DISCOVERING A CURE

THE ALS FORUM

ALS Forum e-Newsletter Volume 78 **January 25, 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:

NEW Resource Added!! Visit the PRO-ACT Database at www.ALSDatabase.org

NEALS Biofluid Repository Available to Researchers

NINDS Fibroblast Repository

Funding News:

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

Upcoming Meetings:

February 3-8, 2013: Santa Fe, NM: Keystone Symposia Joint Meeting: Neurogenesis & New Frontiers in Neurodegenerative Disease Research

February 10-12, 2013: San Francisco, CA: 7th Annual Drug Discovery for Neurodegeneration

Conference News

Chicago-Devilish Duo: Two Mutations Add Up to Familial ALS
Researchers and clinicians gathered at the 23rd International Symposium on ALS/MND held in Chicago, IL from December 5-7 to discuss the latest ALS research topics, including the complicated genetics of ALS. We now have a growing list of genes that are considered to be ALS risk factors. To add to the complexity, Michael van Es from the University Medical Center in Utrecht, the Netherlands, suggested that in certain cases of ALS, two ALS risk factors might contribute to the development -- and even the phenotype -- of the disease. Read more about the ALS risk factors involved, as well as why this is somewhat controversial here.

Chicago-Dynamic Repeats: C9ORF72 Expands and Shrinks in ALS
It's been a little over a year since the discovery of the ALS risk factor, C9ORF72, and researchers are just beginning to understand how hexanucleotide repeat expansions in C9ORF72 influence the development of ALS and FTD. At the 23rd International Symposium on ALS/MND, Mariely Dejesus-Hernandez from the Mayo Clinic in Jacksonville, Florida presented some compelling findings that further complicate the C9ORF72 story. Dejesus-Hernandez found that the length of the repeat expansion not only varies between people, but even more surprisingly, the length of the repeat varies between tissues isolated from the same person! Read more about the potential origin of these tissue-specific repeat length differences, and the implications these findings have on the development of patient-based cellular models, as well as on diagnosing a person with ALS, here.

Chicago-RNA Inclusions Offer Therapeutic Target in ALS
Many researches are feverishly working to understand the mechanism of how C9ORF72 contributes to the development of ALS and FTD. Although we still don't have a clear picture of the role that C9ORF72 plays in these diseases, that hasn't stopped two different research groups from developing potential therapies to target C9ORF72. At the 23rd International Symposium on ALS/MND, John Ravits' group at the University of California, San Diego and Jeffrey Rothstein's group at

Conference

February 19-20, 2013: Manchester, UK: 8th Annual Biomarkers Congress

March 6-7, 2013: Washington, DC: The Traumatic Brain Injury Conference

March 16-23, 2013: San Diego, CA: 65th Annual American Academy of Neurology Meeting

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Johns Hopkins University both presented their progress towards developing antisense oligonucleotide therapies targeting C9ORF72. Both groups are independently working with Isis Pharmaceuticals to develop these potential therapies.

Research News

Hereditary Spastic Paraplegia with Ataxia Potentially Linked to Calcium Dysregulation

Two independent research groups recently found that mutations in β-glucocerebrosidase 2 (GBA2) contribute to the development of hereditary spastic paraplegia (HSP) with ataxia. Between the two studies, these groups identified a total of 8 mutations in GBA2. Three of these mutations were substitutions that the researchers believe are most likely loss-of-function mutations, and the remaining five were truncations. The mechanism of how these mutations are contributing to the development of complex HSP with ataxia is still unclear, although the researchers suggest it could be a result of dysregulated levels of glucosylceramides that potentially contribute to an imbalance in calcium homeostasis. Toxicity resulting from dysregulated levels of calcium is thought to contribute to neuronal death in a number of neurodegenerative diseases, including ALS. Read the full story of how these GBA2 mutations were identified and the emerging role of lipids in HSP with ataxia here.

Drug News

Cut to the Chase: Therapies Go Directly to Central Nervous System

One of the biggest challenges for neurodegenerative diseases is drug delivery. In these diseases, neurons are often the target; however, reaching these neurons with therapeutics is a challenge because of the blood-brain barrier (BBB). Prize4Life funded science writer, Dr. Amber Dance, covers the latest techniques used by companies, including Medtronic, NeuroPhage, Isis Pharmaceuticals, Ceregene, and NsGene Inc. to bypass the BBB and directly deliver therapeutics to the target neurons. Read more about these techniques, as well as the advantages and limitations of these approaches here.

Despite the Recent Failure of Biogen Idec's ALS Clinical Trial the Company is Determined to Stay the Course

Over the years, ALS has resisted all efforts to develop a treatment. With Biogen Idec's recent announcement that the drug Dexpramipexole was also unable to impact the disease, it is easy to see why those who design and oversee ALS clinical trials are frustrated. "All of the drugs that have failed recently in Phase III looked promising at Phase II. Dex slowed down the disease in over 30 percent of the patients in the Phase IIb trial," said Dr. Steve Perrin, CEO and CSO of ALS TDI. "The lesson here is that we need to change the design in Phase II, especially if companies plan to test the drug in different doses." Despite this setback, Biogen Idec CEO George Scangos told investors that the failure of Dexpramipexole "has not dampened our determination to do something about this disease. We continue to work on the biology to come forward

with rationally designed compounds." He also highlighted the company's newly announced $10 million investment in a research collaboration searching for new ALS disease targets.

FDA Approves Neuralstem, Inc. to Begin Phase I Spinal Cord Injury Clinical Trial

Neuralstem, Inc. just announced that they have received approval from the FDA to start a safety trial of the company's potential stem cell therapy in people with chronic spinal cord injury. This announcement comes on the heels of the completion of Neuralstem's Phase I trial, which was designed to test the safety of injecting human stem cells directly into the spinal cord of people with ALS. In addition, the NIH has already agreed to fund a majority of the Phase II portion of the clinical trial, which will further examine this potential stem cell therapy in people with ALS. Neuralstem, Inc. plans to begin recruiting for the Phase II trial once their protocol is approved by the FDA.

Amorfix In Process of Developing Potential ALS Diagnostic Tool

On average it takes about 12 to 14 months to diagnose a person with ALS after their first symptoms appear. With a disease that is often fatal within 3 to 5 years, ALS patients can't afford to lose this time. There is an estimated $250 million market for the development of a diagnostic test that can reduce the time between first symptoms and clinical diagnosis. Amorfix recently announced their entry into this market. Amorfix is known for their development of antibodies that recognize and target misfolded SOD1. On Tuesday, January 22, Amorfix announced that they successfully completed the first steps towards developing a blood test that could be used to diagnose ALS using these antibodies that bind misfolded SOD1. Read more about the diagnostic that Amorfix is developing here.

Correction: In the last edition of the ALS Forum e-Newsletter, we reported that BrainStorm Cell Therapeutics received a $3 million grant from Israel's Office of the Chief Scientist. In fact, the grant was in the amount of 3 million Israeli shekels, not U.S dollars. We apologize for this error.

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