoints Development (TED) Award, combines leaders from universities, industry, and patient advocacy organizations in an effort to create comprehensive databases that can serve as a key resource for developing better tools and standards for TBI clinical trials. Click [here](#) to read more about this exciting initiative.

[NeuroLINCS Program Established to Create Database of Human Neuronal Signatures](#)

The University of California, Irvine (UCI) received an \$8M award from the NIH to establish and spearhead a Library of Integrate Network-Based Cellular Signatures (LINCS) program focused on human neurons. The goal of the program, called NeuroLINCS, is to create a database of cellular and molecular activity in motor neurons and their responses to perturbations caused by drugs or genetic mutations. The common patterns, or signatures, that emerge will expand our understanding of motor neuron characteristics and how they are affected in ALS and other motor neuron diseases. The NeuroLINCS program will be a consortium of researchers from UCI, Cedars-Sinai Medical Center's Regenerative Medicine Institute, the Gladstone Institute of Neurological Disease, UC San Francisco, Johns Hopkins University and the Massachusetts Institute of Technology. Click [here](#) to read more.

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