DISCOVERING A CURE

THE ALS FORUM

ALS Forum e-Newsletter Volume 67 **August 9, 2012**

We have returned after our summer hiatus! We didn't want you to miss any of the groundbreaking ALS research that happened while we were gone, so we will be publishing two back-to-back issues of the e-Newsletter that are jam-packed with exciting ALS research news!

In this issue, you will find summaries of important ALS research stories from July. In addition, we have included links to interesting news stories that happened in May. In our next issue, we will highlight the most recent cutting-edge ALS research articles, as well as provide links to research articles published in June. 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

Clinical Testing and Spinal Cord Removal in a Mouse Model for Amyotrophic Lateral Sclerosis (ALS)

Upcoming Meetings:

August 11-12, 2012: Waterville, ME: Gordon Research Conference: Brain Energy Metabolism & Blood Flow

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

Research News

Research Brief: Does Loss of TDP-43 Cause ALS-Like Disease in Mice?

Researchers from Taiwan have succeeded in knocking out the TDP-43 gene in mouse motor neurons. Generating the mice was not an easy task, as TDP-43 is essential and TDP-43 null mice are embryonic lethal. The researchers used a mouse that started with only one copy of the TDP-43 gene. Using Cre recombinase they were able to selectively delete the remaining copy of the TDP-43 gene in about 60% of motor neurons. These mice had a phenotype that resembled ALS in many respects, including muscle weakness, weight loss, and motor neuron death. The authors suggest that TDP-43 might play an early role in the onset of ALS.

ALS-Linked Ataxin Repeats Stick It to TDP-43 in Stressed Cells

Researchers have gained new insight into how a few extra polyglutamine codon repeats in ataxin-2 may lead to ALS. Scientists at the University of Pennsylvania and at Stanford University showed in three different cell models that an intermediate number of glutamine repeats (between 27 and 33) in ataxin-2 seems to lower the cell's tolerance to stress. The decreased stress tolerance makes the cell prone to activating caspase-3 and moving TDP-43 into stress granules. The activation of these events ultimately leads to TDP-43 fragmentation and phosphorylation, hallmarks of ALS. These findings suggest that preventing caspase activation may be helpful in ALS.

Oligodendrocytes More Than Myelinators, Potential Players in ALS

Two recent *Nature* papers uncovered an unknown role for oligodendrocytes: provider of lactate to axons for energy. It was

European Federation of Neurological Societies Congress

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

FUNDING NEWS:

ADDF/AFTD: Accelerating Drug Discovery for Frontotemporal Dementias

MJFF: Target Validation and Therapeutic Development Initiative Programs

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

MNDA PhD Studentship

MGH's Neurology Clinical Trials Unit Calls for ALS Clinical Trial Applications

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previously thought that the lactate transporter, monocarboxylate transporter 1 (MCT1), was localized to astrocytes. These new findings show that MCT1 is primary localized in oligodendroglia. The oligodendroglia in turn use these transporters to supply lactate to axons and neurons. Neurons apparently require the oligodendrocytes to survive, as knockdown of MCT1 results in neuronal death. Previous studies had suggested that oligodendroglia might be injured in SOD1 mice. The authors of one of the *Nature* papers went on to show that MCT1 expression and mRNA levels are reduced in both patients with sporadic ALS and SOD1(G93A) transgenic mice. These findings suggest an important role of MCT1 in keeping neurons happy and ultimately alive.

Case Studies Crystallize Trial Ideas at FTD Conference
You may want to check out the entire five-part Alzheimer Research Forum series covering the exciting discussions that transpired at a joint meeting of the Association for Frontotemporal Degeneration and the National Institute of Neurological Disorders and Stroke (NINDS) in Washington, D.C., but you should definitely read the third part of the series here, which provides a summary of the clinical trials in progress and the potential therapies in development for FTD.

Research News Updates from May

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

In-Vitro Innervation: Stem Cell-Derived Motor Neurons Meet Muscles

Grasping at the Future of Brain-Computer Interfaces

New Treatment Restores Movement to Paralyzed Rats

Drug News

Breaking News: Ceftriaxone Clinical Trial Stopped
In disappointing news that broke yesterday, the NINDS-supported Phase III ALS clinical trial of the antibiotic ceftriaxone has been stopped. Pre-clinical studies suggested that ceftriaxone could be a promising treatment for ALS. Unfortunately, the results from the ceftriaxone clinical trial did not meet the efficacy standards set for the trial. Ceftriaxone is currently approved by the FDA for the treatment of bacterial infections.

Initial results in clinical study show promise for stem cell therapy for treatment of ALS
BrainStorm Cell Therapeutics' NurOwn technology, developed for the treatment of ALS, shows hints of promising results in its current Phase I (safety) clinical trial. These preliminary results, in a small number of patients, suggest that BrainStorm's stem cell therapy could help slow the progression of ALS. The next steps will be to test different doses, as well as conduct a larger Phase II study to evaluate efficacy and safety.

Biogen Idec searching for genetic causes of ALS
Biogen Idec, Duke University, and the HudsonAlpha Institute for Biotechnology have agreed to sequence the genomes of 1,000 ALS

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patients. The goal of the ambitious collaboration is to identify and better understand the causes of ALS at the genetic level. The team hopes that this additional information will help with identifying potential new ALS therapies.

Patent for neuronal cell transplantation approved

Pioneering stem cell company Neuralstem, was just issued patent number 12/710,097 entitled "Transplantation of Human Neural Cells for Treatment of Neurodegenerative Conditions." The patent covers technology that allows for neuronal cells grown in the lab to be transplanted into the spinal cord of a patient. Neuralstem is currently running an ongoing Phase I clinical trial of its stem cell technology, and just treated their seventeenth patient. Read more about the clinical trial here.

Recent findings suggest that mitochondria play an important role in neurodegenerative disease

Mitochondria are known as the powerhouses of the cell because they generate the energy required for cells to survive. It has been proposed that mitochondrial dysfunction might contribute to neuronal death and disease progression in diseases such as ALS. Trophos SA initiated the MitoTarget Project to determine if mitochondria do contribute to neurodegeneration. The conclusions from the study clearly show that mitochondrial dysfunction has a direct role in neuronal death and the progression of neurodegenerative diseases.

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