

THE ALS FORUM

ALS Forum e-Newsletter Volume 80

February 22, 2013

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:

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

[NEALS Biofluid Repository Available to Researchers](#)

[NINDS Fibroblast Repository](#)

Funding News:

[2013 AAN Foundation ALS-Richard Olney, MD Clinician Scientist Development Three Year Award](#)

Upcoming Meetings:

March 6-7, 2013: Washington, DC: [The Traumatic Brain Injury Conference](#)

March 16-23, 2013: San Diego, CA: [65th Annual American Academy of Neurology Meeting](#)

April 9-11, 2013: Washington, DC: [3rd Annual World Orphan Drug Congress](#)

Research News

[In Case You Wondered: Most Neurodegenerative Diseases Are Not Contagious](#)

There is growing evidence from a number of laboratories indicating that certain neurodegenerative disease-associated proteins, including TDP-43, A β , and α -synuclein, "spread" toxicity between neurons in the brain. The obvious question on everyone's mind is: can these diseases spread between people? A study out of Dr. John Trojanowski's lab at the University of Pennsylvania provides strong evidence that Alzheimer's disease and Parkinson's disease most likely are not transmissible between people. What about ALS? Read a full summary of this interesting story, and find out what the researchers discovered about the transmissibility of ALS [here](#).

[RNA Twist: C9ORF72 Intron Expansion Somehow Makes Aggregating Protein](#)

Just two weeks ago we learned from two bioinformatics studies the [protein family](#) that C9ORF72 most likely belongs to! Although these two studies shed some light on the potential biological role of C9ORF72, they didn't clarify the nature of the disease mechanism for the hexanucleotide repeats within C9ORF72, and whether it is gain of function (RNA-mediated) or loss of function. Now a new study suggests that C9ORF72's disease mechanism could in fact be "a gain of toxic protein function," as described by genetics expert Dr. John Hardy, who was not involved in the study. This new study, which was published online on February 7 in *Science*, shows that the hexanucleotide repeat expansion in C9ORF72 is translated into dipeptide repeat (DPR) proteins, despite the fact that the hexanucleotide repeat sequence is located in an intron. The authors of the study found that carriers of the hexanucleotide repeat expansion also harbored inclusions positive for DPR proteins. Read the complete story to find out which DPR protein was preferentially translated (Gly-Ala, Gly-Pro, or Gly-Arg) [here](#).

[Second Study Sees Intron in FTL Gene Translated](#)

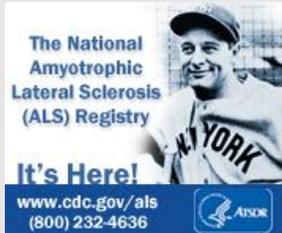
If you need additional evidence to convince you that the hexanucleotide repeat expansion in C9ORF72 really is translated, just pick up the

April 14-19, 2013: Les Diablerets, Switzerland: [Oxidative Stress & Disease, Program: The Metabolic-Inflammatory Axis in Brain Aging and Alzheimer's Disease](#)

April 21-24, 2013: Washington, DC: [MDA Scientific Conference: Therapy Development for Neuromuscular Diseases: Translating Hope Into Promise](#)

Upcoming Webinar:

[Register for the ALS TDI Gladstone Institutes Collaboration Webinar on February 26, 2013 at 4:00 PM EST](#)



Download your free copy:



SUPPORT THE ALS FORUM



Send the ALS Forum e-Newsletters to your colleagues!

February 12 issue of *Neuron*! Dr. Leonard Petrucelli, Professor of Neuroscience at the Mayo Clinic in Jacksonville, Florida, led this second study, which also shed light on the mechanism of how DPR proteins might be translated. Want to know which DPR proteins the Mayo researchers identified in the carriers of the hexanucleotide repeat expansions (hint, it is a different sequence than the DPR proteins identified in the *Science* study)? How about if these DPR proteins could ever serve as biomarkers? And last but not least, how does the unprocessed C9ORF72 pre-mRNA potentially get out of the nucleus in the first place? Click [here](#) to find out!

[In a Funding Twist, NIH Awarded \\$400,000 to Perform Exome Sequencing on ALS Patients](#)

The Muscular Dystrophy Association recently [granted](#) the NIH's Bryan Traynor \$400,000 to conduct exome sequencing on 1,000 sporadic ALS cases. The goal of the one year project is to identify novel ALS-linked genes. In July 2012 Biogen Idec [announced](#) they are collaborating with Duke University and the HudsonAlpha Institute for Biotechnology to sequence the genomes of 1,000 ALS patients over the course of five years. Hopefully, these two projects will yield important findings that help us to better understand the causes of ALS at the genetic level, and provide insights towards identifying potential new ALS therapies.

Drug News

[ALS TDI Receives FDA Approval to Test Multiple Sclerosis Drug Gilenya in ALS Patients](#)

"It was exciting to see how expeditiously the FDA reviewed our application to [test Gilenya in ALS patients](#)," said ALS TDI CEO and CSO Dr. Steve Perrin regarding the approval of a Phase IIa clinical trial to test Novartis' multiple sclerosis drug Gilenya (also known as fingolimod). In 2011, ALS TDI began preclinical testing of Gilenya in mice because the drug's mechanism of action seemed relevant. The results of these preclinical studies were positive, and in early 2012 ALS TDI announced that Gilenya might be a potential drug for people with ALS. ALS TDI plans to start [enrolling](#) patients soon at sites located in Massachusetts, California, Georgia, and Texas. To learn more about the Phase IIa clinical trial, including inclusion and exclusion criteria, click [here](#).

[Phytopharm's Cogane Fails to Show Efficacy in Parkinson's Trial](#)

Phytopharm just finished their [Phase II clinical trial of Cogane](#) for the treatment of Parkinson's disease. Unfortunately, the trial, which included over 400 people with Parkinson's disease, [failed to show efficacy](#). Phytopharm's Chief Executive Tim Sharpington said "Cogane had demonstrated encouraging efficacy in a wide range of industry standard preclinical models but this promise has not translated into clinically meaningful efficacy." This is disappointing news not only for the Parkinson's disease community, but also for the ALS community. In 2011, Cogane was [granted orphan drug status](#) for the treatment of ALS, and last December Phytopharm announced their plans to further develop Cogane for the treatment of ALS. However, in the wake of this recent announcement, Phytopharm has stopped all research activities while they reevaluate their pipeline.

[Neuralstem CEO Comments on Challenges of Drug Approval Process](#)



Forward to a Friend

Neuralstem Inc. just wrapped up their [Phase I clinical trial](#) testing the safety of injecting their human spinal cord neural stem cells (NSI-566) directly into the spinal cord for the treatment of ALS. Neuralstem is eager to start a Phase II study so they can get their stem cell therapy to ALS patients as soon as possible. In fact, they have already [secured funding](#) for the Phase II trial. Recently, Richard Garr, Neuralstem's CEO, wrote a blog post where he commented on the stark contrast between the FDA's "institutional" drug approval process, and the immediate urgency of patients to have access to drug options. Mr. Garr commented in his blog, "It is too easy to lose sight of the human cost from this disease in these institutional settings." To read Garr's provocative blog post, click [here](#).

[New Study Suggests Some Mouse Models May Not Be Predictive of Human Disease](#)

A recent and somewhat controversial new *Proceedings of the National Academy of Sciences* study has many researchers wondering whether [mice are an appropriate model for human disease](#). The study found that some mouse models of disease may not recapitulate the response observed in human disease. This discovery could have relevance for ALS research. Drug testing for potential ALS therapies often begins in the SOD1 G93A mice - the gold standard for preclinical ALS studies - and Prize4Life has been a longtime advocate for the value of well-designed preclinical studies using mice. While the new study provided unexpected results, it will likely not significantly affect current ALS research efforts in the short term. However, as researchers learn more about the molecular underpinnings of ALS these findings provides some sobering "food for thought" with regard to the current system of drug development, especially in the complex and challenging neurodegenerative disease space.

The ALS Forum was developed by Prize4Life, Inc.
P.O. Box 425783 Cambridge, MA 02142

www.prize4life.org

Identified content provided through a partnership with the [Alzheimer Research Forum](#).

[Forward email](#)