



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.

Conference News

Resources:

Visit the new ALSGene tool at www.ALSGene.org

Visit the PRO-ACT Database at www.ALSDatabase.org

[NEALS Biofluid Repository Available to Researchers](#)

[NINDS Fibroblast Repository](#)

[VABBB Tissue Request Information Site](#)

Funding Opportunities:

[Frick Foundation for ALS Research Grants](#)

[The Association for Frontotemporal Degeneration RFPs](#)

[ALS Association ALS Clinical Research Training Fellowship](#)

Webinars:

[ALSTDI Research and Clinical Trial Update: June 18th, 2014, 2pm EST](#)

[ALSTDI Pipeline Update](#)

[12th Annual ENCALS Meeting: Stem Cell Therapy for ALS: Theory and Practice](#)

Dr. Neta Zach, Chief Scientific Officer of Prize4Life-Israel, attended the [12th Annual European Network for a Cure for ALS \(ENCALS\) Meeting](#) on May 22-24th in Leuven, Belgium, and brings us the highlights of an intriguing presentation by Jonathan Glass, M.D., the invited speaker of the Thierry Latran Foundation and Professor, Neurology and Pathology, Emory University School of Medicine, Atlanta, Georgia on "Stem Cell Therapy for ALS: Theory and Practice". ALS patients often approach their physician and request treatment with stem cell therapy. Despite the fact that these treatments are still unapproved and information is still lacking about their safety and efficacy, they are almost magically attractive to patients. But what are the facts about the benefits of stem cell therapy? Click [here](#) to read the full report from the conference.

Research News

[New Method for Reprogramming Cells to Model Neurodegenerative Diseases](#)

Induced pluripotent stem cells (iPSCs), adult cells genetically reprogrammed into an embryonic stem cell-like state, are becoming a powerful tool for research and drug development in ALS. iPSCs derived from sporadic and familial ALS patients are being used to understand mechanisms of the disease and to screen for candidate ALS drugs (for a recent example, see [April 2014 News](#)). However, motor neurons derived from iPSCs often resemble embryonic rather than mature motor neurons affected in ALS. A new study published May 12 in *Development* online and led by Anna Philpott from the University of Cambridge, UK, describes a method to accelerate differentiation and maturation of neurons from fibroblast-derived from iPSCs. By modifying one of the key reprogramming transcription factors, the researchers were able to make the cells more prone to differentiation. To read more about the research behind the new approach for promoting neuronal maturation of iPSCs, click [here](#).

Upcoming Meetings:

June 14-15, 2014: New London, NH: [Gordon Research Seminar: Barriers of the CNS, The Neurovascular Unit: Partners for Life](#)

June 15-19, 2014: Halifax, Nova Scotia, Canada: [The 9th International Motoneuron Meeting - Motoneurons: from Molecule to Man](#)

June 15-20, 2014: New London, NH: Gordon Research Conference: [Barriers of the CNS. Expanding the Understanding of CNS Barriers in Health and Disease](#)

June 17, 2014: Cambridge, MA: [US-India BioPharma & Healthcare Summit](#)

June 22-27, 2014: Waterville Valley, NH: [Cell Biology of the Neuron: Mechanistic Insight into Neuronal Development, Plasticity, Disease and Regeneration](#)

June 27-28, 2014: Cracow, Poland: [Advanced in Clinical Neuroimmunology ACN 2014](#)

June 29 - July 4, 2014: Hong Kong, China: [Gordon Research Conference: Molecular & Cellular Neurobiology, Mechanisms of Neural Development, Circuit Assembly, Synaptic Plasticity and Neuropsychiatric Disorders](#)

July 2014

July 5-10, 2014: Nice, France: [The 13th International Congress on Neuromuscular Diseases - ICNMD 2014](#)

[Tau Joins the Ranks of Prion-like Proteins in Neurodegenerative Diseases](#)

Misfolded proteins that have prion-like characteristics are not strangers to neurodegenerative diseases. Work from Neil Cashman's laboratory has shown that superoxide dismutase (SOD1), which is mutated in 20% of familial ALS cases, can spread in its misfolded state between cells and disrupt native SOD1 folding via a prion-like mechanism (see [February 2014 News](#)). TDP-43 also contains a prion domain, has a propensity to aggregate and spreads across neurons (see [July 2010 News](#), and [January 2014 News](#)). However, evidence that these pathological proteins act like true prions, which maintain their conformation when transmitted between individuals and are infectious, has until now been lacking. A new study published in the May 22 *Neuron* online and led by Marc Diamond from Washington University in St. Louis, shows that the tau protein, which is associated with a class of neurodegenerative diseases called tauopathies, behaves like a true prion in that it maintains its unique conformation (or strain) even when transmitted between animals. Different strains of the protein appear to underlie different clinical manifestations, which may explain the phenotypic diversity observed in tauopathies. Click [here](#) to read more about these intriguing findings.

[Team Effort to Dispose of Misfolded Proteins in the Cell](#)

Misfolded proteins disrupt cellular functions in ALS and other diseases, but the precise mechanisms by which the cell recognizes and targets them for disposal are not well understood. In a new study published online May 29 in *Molecular Cell*, researchers led by Xiaolu Wang from University of Pennsylvania have identified a molecular tag team that removes misfolded proteins and protects from neurotoxicity. PML/TRIM19 recognizes aberrant properties of misfolded proteins, such as exposed hydrophobic residues, and marks them for degradation with small ubiquitin-like modifiers (SUMOs). These tagged proteins are then marked by RNF4 with ubiquitin residues and then degraded by the proteasome machinery. The researchers demonstrate that deficiency in this pathway exacerbates neurodegenerative processes in a mouse model of spinocerebellar ataxia 1 (SCA1). Interestingly, this molecular pathway targets most types of misfolded proteins and protects the cells against their toxicity. Could defects in this machinery play a role in ALS? Click [here](#) to read more.

[Problems in DNA Repair Linked to Two Childhood Neurodegenerative Diseases](#)

Researchers led by Peter McKinnon from St. Jude Children's Research Hospital have discovered a previously unknown player in two devastating rare childhood neurodegenerative diseases, ataxia telangiectasia (A-T) and spinocerebellar ataxia with axonal neuropathy 1 (SCAN1). Topoisomerase 1 cleavage complex (Top1cc), which normally creates reversible breaks in DNA to enable it to unwind for cell division or transcription, accumulates in neurons of both A-T and SCAN1, and is surprisingly a common mediator of DNA damage. It was previously known that A-T is caused by a mutation in *Atm*, while SCAN1 is caused by a mutation in *Tdp1*, and the disease mechanisms were not previously considered related. This work, published online May 4, 2014 in *Nature Neuroscience*, reveals that these two proteins work

July 6-11, 2014: Easton, MA: [Gordon Research Conference: Intrinsically Disordered Proteins, Understanding Intrinsically Disordered Regions \(IDRs\) at Different Scales: From Single Molecules to Complex Systems](#)

July 12-17, 2014: Copenhagen, Denmark: [Alzheimer's Association International Conference](#)

July 13-15, 2014: Prince Edward Island, Canada: [Biotechnology & Human Health Symposium](#)

July 27 - August 1, 2014: Girona - Costa Brava, Spain: [Gordon Research Conference: Neurobiology of Brain Disorders, Neurodegeneration and Aging-related Disorders of the Nervous System](#)

August 2014

August 3-8, 2014: Andover, NH: [Gordon Research Conference: Musculoskeletal Biology & Bioengineering, Identifying and Overcoming Barriers to Translation](#)

August 3-8, 2014: Waterville Valley, NH: [Gordon Research Conference: Synaptic Transmission, Synapses in Networks](#)

August 10-15, 2014: Newport, RI: [Gordon Research Conference: Neural Development, From Stem Cells to Circuits](#)

coordinately to repair breaks in DNA, and when either is absent, levels of Top1cc increase dramatically, leading to DNA damages and ultimately to neuronal apoptosis. Impairments in DNA repair mechanisms have also been linked to ALS and adult onset neurodegenerative diseases (see [February 2013 Conference News](#)). Click [here](#) to read more.

Drug News

[Kinemed and CHDI Expand Huntington's Disease Partnership](#)

[Kinemed](#), an Emeryville, CA-based biotechnology company, has expanded its partnership with the [CHDI Foundation](#), a non-profit research organization focused exclusively on accelerating therapy development for Huntington's disease (HD). The initial collaboration leveraged Kinemed's platform for analyzing microtubule dynamics to identify disease biomarkers in the cerebrospinal fluid (CSF) of HD models. The extension aims to identify pharmacodynamic biomarkers that can be used in clinical trials by combining biomarker studies with therapeutic interventions. Kinemed has already explored applications of this technology for ALS: In 2007, Kinemed was one of the winners of the Prize4Life 'thought' prizes of the [\\$1M ALS Biomarker Prize](#). Hopefully we will see the company expands its current biomarker discovery efforts into the field of ALS! Click [here](#) to read more.

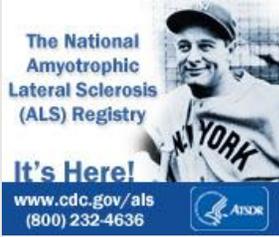
[ALSA and ALSTDI Convene ALS Biomarker Meeting](#)

The ALS Association and ALS Therapy Development Institute convened 24 leaders from academia, government and the pharmaceutical and biotechnology industries to identify approaches to accelerating biomarker development for ALS. Areas identified as particularly important for cooperation were standardized collection of biospecimens and harmonization of data collection methods during clinical trials. Another discussion point was the different type of ALS biomarkers and their distinct applications: biomarkers for distinguishing different subtypes of ALS could help in patient selection for clinical trials, while biomarkers for target engagement would help determine whether a drug is reaching its target and affecting the desired disease pathway. Prize4Life's contributions to the efforts to identify biomarkers through the [\\$1M ALS Biomarker Prize](#) were also mentioned. To read the full report from ALSA, click [here](#).

[Rodin Therapeutics Tackles Epigenetics in CNS Disorders](#)

Cambridge, MA-based Rodin Therapeutics has secured \$12.9M in series A funding to bring its small molecule epigenetic modulators from preclinical studies in humans. The company was launched last year with the backing of Atlas Ventures and Johnson & Johnson Development Corp., who are also leading this round of funding. The company's lead compound is a modulator of an epigenetic target that regulates transcription of genes involved in memory, and has been shown in preclinical studies to improve performance on learning and memory tasks. In addition to developing their own pipeline of modulators, they have also in-licensed promising compounds from the Broad Institute. As primary indications, Rodin aims to treat Alzheimer's disease, but other neurological disorders are also on the horizon. Click [here](#) to read more.

[Bryologs at the Center of New Licensing Deal Between Neurotrope and](#)



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Stanford

Neurotrope has closed an exclusive licensing deal with Stanford University for rights to develop bryostatin analogs, called "bryologs", for applications in disorders of the central nervous system. Bryostatin, a natural product that is thought to inhibit PKC epsilon signaling, is currently in Phase II clinical trials by Neurotrope for treating Alzheimer's disease. Neurotrope has now gained exclusive rights to make and sell a set of less complex chemical compounds with potential to mimic bryostatin's activity, developed over the years in Paul Wenders' laboratory at Stanford University. Neurotrope aims to advance a candidate bryolog-based therapy into clinical development by 2015. Click [here](#) to read more.

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