DISCOVERING

THE ALS FORUM

A CURE

ALS Forum e-Newsletter Volume 91 **August 9, 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:

National Institute of Environmental Health Sciences (NIEHS) released a new RFA: Research Linking Environmental Exposure to Neurodegenerative Disease (R21). Letter of Intent due September 30, 2013.

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

NCATS Therapeutics for Rare and Neglected Diseases seeks collaborative partnerships with academic laboratories, not-for-profit organizations, and for-profit companies. Letter of Intent dueSeptember 16, 2013.

Research News

Neuronal Recycling Determines Vulnerability to Misfolded Proteins

New research out of Dr. Steven Finkbeiner's laboratory at the University of California, San Francisco suggests that the difference in vulnerability to cell death among various neuronal subtypes correlates with the rate of breakdown and clearance of toxic neurodegenerative disease-linked proteins. The researchers found that neuronal subtypes that were less effective at clearing toxic proteins were more susceptible to cell death. Dr. Finkbeiner's group primarily focused on examining the clearance of mutant huntingtin (Htt) in Huntington's disease (HD); the results of which were recently published in *Nature Chemical Biology* in July. However, Dr. Finkbeiner's group is also interested in looking at how clearance of TDP-43 affects the death of neuronal subtypes in ALS. Click here to read about the clever method that first author and postdoctoral fellow Dr. Andrey Tsvetkov used to look at protein turnover in the neurons.

NIH Considers Reproducibility Requirement

Last year, Amgen published a study showing that they failed to "replicate 89% of the findings from 53 landmark cancer papers." Is this really a surprise? We all know about this dirty little secret, but somehow we brush the topic under the carpet. With the immense pressure to publish or perish, who has time (and money) to address the reproducibility problem? Well, the NIH does. The NIH is "considering adding requirements to grant applications to make experimental validation routine for certain types of science, such as the foundational work that leads to costly clinical trials." Although the debate has just begun, there could be enormous benefit to requiring experimental validation, especially when translating ALS preclinical findings to the clinic. Preclinical studies in ALS are challenging for a number of reasons (for a comprehensive overview, check out the 2008 Scott paper and the "Working with ALS Mice" manual). Prize4Life supports external validation of foundational preclinical findings. For our $1M ALS Treatment Prize competition, Prize4Life will pay to have selected treatments validated in external laboratories. If we can potentially prevent some clinical trial failures through external validation of preclinical studies, we could save money, time, and resources - and potentially even attract more investment into the ALS space.

Upcoming Short Meeting:

What's Happening with Big Pharma and Neuroscience Development?
McGovern Institute at MIT, Thursday, August 15, 2013 from 5:30pm to 9:00pm EST.

Upcoming Meetings:

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 Leadership Summit

October 14-15, 2013: Tel Aviv, Israel: BrainTech Israel 2013

November 3-5, 2013: New York, NY: FasterCures: Partnering For Cures

November 7-8, 2013: San Diego, CA: 8th Annual Brain Research Conference: RNA Metabolism in Neurological Disease

November 7-8, 2013: San

A Little Fish is a Big Model for ALS Research
Over the past twenty years, the common zebrafish (*Danio rerio*) has become one of the most important animal models for research in neuroscience, including ALS. Zebrafish have a number of advantages, including that they grow quickly in the laboratory and their larvae are transparent, which makes it easy to study their development. In addition, zebrafish have a well-characterized genome, and their nervous system is very similar to the nervous system in humans. Now, the Packard Center for ALS research at Johns Hopkins University presents a three part seriesson the contributions zebrafish are making to ALS research. Part 1 focuses on how a group of researchers used zebrafish to investigate the functional role of C9orf72. Part 2 examines the fascinating ability of zebrafish to regenerate neurons using the neurochemical dopamine, and the implications these findings have for ALS. Finally, Part 3 covers how zebrafish are enabling researchers to understand how mutations in the ALS-linked gene FUS may cause ALS.

Short Peptide Rescues Microtubule Breakdown in ALS Mice
Microtubule network breakdown and axonal transport defects are hallmarks of disease-associated processes that occur in neurodegenerative diseases such as ALS and Alzheimer's disease. Potentially, rescuing such defects may provide therapeutic benefit in these and other neurodegenerative diseases. A study out Dr. Illana Gozes' laboratory at Tel Aviv University (TAU) and published recently in*Neurobiology of Disease* suggests that this is indeed the case. Dr. Gozes, along with Dr. Yan Jouroukhin and TAU graduate student Regin Ostritsky, showed that an eight amino acid peptide derived from activity-dependent neuroprotective protein (ADNP), called Davunetide or NAP, prevents the breakdown of -- and can even repair -- the microtubule network. Treatment of SOD1 G93A mice with NAP modestly prolonged the survival of these mice. In addition, using manganese-enhanced MRI the researchers found that NAP improved axonal transport in the SOD1 mice. So far, NAP has had mixed reviews in patients. NAP showed positive results when it was tested in people with mild cognitive impairment, a pre-Alzheimer's disease symptom. However, the Phase III trial of NAP for Progressive Supranuclear Palsy recently failed. The jury is still out on whether to test NAP clinically for ALS. Click here to read the full story.

Could Stem Cells Stem the ALS Tide?
Stem cells are a perennial hot topic in ALS. ALS-TDI recently posted a comprehensive overview on their blog detailing the current uses and potential of stem cell therapies for treating ALS. The post covers the history of stem cell therapies, from the earliest successes in the treatment of leukemia to more modern advances with skin grafts. It then goes on to talk about the history of stem cell therapies in efforts to diagnose and treat ALS. The hope is that stem cell-based models could be used to help identify new drugs and treatments, and stem cells themselves are already being tested as therapies by both Neuralstem and BrainStorm for the treatment of ALS. Click here to read the post.

Drug News

Knopp Continues to Hold Out Hope for Dex
Knopp Neurosciences Inc. licensed its drug Dexpramipexole (Dex) to Biogen Idec in 2010 after the compound (formerly known as KNS-760704)showed promising Phase II clinical results in people with ALS. In

Diego, CA: Workshop, Introduction to Stereology for Neuroscientists

November 9-13, 2013: San Diego, CA: Society for Neuroscience Annual Meeting: Neuroscience 2013

December 6-8, 2013: Milan, Italy: 24th International Symposium on ALS/MND

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2011, Biogen and Knopp began enrolling ALS patients in a Phase III Dex trial. This past January, Biogen Idec announced that the Phase III Dex trial failed to meet its primary and secondary endpoints for function and survival, and Biogen decided to discontinue the development of the drug. However, Knopp isn't ready to give up on Dex. In fact, Knopp is convinced that Dex had a statistically significant benefit in a subgroup of the 943 ALS patients that participated in the Phase III trial. Specifically, the subgroup of patients on riluzole with a fast disease trajectory whose ALS had already affected multiple body parts. Stay tuned to the ALS Forum e-Newsletter for more updates around the evolving Dex story.

Three Companies Granted FDA Approval to Market Riluzole

Riluzole is the only FDA-approved drug available for people with ALS. Riluzole had been marketed exclusively by Sanofi from its approval in 1995 until earlier this year when, in advance of the impending patent expiration on June 18, 2013, Sanofi sold Rilutek® (riluzole) to the Switzerland-based pharmaceutical company Covis Pharma Sarl. Although Covis enjoyed several months of exclusive rights to market riluzole, the honeymoon is now over. On the same day of the patent expiration, the US Food and Drug Administration (FDA) granted approval to three companies to market generic versions of riluzole. The three companies include Sun Pharmaceutical Industries, Apotex Corp., and Glenmark Generics. Hopefully, this healthy competition will benefit patients through lower drug costs.

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