DISCOVERING A CURE

THE ALS FORUM

ALS Forum e-Newsletter Volume 68 **August 16, 2012**

We are working hard to catch you up on the ALS research and drug news that happened while we were on hiatus. This is the second of our two back-to-back issues of the eNewsletter. In this issue, you will find summaries of the latest ALS research stories from July and August. In addition, we have included links to interesting news stories that happened in June. Our next issue will be published on August 30, 2012, when we will return to our biweekly eNewsletter schedule. As always, you can find all of these research stories, as well as drug and conference news, on the ALS Forum.

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:

NEALS Biofluid Repository Available to Researchers

Upcoming Registration Deadline:

September 12th for the Keystone Symposia: Multiple Sclerosis in January

Upcoming Meetings:

September 5-7, 2012: Manchester, UK: 8th International Conference on Frontotemporal Dementias

September 6-7, 2012: Dublin, Ireland: Neurons Under Stress 2012

September 8-11, 2012: Stockholm, Sweden: 16th European Federation of Neurological Societies Congress

Research News

iPSC Disease Models Up and Coming for AD, Down's, ALS

Patient-derived induced pluripotent stem cells (iPS cells) are quickly becoming a promising new method for modeling human diseases in culture. This is especially true for neurodegenerative diseases, including Alzheimer's disease, Down's syndrome, and ALS. Recently, researchers from Kyoto University published an article in *Science Translational Medicine* on the generation of nine iPS cell lines from three different patients with familial ALS. Each of the three patients were heterozygous for a mutant Tar DNA binding protein-43 (TDP-43) allele. The researchers generated motor neurons from the iPS cells that showed a characteristic phenotype of neurons expressing a mutant TDP-43 protein, including shortened neurites as well as TDP-43 aggregates in the cytosol. They screened the neurons against several histone acetyltransferase inhibitors, and they identified that anacardic acid seemed to reverse some of the TDP-43 related defects in the neurons.

When Is a C9ORF72 Repeat Expansion Not a C9ORF72 Repeat Expansion?

On July 15th, at the Alzheimer's Association International Conference in Vancouver, CA, Stuart Pickering-Brown from the University of Manchester presented some interesting new data for the FTLD and ALS linked gene, C9ORF72. Pickering-Brown's data suggests that the hexanucleotide GGGGCC repeat expansions in C9ORF72, which are linked to FTLD and ALS, may have alternative repeat expansion sequences. Pickering-Brown was genotyping individuals with FLTD and found two brothers that appeared to lack the large hexanucleotide repeat expansions found in people with FTLD or ALS. By Southern blot analysis, researchers showed the two individuals in fact had large hexanucleotide expansions in the C9ORF72 gene - upwards of 800 to 950 repeats. They determined that a mutation in the hexanucleotide

September 21-22, 2012: Quebec, Canada: Annual Foundation Andre-Delambre ALS Symposium: Causes and Therapeutic Perspectives

Training Program:

Interested in drug discovery and development for nervous system disorders? Apply to the NIH Blueprint-funded training program! Application deadline: October 1, 2012.

Funding News:

ADDF/AFTD: Accelerating Drug Discovery for Frontotemporal Dementias: Letter of Intent Due September 6, 2012

MJFF: Target Validation and Therapeutic Development Initiative Programs: Proposals Due September 12, 2012

MGH's Neurology Clinical Trials Unit Calls for ALS Clinical Trial Applications: Application Due September 17, 2012

2013 AAN Foundation ALS-Richard Olney, MD Clinician Scientist Development Three Year Award

MNDA PhD Studentship

repeat most likely interfered with annealing of the PCR primer. The next step is to identify the exact sequence of the repeat.

Profilin Gene Is Actin' in ALS
A team of scientists led by Dr. John Landers of the University of Massachusetts Medical School in Worcester identified a new gene linked to 1 to 2% of familial ALS cases. The researchers identified four mutations in the gene profilin 1 (*PFN1*), an-acting binding protein responsible for remodeling and growth of the actin cytoskeleton. The mutations C71G, M114T, G118V, and E117G are all localized to the actin-binding domain of profilin. Three of the mutations, C71G, M114T, and G118V, were the most penetrant, and when these mutants were expressed in N2A cells or in mouse primary motor neurons, they formed highly ubiquitinated aggregates that often contained TDP-43. These results suggest that defects in the cytoskeleton could be associated with ALS.

Research News Updates from June

Check out the full stories on the ALS Forum by clicking the links below!

ALS Immunotherapy: Vaccination Delays Disease in Mice

Hometown Loyalty: Astrocytes Stay Put During Development, After Injury

Sorting Cell Rescue in Spinal Muscular Atrophy

One, Two, Three...Four? Peripherin Jams With Neurofilament in Quartet

C9ORF72 Update: ALS Gene Is a Variable, and Global, Phenomenon

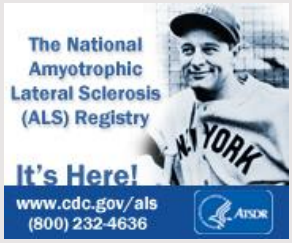
Staying Alive: Freed of a Single Gene, Severed Axons Defy Death

New Treatment Restores Movement to Paralyzed Rats

Drug News

Another Potential Neurodegenerative Disease Drug Fails in Clinical Trials
On the heels of the disappointing announcement that the Phase III ALS clinical trial of the antibiotic ceftriaxone has been stopped, a Phase III clinical trial of the potential Alzheimer's disease therapeutic, bapineuzumab, has also been halted. Bapineuzumab is an antibody that targets the Abeta peptide and was being tested for the treatment of patients with mild to moderate Alzheimer's disease. Although the results of the Phase II efficacy trial were promising, the Phase III study failed to show any effect on daily function or cognition in people with Alzheimer's disease.

Neuralstem's ALS Stem Cell Therapy is Helping Their Second Quarter Numbers



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At the close of the second quarter, Neuralstem, Inc. is reporting good news. They have now treated 17 patients in their ongoing clinical trial for their ALS stem cell therapy. The company is humble about their second quarter numbers, attributing their success to the ALS patients and their families who are participating in the trials, as well as the scientists leading the study, including Dr. Eva Feldman (University of Michigan), Dr. Jonathan Glass (Emory University), Dr. Nicolas Boulis (Emory University), and Dr. Maurizio Fava (Harvard University).

Isis Pharmaceuticals Develops Anti-sense Drug for Muscular Dystrophy and ALS

Isis Pharmaceuticals, in collaboration with Genzyme and researchers at the University of Rochester Medical Center, has developed a new anti-sense oligonucleotide drug to treat the most common form of muscular dystrophy, degenerative myotonic dystrophy type 1. The therapy was shown to help restore muscle movement in mouse models of the disease. Isis has also developed an anti-sense oligonucleotide therapy for people with ALS, called ISIS 333611. The Phase I clinical trial results for ISIS 333611 were just released in June. The conclusions from the trial were promising, suggesting that the therapy is safe to use and well-tolerated. Read more about it here.

FDA Can Now Regulate Stem Cell Clinics

A district court ruled that the FDA can regulate clinics that use stem cell-based therapies. The ruling now identifies stem cell as drugs. This decision ensures that stem cell therapies are subject to the FDA regulatory standards of other drugs, including that they are subject to the clinical trial process and have been approved for use. This ruling is especially important to ALS patients for two reasons, 1) many potentially promising ALS therapies are based on stem cells, and 2) there has been an unfortunate recent history of unregulated, unsafe, and disreputable stem cell treatments being offered to ALS patients.

The ALS Forum was developed by Prize4Life, Inc.
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