DISCOVERING A CURE

THE ALS FORUM

ALS Forum e-Newsletter Volume 75 **November 30, 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.

Funding News:

Opportunities available to be a contract collection site for the NMH, NICHD and NINDS Brain and Tissue Repository. Deadline: January 22, 2013

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

HNDC and the MGH NCRI announced an RFA for the 2013 Neurodegenerative Disease Pilot Study Grant Program. Proposal Deadline: December 6, 2012

Rare Disease Challenge Be HEARD. Proposal Deadline: December 15, 2012

Upcoming Webinars:

ALS Clinical Trials and Expediting Therapy Development Webinar.
Friday, November 30, 2012, 3:00 PM EST.
Register here.

Research News

Contest Winners Offer Solutions for Tracking ALS

Prize4Life announced the winners of their DREAM-Phil Bowen ALS Prediction Prize4Life Challenge (or ALS Prediction Prize) at the 7th annual DREAM Conference, held November 12-15 in San Francisco, CA. The ALS Prediction Prize challenged solvers to develop algorithms that could predict the future rate of ALS disease progression using three months of clinical data collected from completed phase II and phase III ALS clinical trials. Over 1,000 solvers participated in the ALS Prediction Prize, 39 unique solutions were submitted, and the top three solutions were awarded. Read more about the ALS Prediction Prize Challenge winning solutions here. Interested in learning more about the ALS Prediction Prize Challenge? Read the ALS Prediction Prize FAQs here.

Do you want access to the ALS clinical trial data used in the ALS Prediction Prize? The ALS Prediction Prize Challenge was based on a subset of the data that will be available in the PRO-ACT database. On December 5, the full PRO-ACT database will go live and will be freely available to the global scientific community! PRO-ACT will house clinical data collected from over 8,500 ALS patients from completed late-stage clinical trials. PRO-ACT is a collaboration between Prize4Life, the Northeast ALS Consortium (NEALS), and the Neurological Clinical Research Institute at Massachusetts General Hospital, and is supported by funding from the ALS Therapy Alliance.

Enter the New Alzheimer's Gene: TREM2 Variant Triples Risk

In two back-to-back papers that were published online on November 14 in *The New England Journal of Medicine*, two groups independently reported that mutations in the triggering receptor expressed on myeloid cells 2 (*TREM2*) gene triples the risk of developing Alzheimer's disease (AD). One of these studies was led by Dr. John Hardy, a professor at the University College London, UK. Dr. Hardy also led another recent study that identified *TREM2* as a risk factor for FTD; the findings of which were published online on October 8 in *Archives of Neurology* (read the related story here: Mutations in TREM2 Cause Frontotemporal Dementia). In

ALS Associations' December Research Update Webinar featuring Andreas Jeromin, CSO at NextGen Sciences DX. Thursday, December 13, 2012, 4:00 PM EST. Register here.

Early Registration Deadline:

Early Registration Deadline is December 4th for the Keystone Symposia Joint Meeting: Neurogenesis & New Frontiers in Neurodegenerative Disease Research

Upcoming Meetings:

December 3-5, 2012: West Palm Beach, FL: The World Stem Cell Summit

December 5-8, 2012: Cold Spring Harbor, NY: Blood Brain Barrier

December 5-7, 2012: Chicago, IL: 23rd International Symposium on ALS/MND

December 17, 2012: London, UK: Mitochondria and the Central Nervous System

January 11-16, 2013: Big Sky, MT: Keystone Symposia: Multiple Sclerosis

January 15-19, 2013: Hokkaido, Japan: The Society of Neuromuscular Sciences Incorporated 7th Annual Scientific Meeting

February 3-8, 2013: Santa Fe, NM: Keystone Symposia Joint Meeting: Neurogenesis & New

fact, it was the *TREM2*-FTD finding that led Dr. Hardy to look for *TREM2* mutations in Alzheimer's. In collaboration with a team at Washington University in St. Louis, the groups examined the sequences from 1,092 people with AD, as well as the sequences of 1,107 controls. The groups found that a particular TREM2 mutation, R47H, was strongly associated with AD. Mutations in *TREM2* were originally linked to Nasu-Hakola disease, which causes changes in bone structure and dementia. Now we are finding out that *TREM2* has a role in multiple neurodegenerative diseases. Although not much is known about the function of TREM2, it is thought to potentially control the microglial immune response. These findings suggest that inflammation might be a common pathway in FTD and AD.

Part 3 of a 6 Part Series on CTE: CTE: Trauma Triggers Tauopathy Progression

Chronic traumatic encephalopathy (CTE) is emerging as an independently-defined neurodegenerative disease, characterized by a tauopathy that progressively spreads throughout the brain (see Part 1). CTE is primarily observed in the brains of military veterans and athletes that play contact sports, as well as in people that have a history of repeated brain injuries. In 2007, Dr. Ann McKee of Boston University started studying brains that had been donated to the University' Center for the Study of CTE. To date, 136 brains have been donated to the center, by a mix of football players (high school to NFL), hockey players, and veterans. Dr. McKee has analyzed 100 of these brains thus far, and has found that 80% have CTE. By studying these brains, Dr. McKee found that CTE has a distinct pathology that can be divided into specific stages of disease progression. In addition to the massive tauopathy, she often also observes TDP-43 deposition. In some cases, the CTE brains show a second pathology, including ALS, FTD, or AD pathologies. This might suggest that the recent study that reported NFL football players have a nearly 4-times higher risk of developing ALS might be skewed. The findings in this report were based on medical records and not on the analysis of the brain tissue -- potentially some of these players could have had a mixed CTE-ALS pathology. McKee presented these findings at the first research conference on CTE held in Las Vagas, Nevada. This is Part 3 of a six-part coverage of the conference. See also Part 1, Part 2, Part 4, Part 5, and Part 6.

$1 Million Goes to ALS Research

In 2005, the University of Miami ALS Research Foundation joined forces with the ALS Recovery Foundation to create the ALS Recovery Fund. That same year, the ALS Recovery Fund pledged $1 million to the Department of Neurology at the University of Miami's Miller School of Medicine to establish the Walter Bradley Endowed Chair for ALS Research. Dr. Michael G. Benatar, associate professor of neurology and chief of the Neuromuscular Division, currently holds this position. Now, seven years later, the ALS Recovery Fund has contributed another $1 million to the Department of Neurology. The gift will be used to provide support for ALS patients, as well as provide funds for ALS research. The president of the ALS Recovery Fund, Adam J. Silverman, said "Not enough is done in the area of ALS research. There are no survivors or success stories in ALS. This gift continues to build on the world-class ALS programs at the Miller School, and through our continued partnership, we will solve the mystery surrounding this terminal illness."

Frontiers in Neurodegenerative Disease Research

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

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

Resources:

NEALS Biofluid Repository Available to Researchers

NINDS Fibroblast Repository

Download your free copy:

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Drug News

Companies Are Investing in ALS Drug Development
Dr. Steve Perrin, CEO and CSO of the ALS Therapy Development Institute (ALS-TDI), recently said "For anyone working in the ALS field, it's a real time of hope and promise." He is correct - this is an exciting time! For example, Biogen Idec, Cytokinetics, Inc., and Neuraltus Pharmaceuticals are just three of a number of companies actively working on developing ALS therapies. Biogen is currently the most advanced company in this respect. They plan to complete their Phase III study of dexpramipexole in over 900 people with ALS early next year. Cytokinetics is currently enrolling people with ALS in the Phase IIb study of tirasemtiv. Cytokinetics expects to know the results of this study by the end of 2013. Neuraltus just announced the results from their Phase II clinical trial of NP001 in people with ALS. The study showed encouraging results in a subset of patients. After discussions with the FDA, Neuraltus has decided to move forward with a Phase III study of their drug, which will start enrolling in 2013. ALS-TDI is teaming up with Novartis to study fingolimod (Gilenya), for the treatment of ALS. Fingolimod is already FDA approved for the treatment of MS. The results of this study are expected by the middle of 2013. Read more details about each study here.

Positive Data From Phase IIA Study of Cytokinetics' Tirasemtiv
Cytokinetics, Inc. just announced positive results of their Phase IIa study of tirasemtiv (formerly CK-2017357) in people with the autoimmune neuromuscular disease, generalized myasthenia gravis. Tirasemtiv has been shown to activate skeletal muscle, as well as reduce and delay the onset of muscle fatigue. In April, the FDA granted an orphan drug designation and fast track status to tirasemtiv for the potential treatment of ALS. Cytokinetics is currently recruiting participants for their Phase IIb study of tirasemtiv in people with ALS. Cytokinetics plans to enroll around 400 people with ALS in the clinical trial. Read more about this international clinical trial here.

Isis Pharmaceuticals Continues To Pursue ALS Therapy Development
Isis Pharmaceuticals is currently developing therapies for both ALS and Huntington's disease. Their novel approach uses technology called antisense oligonucleotides (ASOs) to target and regulate specific RNAs inside neurons. Isis just completed a Phase I study of their ASO drug (ISIS SOD1Rx) in people with ALS caused by mutations in the SOD1 gene. The results of the study were positive - the ASO drug was shown to be well tolerated and safe. However, the ISIS SOD1Rx drug can only be used to treat about 2% of all ALS patients. Isis currently has plans to develop additional ALS therapies that would reach a larger population. Read an interview with senior vice president of research at Isis, Dr. Frank Bennett, here.

Amorfix Collaborates with Columbia University on Potential ALS Therapeutic
Approximately 20% of inherited ALS cases are caused by the misfolding of mutant SOD1 proteins. To prevent the toxicity of these misfolded

proteins, Amorfix Life Sciences Ltd. developed anti-SOD1 antibodies that target and bind to misfolded SOD1. However, the details of how the antibodies are working to prevent toxicity at the cellular level are still unknown. To determine how these antibodies work, Amorfix turned to Dr. Serge Przedborski at Columbia University. Dr. Neil Cashman, Amorfix's Chief Scientific Officer and founder, said "This collaboration is designed to help answer key questions about the pivotal role of misfolded SOD1 in ALS. Understanding the disease from a mechanistic perspective will greatly facilitate the development of new treatments that can effectively treat ALS patients and hopefully prevent further decline in neurological function." Biogen Idec is currently licensing Amorfix's anti-SOD1 antibodies to pursue the development of antibody-based ALS therapeutics.

Knopp Investigating Dex for the Treatment of Other Neurodegenerative Diseases

In 2010, Biogen Idec licensed dexpramipexole (Dex) from Knopp Biosciences for $80 million to further develop the drug candidate for the treatment of ALS. After promising Phase II results, Biogen launched a global Phase III study of Dex in over 900 people with ALS. Although the Phase III trial is still ongoing, Knopp has started to raise funds to support studies that would test Dex for the treatment of other neurodegenerative diseases. Knopp's goal is to raise $30 million, and they are about halfway there. Hopefully these additional studies will provide further insights into the results of the soon-to-be-announced Dex ALS study!

San Francisco Is An ALS Research Hub

San Francisco is a hotbed for ALS research! Nine different groups - five companies and four research institutes, all located in or near San Francisco - are working on finding a cure for ALS. Although they all of have a common goal, their approaches towards this goal vary widely. For example, one of these companies, KineMed, is developing a biomarker to track disease progression in people with ALS. Others, such as Cytokinetics, Inc., are working to find ways to activate skeletal muscle. In addition to these more established companies, startups such as Coyote Pharmaceuticals Inc. and Xalud Therapeutics Inc. are breaking into the ALS research space. Let's hope all of these companies can reach their goal of curing ALS! Read the full article here (paid subscription required).

The ALS Forum was developed by Prize4Life, Inc.
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