THE ALS FORUM

Discovering a Common Goal, Discovering a Cure

ALS Forum e-Newsletter Volume 115 **October 31, 2014**

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:

The ALSGene tool: www.ALSGene.org

The PRO-ACT Database: www.ALSDatabase.org

NEALS Biofluid Repository Available to Researchers

NINDS Fibroblast Repository

VABBB Tissue Request Information Site

Funding Opportunities:

ALS ACT, ALSA, NEALS and the ALS Finding a Cure Foundation RFP: Phase II Clinical Development of Novel, High-Potential Treatments for People with ALS. Letter of Intent due January 9, 2015.

NCATS Small Business Contract Funding.Applications due November 5, 2014.

Upcoming Meetings:

November 2014

November 7, 2014: Boston, MA: 10th Annual ALS TDI Leadership Summit

Research News

Original Approach Identifies Tubulin as New ALS Gene

The microtubule cytoskeleton is essential for maintaining structural integrity and for protein transport in the cell, and damage to microtubules is associated with ALS and other neurodegenerative diseases (see Oct 2012 news story). A new paper published October 22 in *Neuron* directly links mutations in the gene encoding the microtubule protein Tubulin Alpha 4A (TUBA4A) to ALS. The researchers, led by John Landers from University of Massachusetts Medical School in Worcester, MA, Vincenzo Silani from the University of Milan Medical School in Milan, Italy and Christopher Shaw from King's College London, UK, utilized a novel exome sequencing approach followed by a genome-wide association study to identify genes with rare mutations that are enriched in ALS patients. They picked up TUBA4A as a risk gene, as well as a positive control from familial ALS patients - the superoxide dismutase 1 (SOD1) gene. A major challenge was how to distinguish benign gene variants from disease-linked mutations. Click here to learn more about their strategy and exciting findings.

Viral Protein Salvages Mitochondria and Protects Neurons in Mouse Model of PD

Many viruses have evolved specialized mechanisms for preventing cellular apoptosis in order keep their hosts alive. A new study published in the 21 October *Nature Communications* presents a compelling example of such a viral anti-apoptotic protein that can be utilized as a protective agent to prevent neuronal degeneration in a mouse model of Parkinson's disease. When Daniel Gonzalez-Dunia at INSERM in Toulouse, France and colleagues administered protein X from the Borna disease virus (BDV) into the substantia nigra of mice prior to administration of the neurotoxin MPTP, they found that protein X salvaged dopaminergic neurons. This protein targets mitochondria, and could serve as a therapeutic lead not only for PD but also for ALS, where mitochondrial dysfunction is known to play a role (see Mar 2013 news story; Oct 2014 news story). Further work is needed to characterize the protein's properties and devise an approach to translate these findings into a new therapeutic for humans. Click here to read more.

November 13-14, 2014: Arlington, VA: 9th Brain Research Conference Neuroprotection: Basic mechanisms and translational potential

November 14, 2014: Washington, DC: Advances in ALS and FTD Genetics Workshop

November 15-19, 2014: Washington, DC: The Annual Society for Neuroscience Meeting

November 16-18, 2014: New York, NY: Partnering for Cures

December 2014

December 3-5, 2014: San Antonio, TX: World Stem Cell Summit

December 3-6, 2014: Cold Spring Harbor, NY:Neurodegenerative Diseases: Biology & Therapeutics

December 5-7, 2014: Brussels, Belgium:International Conference on ALS/MND

December 17-20, 2014: Hotel Vila Galé Coimbra, Portugal: Mitochondria, Metabolism and Disease

January 2015

January 13-17, 2015: Hokkaido, Japan: Society for Neuromuscular Sciences 8th Annual Scientific Meeting

January 25-30, 2015: Taos, New Mexico:Neuroinflammation in Diseases of the Nervous System

February 2015

Blood Test for Alzheimer's Disease Enables Presymptomatic Diagnosis

A major obstacle to identifying effective and disease-modifying therapies for ALS is the long delay between initial onset of symptoms and diagnosis. The earlier the diagnosis, the earlier patients could receive therapeutic interventions to attenuate or potentially reverse neuronal damage. A new early diagnostic blood test for Alzheimer's disease (AD) is a major advance in that direction. In work published October 28 in *Molecular Psychiatry* online by Andrew Hill and colleagues from the University of Melbourne, Australia, microRNAs (miRNAs) from circulating exosomes in human serum were sequenced, and the sequences were compared between AD patients and controls. The team identified a 16 microRNA signature that together with other risk factors could detect AD with 91% accuracy. Similar approaches could be applicable to ALS, where miRNAs also play an important role (see Nov 2013 news story). Click here to read more about the exciting plans to further improve this diagnostic test.

Activation of mTOR Signaling by Mutant Huntingtin Exacerbates Huntington's Disease

A new study published October 28 in *Science Signaling* online provides new insight on how mutant huntingtin (Htt) causes Huntington's disease (HD). The study, led by Srinivasa Subramaniam and colleagues from the Scripps Research Institute in Jupiter, Florida, identifies a direct link between Htt and the mammalian target of rapamycin (mTOR) complex 1 (MTORc1). In a mouse model of HD, activation of mTOR signaling in the striatum accelerates disease onset and exacerbates the behavioral abnormalities of the mutant mice. Interestingly,whether these findings translate to other neurodegenerative diseases is yet to be determined, since mTOR signaling has been shown to play a protective role in ALS (see October 2013 news story). Click here to read more about this potential new therapeutic target for HD.

Drug News

Cytokinetics Planning Phase III Clinical Trial of Tirasemtiv for ALS

Based on promising effects on respiratory function, and follow-up discussions with statisticians, clinicians and the US Food and Drug Administration, Cytokinetics announced its decision to move forward with a Phase III clinical trial of *tirasemtiv* in ALS. Earlier this year, Cytokinetics presented disappointing results of the company's Phase IIb clinical trial to evaluable safety, tolerability and efficacy of *tirasemtiv* for treating ALS (see May 2014 news story). The drug, which increases sensitivity of the fast skeletal muscle troponin complex to calcium and thereby increases skeletal muscle force, did not lead to a significant change in a functional score in ALS patients, called the ALS Functional Rating Scale in its revised form (ALSFRS-R). However, treatment with the drug decreased the rate of decline of Slow Vital Capacity consistently across all subgroups of ALS patients, results which led to the decision to continue development of the drug for ALS. Click here to read about these exciting new developments.

Genervon Announces Promising Results of its Phase IIb Trial of GM6 in ALS and PD

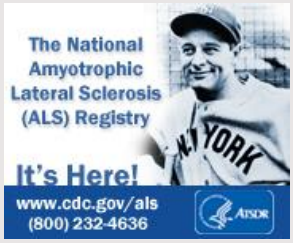
February 1-3, 2015: Cambridge, UK: Biomarkers for Brain Disorders: Challenges and Opportunities

Feb 17-19, 2015: Boston, MA: World CNS Summit 2015

Feb 23-24, 2015: Manchester, UK: 10th Annual Biomarkers Congress

March 2015

March 1-3, 2015: San Diego, CA: 9th Annual Drug Discovery for Neurodegeneration Conference



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In July this year, Genervon announced promising results of its Phase IIb clinical trial of GM6 in ALS and Parkinson's disease (PD) based on biomarker data from the trial (see July 2014 news story). The biotechnology company just released the full results of the study, which provide further support of the disease-modifying effects of this peptide therapy. GM6 is a peptide regulator that modulates inflammatory processes, has potentially beneficial effects on other pathways implicated in ALS, such as apoptosis and hypoxia. In the small trial of 8 patients, GM6 reduced the decline of the ALS Functional Rating Scale in its revised form (ALSFRS-R) compared to historical controls, as well as slowed decline in Forced Vital Capacity. Genervon has both fast track and orphan drug designation for GM6 in ALS, and has submitted the results to the FDA for further guidance on next steps. Click here to read more.

Two Leading Neuroscientists Join Biogen-Idec to Advance Neurodegenerative Disease Research

Biogen-Idec is taking further steps to advance its research and development efforts in neurodegenerative diseases. After appointing Donald Johns to head the ALS iHUB in August (see Aug 2014 news story), Biogen has announced that two world renown neuroscientists have joined the company: Dr. Christopher Henderson joins as Vice President of Neurology and Dr. Richard Ransohoff as senior research fellow of neuroimmunology. Dr. Henderson joins Biogen-Idec from Columbia, where he was the co-founder of the Center for Motor Neuron Biology and Disease, and he is the director of TARGET-ALS. Dr. Ransohoff is a leading neuroimmunologist, who joins the company from the Cleveland Clinic, where he directed the Neuroinflammation Research Center. These two outstanding scientists will now focus on advancing Biogen-Idec's research and drug discovery for neurodegenerative diseases, including ALS. Click here to read more.

Astrazeneca and University of Cambridge Partner on Neurodegenerative Disease Research

Astrazeneca, together with its biologics arm, Medimmune, has expanded its strategic alliance with University of Cambridge beyond oncology into research and development for neurodegenerative diseases. The focus of the four new joint projects will be on biomarkers, drug discovery and personalized medicine. The partnership merges the expertise of world class researchers from the University of Cambridge with drug development expertise and experimental tools from Astrazeneca and Medimmune. As part of the collaboration, Astrazeneca will also share proprietary compounds in its development pipeline, such as mTOR and AKT inhibitors, to potentially identify new uses of these drugs. Hopefully, advances from these projects will also lead to new targets and candidate biomarkers for ALS. Click here to read more.

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