DISCOVERING A CURE

THE ALS FORUM

ALS Forum e-Newsletter Volume 88 **June 14, 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.

The ALS Forum e-Newsletter will not be published on June 28, 2013 in observance of the July 4th holiday. We will return to our normal bi-weekly publication schedule on Friday, July 12, 2013. Wishing everyone a very Happy Fourth of July!

Resources:

Visit the PRO-ACT Database atwww.ALSDatabase.org

NEALS Biofluid Repository Available to Researchers

NINDS Fibroblast Repository

Funding News:

Request for Proposals:Accelerating Drug Discovery for Frontotemporal Dementias. Letter of Intent due before August 22, 2013.

Upcoming Webinar:

The ALS Association's Research Update Webinar Series continues with Dr. Steven Burden of NYU Medical Center who will be discussing MusK agonists as a treatment for ALS. The webinar will be held onTuesday, June 18, 2013 at 4pm EST. Click here to register.

Conference News

11th Annual ENCALS Meeting: TDP-43 Responsible for Spreading ALS?

ALS-linked genes including TDP-43, C9ORF72, SOD1, and FUS were highlighted at the 11th Annual meeting of The European Network for a Cure of ALS (ENCALS) held May 31, 2013 through June 2, 2013 in Sheffield, England. One of these genes, TDP-43, was of particular interest. Dr. Johannes Brettschneider of the University of Ulm in Germanypresented data to suggest that the pathological protein aggregates of TDP-43 spread within motor neurons by travelling along axons. However, the damage caused by TDP-43 doesn't stop there; these aggregates can also travel between motor neurons, perhaps causing the pathological spreading of the disease throughout the body. This is not the first time that people have suggested that ALS-linked proteins can "spread" from one neuron to another. Dr. Neil Cashman, a professor at the University of British Columbia in Vancouver, Canada, presented some compelling data at the 23rd International Symposium on ALS/MND to suggest that misfolded SOD1 can in fact propagate the disease from cell-to-cell via a "template protein misfolding" mechanism. Read more about how misfolded SOD1 could also spread the disease here.

Prize4Life Covers Recent Advances in ALS Presented at the 2013 Neurotech Conference

Prize4Life's Program Officer, Dr. Jessica Goodman, attended the 8th Annual Neurotech Investing & Partnering Conference, hosted by the Neurotechnology Industry Organization (NIO) and NeuroInsights held May 23-24, 2013 in San Francisco, California. Don't miss Dr. Goodman's in-depth coverage of the "Movement Disorders: Parkinson's, ALS, and more" session, which focused on the development of biologics and devices as therapeutic options for neurodegenerative diseases including ALS.

The ALS Association / NEALS PALS Webinar: Dr. James Barry will lead a TDI-132/Gilenya Informational Webinar onJune 26, 2013 at 2pm EST. Click here to register.

Upcoming Meetings:

June 18, 2013: Boston, MA:US-India BioPharma & Healthcare Summit

June 23-27, 2013: Boston, MA: DIA 49th Annual Meeting

June 29-30, 2013:Philadelphia, PA: The ALS Clinical Research Learning Institute

July 7-12, 2013: Smithfield, RI: Gordon Research Conference: Human Genetics & Genomics

August 10-16, 2013: Andover, NH: Gordon Research Conference: Cellular & Molecular Mechanisms of Toxicity

September 4-5, 2013: Helsinki, Finland: 2nd Biannual European Neurotech Investing and Partnering Conference

September 18-20, 2013: Aspen, CO: Accelerating Translational Neurotechnology: Fourth Annual Aspen Brain Forum

September 21-26, 2013: Vienna, Austria: XXIth World Congress of Neurology: Neurology in the Age of Globalization

October 2-4, 2013: Clearwater Beach, FL:2013 Annual NEALS Meeting

October 3, 2013: Boston, MA: 9th Annual ALS TDI

Research News

Methylation a Turn Off for Disease Gene C9ORF72?

New research out of Dr. Ekaterina Rogaeva's laboratory at the University of Toronto in Canada suggests that hypermethylation of C9ORF72 might be "turning off" the transcription of C9ORF72. In their recent publication in the*American Journal of Human Genetics*, the authors identified up to 26 different sites upstream of the hexanucleotide repeat expansion that could be methylated in people carrying the repeat-expansion. Surprisingly, the amount of methylation seems to correlate with disease progression -- "more methylation associated with a faster disease course". The authors believe that hypermethylation reduces C9ORF72 transcription, potentially causing toxicity through a haploinsufficiency mechanism. This is the third research development in just the past few months around understanding C9ORF72's mechanism of toxicity, highlighting the importance of this question. Earlier this year, two groups suggested that the hexanucleotide repeat expansion in C9ORF72 is translated into dipeptide repeat (DPR) proteins, which could be a possible mechanism mediating the neuronal damage (be sure to read the *Science* and *Neuron* stories), while another group showed that the hexanucleotide repeat RNA acts as an "RNA sponge" to sequester important RNA binding proteins, thereby resulting in neurodegeneration (if you missed this story, click here to read it now). Stay tuned to the ALS Forum for future exciting developments in the dynamic C9ORF72 field.

RNA Binding Is Responsible For FUS-Associated Toxicity In ALS

In certain rare cases of ALS and FTLD the normally nuclear DNA/RNA-binding protein FUS is mutated, which causes FUS to mislocalize into cytoplasmic aggregates. Although several studies have suggested that this cytoplasmic mislocalization contributes to toxicity in ALS and FTLD, it was unclear if FUS' RNA binding ability was also contributing to toxicity. Now, new research out of Dr. Udai Pandey's laboratory at the Louisiana State University Health Sciences Center in New Orleans suggests that FUS' ability to bind RNA is essential for FUS-associated neurotoxicity. The researchers generated a variety of FUS variants with combinations of ALS-relevant mutations and mutations in the RNA recognition motif (RRM) sequence. *Drosophila* carrying FUS variants with an ALS relevant mutation had brain morphology defects, motor neuron defects, and eye defects that were not observed in flies carrying FUS variants with the same ALS relevant mutation and additional mutations in the RRM sequence. These data suggest that the RNA binding ability of FUS might be essential for neurotoxicity. Click here to read the full story.

CVS/pharmacy Launches Annual In-Store Fundraising Campaign to Raise Money for ALS

CVS/pharmacy just announced they have launched their annual in-store *Advancing Medical Research* campaign, which will raise funds "to support medical research and help improve the quality of life for those living with amyotrophic lateral sclerosis (ALS)." The money raised will primarily be donated to the ALS Therapy Alliance (ATA), which supports various ALS research initiatives including Prize4Life's PRO-ACT database (www.ALSDatabase.org). CVS/pharmacy will be collecting donations through the end of June. Click here to learn more. Last year

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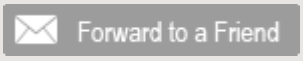

the *Advancing Medical Research* campaign raised more than $5 million dollars for ALS and cystic fibrosis research; let's hope the campaign will be even more successful this year!

Drug News

Knopp Neurosciences Donates Phase III Dex Data to PRO-ACT
Exciting Breaking News! Knopp Neurosciences Inc. has agreed to donate a portion of the de-identified patient data from the recent Phase III clinical trial of dexpramipexole (Dex) in ALS to the PRO-ACT database (www.ALSDatabase.org). Under the agreement, Knopp will donate the clinical data collected from the 468 placebo subjects that participated in the trial to PRO-ACT. In addition, Knopp plans to donate the data from the treatment-arm group of the Phase III trial to PRO-ACT after all studies of Dex in ALS are complete. Currently, PRO-ACT consists of over 8,500 ALS patient records from 17 completed Phase II and Phase III clinical trials conducted by companies including Teva, Novartis, Sanofi, and Regeneron. The addition of these new data will push the number of ALS patient records to over 9,000 in PRO-ACT! If you haven't checked out PRO-ACT, now is the time! There are many outstanding research questions that these new data can help address. In April, Prize4Life and the Neurological Clinical Research Institute (NCRI) were awarded the 2013 Best Practices Award in the Clinical & Health IT category from Bio-IT World for PRO-ACT. PRO-ACT is a collaboration between Prize4Life, the Northeast ALS Consortium (NEALS), and the NCRI at Massachusetts General Hospital, and is supported by funding from the ALS Therapy Alliance.

BrainStorm Shares Exciting News About Phase IIa Trial in ALS
Earlier this year, BrainStorm Cell Therapeutics' Phase I/II trial was fast tracked to a Phase IIa dose-escalating trial by the Israeli Ministry of Health. The Phase IIa trial design includes 12 patients split into three cohorts that will be treated "with increasing doses" of BrainStorm's NurOwn technology. Each group will receive both intrathecal (IT) and intramuscular (IM) injections of NurOwn. BrainStorm just announced that they have successfully treated their eighth patient in the Phase IIa trial and have recruited the final patient for the third cohort. BrainStorm estimates that all 12 patients will be treated by Fall 2013. In addition, BrainStorm just submitted safety data to their Institutional Review Board (IRB), including data from the first cohort treated in this Phase IIa study.

Neuralstem Sees Results in Phase I Trial
Dr. Eva Feldman, Director of Research of the ALS Clinic at the University of Michigan Health System and Principle Investigator on the Neuralstem ALS trial, recently commented that six of the fifteen patients that were injected with Neuralstem's human spinal cord-derived stem cells (NSI-566) during their Phase I trial in ALS seemed to respond. These six patients have "substantially slowed muscle degeneration" and "no significant disease progression" since their treatment nearly two years ago. As it turns out, the six patients that showed this unexpected response were all treated within two years of their diagnosis. Those that were treated five or more years after diagnosis did not appear to show any response to the treatment. Early intervention may be the key. This

past April, Neuralstemannounced that the FDA approved their Phase II trial in ALS. The goal of the Phase II study is to determine the maximum tolerated dose of NSI-566 in people with ALS. In the Phase I trial, Neuralstem examined a maximum of 15 injections of 100,000 cells/injection, while the Phase II study will examine up to 40 injections at up to 400,000 cells/injection. The Phase II trial is expected to begin this summer.

The ALS Forum was developed by Prize4Life, Inc.
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