DISCOVERING A CURE

THE ALS FORUM

ALS Forum e-Newsletter Volume 85 **May 3, 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:

The MNDA just opened their Online Summary Application Form for PhD studentship grants. The deadline is **today, Friday 3 May 2013**.

The ALS Association and the MGH Neurological Clinical Research Institute announce a request for proposals: Phase II Clinical development of novel, high-potential treatments for people with ALS. Letter of intent due May 20, 2013.

Abstract Registration Deadline:

Don't Miss It! The Society for Neuroscience 2013 Annual Meeting Abstract

Research News

Stem Cell Screen Points to ALS Disease Target

Dr. Lee Rubin's group at Harvard University recently developed a small molecule screening system employing motor neurons derived from mouse embryonic stem cells isolated from wild type SOD1 mice and SOD1 G93A mice. Using this system, the researchers screened a 5,000 compound library and identified a number of anti-apoptotic compounds as hits; with one of these compounds, kenpaullone, outperforming the rest. Importantly, kenpaullone also increased the survival of motor neurons generated from patient-derived iPS cells. Dr. Rubin suggests that testing compounds in a human iPS cell system may be a valuable approach to determining how a drug might behave in a clinical trial. Click here to find out how the anti-apoptotic compound kenpaullone is thought to work at the molecular level, as well as to find out how kenpaullone's effects stacked up against olexosime, dexpramipexole, and Riluzole.

Does Progranulin Play Both Sides in AD and FTD?

Progranulin mutations are often linked to frontotemporal dementia (FTD); however a new study out of Dr. Gil Rabinovici's group at the University of California, San Francisco, suggests that mutations in progranulin may increase the risk of another neurodegenerative disease, Alzheimer's disease (AD). The study, which was published online in *JAMA Neurology* on April 22, 2013, identified two people with progranulin mutations who developed sporadic AD symptoms at relatively young ages - 53 and 62. In both cases, these individuals presented with amyloid pathology "consistent with AD." Although this finding is intriguing, additional data needs to be collected to support the hypothesis that progranulin mutations could be a risk factor for AD. These results are potentially encouraging for drug development; if FTD and AD share a common genetic pathway, then there could be a shared drug target in this pathway. Read the full progranulin story here.

Melatonin: An Unexpected Neuroprotectant in ALS Mice

In a surprising new study published online in *Neurobiology of Disease*, researchers in the lab of Dr. Robert Friedlander, a professor at the

submission deadline is May 9, 2013!

The 24th International Symposium on ALS/MND abstract submission deadline is also quickly approaching! The deadline is May 10, 2013!

The RNA Metabolism in Neurological Disease Meeting Abstract deadline is May 31, 2013.

Upcoming Meetings:

May 6, 2013: New York, NY: The New York Academy of Sciences, Translating Natural Products into Drugs for Alzheimer's and Neurodegenerative Disease

May 6-8, 2013: Philadelphia, PA: 9th Annual Biomarker World Congress

May 18-24, 2013: Les Diablerets, Switzerland: Gordon Research Conference: Dendrites: Molecules, Structure & Function

May 19-22, 2013: Boston, MA: Society for Clinical Trials 34th Annual Meeting

May 21-23, 2013: Boston, MA: Translational CNS Summit

May 23-24, 2013: San Francisco, CA: 8th Annual The Neurotech Investing & Partnering Conference, Advances in Drugs, Devices & Diagnostics for the Brain and Nervous System

May 23-24, 2013: Uppsala, Sweden: Neurodegenerative Disorders: Immunotherapy

University of Pittsburg School of Medicine, found that melatonin delayed the onset of symptoms and prolonged survival in SOD1 G93A mice. The researchers reported that melatonin appears to work by preventing apoptosis through a multipronged approach, including inhibiting cytochrome c release, inhibiting the activation of the Rip2/caspase-1 pathway, and by reducing the levels and activation of caspase-3. Furthermore, the group found that disease progression in these mice was associated with melatonin receptor 1A loss and low levels of melatonin in the spinal cord. This work raises intriguing questions around the role of apoptosis in ALS.

Conference News

Human-Derived SOD1 Antibodies Show Promise in ALS Mice
Using antibodies to target pathogenic neurodegenerative disease-associated proteins was just one of the hot topics discussed at the 11th International Conference on Alzheimer's and Parkinson's Diseases held in Florence, Italy from March 6-10, 2013. Although SOD1 mutations account for only 2% of the ALS patient population, there is mounting evidence to support the idea that wild type SOD1 aggregates into pathologic conformations in sporadic ALS cases. Read this short report to learn about Neurimmune's initiatives to identify antibodies that target the misfolded pathogenic SOD1 proteins, as well as learn about their impressive preclinical results with these antibodies in both the SOD1 G93A and SOD1 G37R mouse models (they even adhered to the rigorous preclinical study design in ALS mice that Prize4Life champions). Looks like Amorfix may have some healthy competition!

Drug News

ALS TDI Receives $3.2 Million to Fund ALS Research
The Muscular Dystrophy Association (MDA) just announced that they are providing $3.2 million to the ALS Therapy Development Institute (ALS TDI) to support ALS TDI's preclinical research efforts. The funds are being contributed from the Augie's Quest campaign, which benefits the MDA's worldwide ALS research program. Dr. Steve Perrin, CEO and CSO of ALS TDI, said "Our partnership with MDA has helped us to establish a foundation that paves the way for new discoveries, better powering our research that may lead to effective treatments for patients today." Since 2007, ALS TDI has received over $31 million in funding from the MDA. Learn about how ALS TDI has used these funds to further ALS research here.

Is The Nose The Gateway To The Brain?
Impel Neuropharma recently showed that their "nose-to-brain drug delivery device" could successfully deliver peptides to human brains - completely bypassing the blood-brain barrier. This trial was one of the first of its kind in humans to show that drugs administered through the nose are able to reach the exposed primary neurons located in the upper nasal passage. This advance is an important first step towards targeted

and Biomarkers

May 31, 2013 - June 2, 2012: Sheffield, United Kingdom: 2013 ENCALS (European Network for the Cure of ALS) Meeting

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delivery of drugs to the brain, which in some cases may help minimize side effects that come from taking some drugs orally. Impel Neuropharma is confident that they can delivery larger proteins using their device (maybe those SOD1 antibodies you just read about?). In case you didn't catch it the first time, click here to read Prize4Life's coverage of the Alzheimer's Drug Discovery Foundation's 7th Annual Drug Discovery for Neurodegeneration Conference held in San Francisco, California, which also discussed the benefits of bypassing the blood-brain barrier using nasal drug delivery.

ALS Association's Drug Company Working Group Meets To Discuss ALS Developments

A few weeks ago, at the 65th Annual Meeting of the American Academy of Neurology held in San Diego, California, the ALS Association's Drug Company Working Group met to discuss several important developments in ALS clinical trials and research. Click here to read short summaries about the important findings that came out of the Dexpramipexole trial, the developments around the Phase II Tirasemtiv trial, as well as some recent discoveries around biomarkers -- including the use of an imaging biomarker to monitor levels of the EAAT2 glutamate transporter, and a cell-based biomarker that could be used to monitor ALS-associated changes in the immune system.

European Medicines Agency Recommends Approval of NUEDEXTA in Europe

The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has recommended "NUEDEXTA (dextromethorphan hydrobromide and quinidine sulfate) be approved for the treatment of pseudobulbar affect (PBA), irrespective of neurologic cause." Although this is encouraging news to the European community, the European Commission (EC) will have the final say over whether NUEDEXTA will be approved for use (although the EC usually takes the recommendation of CHMP). NUEDEXTA was approved by the U.S. Food and Drug Administration in October 2010 for PBA, which is a neurologic condition characterized by frequent outbursts of involuntary crying or laughing. PBA occurs in ALS, multiple sclerosis, traumatic brain injury as well as in Alzheimer's disease and Parkinson's disease.

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