DISCOVERING A CURE

THE ALS FORUM

ALS Forum e-Newsletter Volume 71 **September 27, 2012**

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:

NINDS Fibroblast Repository

Upcoming Workshop October 2 and 3: Applying to the NIH SBIR Phase I Program for First-Time Applicants

Upcoming Science Webinar October 3: Translating Genetic Biomarkers to the Clinic: The Promise and Pitfalls of Developing Robust, Reliable Signatures

Upcoming Registration Deadline:

Register Now for the Keystone Symposia, Neurogenesis joint with New Frontiers in Neurodegenerative Disease Research. Registration Deadline is October 4.

Register Now for the 23rd International Symposium on ALS/MND, December 5-7, 2012: Chicago, IL. The program was just released.

Upcoming Meetings:

Research News

Are TDP-43 Mice Living Up to Expectations?

TAR DNA binding protein 43 (TDP-43) was identified five years ago as being linked to ALS. TDP-43 is mutated in some cases of ALS and people with ALS often have TDP-43 containing protein inclusions. After the discovery of the TDP-43 gene, many research groups began generating TDP-43 mouse models as an alternative to SOD1 G93A mice. However, these TDP-43 models have presented unexpected phenotypes. For example, the TDP-43 mice developed by Dr. Robert Baloh at the Cedars-Sinai Medical Center in Los Angeles die from causes that seem unrelated to neurodegeneration, such as bowel obstruction. In addition, some of the TDP-43 models have a highly variable lifespan and reproduction issues. Despite these challenges, some of the TDP-43 models are showing promise. Dr. Jada Lewis' lab at the University of Florida in Gainesville has developed a doxycycline repressible TDP-43 mouse model. The pathology of this mouse model looks very similar to that observed in neurodegenerative diseases associated with aging. It looks like we are getting closer to a TDP-43 mouse model. However, there is still a significant amount of work that needs to be done to characterize these TDP-43 models before they can be used for pre-clinical studies.

C9ORF72 Steals the Show at Frontotemporal Dementia Meeting

It's been hardly a year since the hexanucleotide repeat expansions in C9ORF72 were discovered and linked to ALS and FTD. Yet in this year, many research groups have made significant progress towards understanding C9ORF72 and its involvement in ALS and FTD. The results of many of these studies were presented at the 8th International Conference on Frontotemporal Dementias, held September 5-7 in Manchester, United Kingdom. The discussions ranged from understanding how the hexanucleotide repeat expansions occurs, whether the origin of the expansion is from a single common ancestor, as well as identifying clinical markers that could be used to determine if a patient has the repeat expansion without sequencing. In addition, researchers debated several hypotheses for how the C9ORF72 repeat expansions might be causing cellular toxicity. Although it's clear that progress is being made, there is still much to learn about C9ORF72 and

October 2, 2012: Rockland, MD: 3rd Annual Conference on Clinical Research for Rare Diseases

October 3-6, 2012: Orlando, FL: American Association of Neuromuscular & Electrodiagnostic Medicine Annual Meeting

October 7-9, 2012: Boston, MA: American Neurological Association 2012 Annual Meeting

October 13-17, 2012: New Orleans, LA: Society for Neuroscience Annual Meeting 2012

October 24, 2012: New York, NY: Michael J. Fox Foundation Annual PD Therapeutics Conference

October 24-26, 2012: Clearwater Beach, FL: 11th Annual NEALS Meeting

October 31 - November 1, 2012: New York City, NY: Life Science Summit 2012

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:

MND Association is Calling for Research Project Grants. Summary Applications are due November 2

Massachusetts Neuroscience Consortium

its link to ALS and FTD. Read the full report from the conference here.

Arginine Methylation Distinguishes ALS-FUS From FTLD-FUS
At the 8th International Conference on Frontotemporal Dementias, held September 5-7 in Manchester, U.K., researchers were not only discussing the role of C9ORF72 in ALS, but also the difference between ALS and FTLD with FUS pathology. Dr. Christian Haass and Dr. Dorothee Dormann, from Ludwig-Maximilians-Universitat in Munich, Germany, showed that the arginine methylation state of FUS can be used to differentiate between ALS-FUS or FTLD-FUS. Normally, FUS is localized to the nucleus by the transportin 1, which binds FUS's C-terminal nuclear localization signal (NLS). In certain cases of ALS, the NLS is mutated, which prevents transportin 1 binding, and FUS remains cytosolic. However, in certain cases of FTLD, FUS remains in the cytosol, but the NLS is not mutated, so there must be another explanation for the localization defect. Drs. Haass and Dormann found that the arginine methylation of the NLS influences FUS localization. They identified that in ALS-FUS the cytosolic FUS was methylated. In FTLD-FUS, FUS that localized to cytosolic inclusions was unmethylated. They believe that the hypomethylated FUS can bind strongly to transportin 1, which causes a general defect in nuclear import. These findings may help begin to clarify why certain people with a FUS pathology develop ALS and others develop FLTD. Their findings were published online on September 11 in the *EMBO Journal*.

Drug News

$1 Million Dollar B.R.A.I.N. Prize Announced
On September 12, 2012, Israel Brain Technologies (IBT) announced the launch of its $1 Million dollar global B.R.A.I.N. Prize. The **B**reakthrough **R**esearch **A**nd **I**nnovation in **N**eurotechnology (B.R.A.I.N.) Prize will be awarded to an individual or team that demonstrates an "extraordinary breakthrough in brain technology with global implications." The goal of the Prize is to encourage neurotechnology innovation, with the goal of helping people with Alzheimer's disease, Parkinson's disease, ALS, PTSD, depression, or head trauma. The Prize will be awarded at IBT's Global Brain Technology Conference in 2013. Learn more about the B.R.A.I.N. Prize here.

Neuralstem Treatment Shows Promise in Rats with Spinal Cord Injury, Findings Help Neuralstem Potentially Raise $7 Million
On the heels of Neuralstem's announcement that they just treated their 18th patient and concluded their Phase I Clinical Trial of spinal cord neural stem cells for the treatment of ALS, Neuralstem has more exciting results with their stem cell therapy. Neuralstem's findings, which were published in *Cell*, showed that paralyzed rats treated with Neuralstem's spinal cord stem cells (NSI-566), regained locomotor function, including movement in lower parts of the body. In addition, the transplanted neuronal stem cells showed characteristic features of normal neurons, including "a remarkable number of axons that extended for very long distances." On the same day this research news broke, Neuralstem announced that they are offering 7,000,000 shares of their common stock at a price of $1.00/share. Neuralstem is expected to raise $7

Calls for Proposals. Proposal Deadline: November 16, 2012

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

MNDA PhD Studentship

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million through this direct offering.

The List of the 2012 Top 15 Industry Companies Released
FierceBiotech just released its top 15 companies for 2012, called the "2012 Fierce 15." Several on the list are involved in clinical development relevant for neurodegeneration including En Vivo and Angiochem. Angiochem is targeting diseases of the central nervous system, including Parkinson's disease and Alzheimer's disease. These diseases are especially difficult to target because they require passing treatments across the blood brain barrier -- however, that's not stopping Angiochem. This past year, Angiochem partnered with GlaxoSmithKline to break into the rare-disease market, including working on orphan diseases of the brain. This company is one to watch, maybe in 2013 they might think about entering into the ALS space!

EMD Millipore Licenses iPS Cell Technology
Patient-derived induced pluripotent stem cells (iPS cells) are quickly becoming a promising new approach for modeling human diseases in a culture dish. This is especially true for neurodegenerative diseases, including ALS. Recently, researchers from Kyoto University generated nine iPS cell lines from three different people with ALS. The researchers were able to differentiate the iPS cells into neurons that they used to screen drugs that could reverse some of the ALS-related toxicity, a technique that has significant amount of promise for identifying potential drug candidates for neurodegenerative diseases. EMD Millipore recently licensed this technology from iPS Academia Japan Inc., which is an affiliate of Kyoto University. Maybe EMD Millipore has plans to use this technology to identify potential ALS therapeutics?

The ALS Forum was developed by Prize4Life, Inc.
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Identified content provided through a partnership with the Alzheimer Research Forum.

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