ALS Forum e-Newsletter Volume 122 **February 27, 2015**

We value your feedback! In order to continue to improve the ALS Forum and e-Newsletter, we would greatly appreciate your responses to our survey here.

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.

Please provide your feedback on the ALS Forum here!

Resources:

ALS Drugs in Development Database

The ALSGene tool: www.ALSGene.org

The PRO-ACT Database: www.ALSDatabase.org

NEALS Biofluid Repository Available to Researchers

Funding Opportunities:

EU Joint Programme-Neurodegenerative Disease Funding. Pre-proposal due Mar 10, 2015.

New York Stem Cell Foundation Stem Cell Investigator Award.Applications due Mar 18, 2015.

CDC Grant: Analyze and Evaluate Potential Risk Factors for ALS. Applications due Apr 6, 2015.

California Stem Cell Agency (CIRM) 2.0 Awards. Due last business day of each month.

Webinars:

Research News

Largest Exome Sequencing Project To Date Reveals New ALS Gene
An international collaborative effort, led by researchers from Columbia University in New York, HudsonAlpha Institute for Biotechnology in Huntsville, Alabama, and Biogen Idec in Cambridge, Massachusetts, has identified a new ALS gene called TANK-binding kinase 1, or TBK1. According to the publication in the February 19 ScienceExpress online, the largest exome sequencing project of ALS patients to date revealed TBK1 mutations in approximately 1% of sporadic ALS patients. Since TBK1 is requires for both inflammatory (see May 2011 Webinar) and autophagy pathways (see July 2014 news story; June 2010 news story), the new findings further implicate dysfunction in these cellular processes in ALS pathophysiology. Click here to read more about this exciting new discovery.

Brain Banks Rapidly Evolving But Facing Funding Challenges
Brain banks have been a valuable resource for researchers and clinicians for decades. Banked tissue from ALS patients contributed to the discovery of TDP-43, and FTD patient samples helped identify the role of C9ORF72 repeats expansions in ALS and FTD (see Sept 2011 news story). Autopsy tissue is being used to characterize and improve brain imaging agents, to improve patient diagnosis and treatment, and to highlight potential new therapeutic approaches. However, the public funding that has supported these banks is gradually drying up, and brain banks are facing the need to scale down, even at a time when the demand for tissue is high. Click hereto read about the history and purpose of brain banks, as well as existing brain banking networks worldwide.

TMEM106B Affects TDP-43 Pathology Beyond FTD
Transmembrane protein 106B (TMEM106B) variants were originally identified as genetic risk factor for frontotemporal dementia (FTD) in patients with frontotemporal lobar degeneration (FTLD) with TDP-43 pathology (see Aug 2012 news story; Feb 2010 news story). However, little is known about the protein's function and how it affects TDP-43 pathological spreading in the central nervous system. According to a publication in the February 4 Neurology online by Julie Schneider and colleagues at the Rush Alzheimer's Disease Center in Chicago, TMEM106 variants contribute to TDP-43 pathology above and beyond FTD. The researchers further confirm that TMEM106 acts upstream of progranulin, another known FTD gene (see Nov 2014 conference

ALSA/NEALS Webinar: Clinical Trial Design and Evaluation of Small Trials. March 9, 2015, 3:00-4:00pm EST.

Upcoming Meetings:

March 2015

March 11-14, 2015: Washington, DC: MDA Scientific Conference.

March 18-20, 2015: Newcastle upon Tyne, UK:8th Annual MRC Neuromuscular Translational Research Conference.

March 18-22, 2015: Nice, France: 12th international Conference on Alzheimer's and Parkinson's Diseases.

April 2015

April 7-11, 2015: Soelden, Austria: The 17th International Neuroscience Winter Conference.

April 7-8, 2015: San Francisco, CA: The 10th Annual Neurotech Investing and Partnering Conference.

April 18-25, 2015: Washington, DC: The American Academy of Neurology (AAN) Annual Meeting.

April 21-23, 2015: Boston, MA: BioIT World Conference & Expo.

April 27-29, 2015: Boston, MA: Stem Cell Summit '15.

May 2015

May 5-7, 2015: Philadelphia, PA: Biomarker & Diagnostics World Congress 2015

news).Further work is needed to elucidate exactly how TMEM106B and progranulin contribute to TDP-43 pathology. Click here to read more.

NAD+ Depletion Underlies Neuronal Death Triggered by Misfolded Prion Proteins

Misfolded proteins, which accumulate in neurodegenerative diseases such as ALS, Alzheimer's and Parkinson's disease, can trigger misfolding and aggregation of their non-mutant protein counterparts in a prion-like manner. In ALS, both TDP-43 and SOD1 demonstrate prion-like properties (see Feb 2014 news story; Nov 2013 news story) and may contribute to the characteristic spreading of neurodegeneration in the central nervous system. A new study published February 11 in Brain reveals a mechanism underlying toxicity of prion proteins that may also apply to other protein misfolding neurodegenerative diseases. Researchers led by Corinne Lasmézas and colleagues at the the Scripps Research Institute in Jupiter, Florida demonstrate that in both neuronal cultures and in mouse models infected with a toxic misfolded prion protein (TPrP), depletion of nicotinamide adenine dinucleotide (NAD+), a metabolite necessary for energy production, drives neuronal death. TPrP-induced neuronal death could be prevented by NAD+ supplementation. The team is now developing screening assays for compounds that can restore NAD+ levels and may have therapeutic promise for diseases linked to protein misfolding. Click here to read more.

Drug News

OptiKira to Develop Therapeutics Targeting the Unfolded Protein Response

A new startup company developing therapeutics with potential applications to ALS has just been launched! The company, OptiKira, is developing small molecules that can prevent cell death due to misfolded or unfolded proteins. The scientific founding team, which includes Scott Oakes and Feroz Papa from University of California, San Francisco (UCSF) and collaborators from UCSF and University of Washington, have made seminal discoveries on the role of the unfolded protein response (UPR) in cellular metabolism and mechanisms by which overactivation of the UPR leads to cell death. The platform company will initially focus on inhibitors of inositol-requiring enzyme-1α (IRE1α), a key activator of the UPR. OptiKira's platform could have direct applications to ALS, based on increasing evidence that inhibition of the UPR may be a promising therapeutic avenue in neurodegenerative diseases linked to protein misfolding (see Oct 2013 news story; June 2008 news story). Click here to read more.

Skin Biopsies May Hold Promise as Diagnostic Test in Alzheimer's and Parkinson's Diseases

A new study to be presented in April at the American Academy of Neurology Meeting in Washington, DC, suggests that skin biopsies may help diagnose Alzheimer's (AD) and Parkinson's disease (PD). Researchers led by Ildefonso Rodriguez-Leyva at the Central Hospital at the University of San Luis Potosi in Mexico hypothesized that due to the shared embryonic origin of skin and brain tissue, misfolded proteins characteristic of neurodegenerative diseases may also be present in the

May 21-23, 2015: Verbania, Italy: European Network for the Cure for ALS (ENCALS) Annual Meeting.

June 2015
June 19 - 24, 2015: Breckenridge, Colorado:Keystone Symposia: Autophagy

September 2015

Sept 19-20, 2015: Montreal, Canada: 10th Annual Symposium of the Fondation Andre-Delambre.

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skin. In a small study of AD and PD patients as well as patients with other forms of dementia and healthy controls, the researchers found elevated levels of tau protein in AD patient skin samples. Similar results were obtained with alpha-synuclein in the PD skin biopsies. Further confirmation of these findings in a larger cohort is necessary, but if confirmed, this approach could hold promise not only for AD and PD, but also for other protein misfolding diseases, such as ALS. Click here to read more.

New Speech Generating App Uses Patient's Own Voice

UK company Therapy Box has just launched a new application to replace standard text-to-speech devices with a speech generator based on the user's own voice. The Predictable 4 app is a text based Augmentative and Alternative Communication application specifically designed for people with speech impairments resulting from ALS, stroke or other causes. The app now incorporates a program called ModelTalker, which enables users to create a personalized synthetic voice based on their own voice to use in text-based communication. This is an exciting new development this is a significant milestone for patients who have until now relied on generic voices available in speech generating devices. Click here to read more.

Amarantus and Anavex Partner to Develop Alzheimer's Disease Diagnostics

Clinical stage biotechnology company Anavex Life Sciences has partnered with Amarantus Bioscience Holdings to provide biomarker services for Anavex's Alzheimer's disease (AD) drugs. Anavex's sigma-1 receptor agonist, Anavex 2-73, is in Phase II trials for Alzheimer's disease and is in preclinical development for ALS (see March 2014 news story). The company will use Amarantus' LymPro Test to examine the effect of Anavex 2-73 and Anavex Plus on CD69 biomarker expression in peripheral blood lymphocytes of AD patients. The companies have also agreed to work together on blood-based biomarkers for a potential Phase III clinical trial of these drug candidates. This partnership could help lay the ground for biomarker studies in a future ALS clinical trial. Click here to read more.

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