ALS Forum e-Newsletter Volume 129 **June 12, 2015**

Visit the ALS Forum website to read the complete stories featured in this e-newsletter. Please let your friends and colleagues who may be interested in learning more about ALS know about the ALS Forum. It is easy to sign up for the newsletter 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

VABBB ALS CNS Tissue Request Information Site

Funding Opportunities:

CreATE Consortium ALS Biomarker RFA. Letter of Intent Due: June 26, 2015.

CDC Presolicitation: Establishing a Biorepository of ALS. Full solicitation to be posted around June 16, 2015.

ALS Therapy Alliance (ATA) RFP. Applications due Oct 15, 2015.

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

Research News

Could Skin Be a New Diagnostic Tissue for Neurodegenerative Disease?

Many of the neurodegenerative disease proteins that could provide crucial diagnostic information are not detectable via affordable, non-invasive methods, such as blood tests. At this year's American Academy of Neurology Annual Meeting, several groups of scientists presented intriguing data on the potential of skin samples for diagnosing neurodegenerative diseases. Nicolas Dupré, François Gros-Louis, and colleagues of Laval University, Québec examined skin biopsies from healthy controls, sporadic ALS patients and from pre-symptomatic C9ORF72 mutation carriers. In all but the healthy controls, the skin cells contained TDP-43 cytoplasmic inclusions, a pathological hallmark of ALS (see Jan 2010 news story). They next used a tissue engineering approach to develop organized skin tissue in culture from human fibroblasts, and found that fibroblasts from ALS patients failed to fully differentiate to form mature skin. Strikingly, the synthetic skin from the sporadic ALS patients and presymptomatic mutation carriers also contained cytoplasmic TDP-43 inclusions. In a separate study, researchers from the Universidad Autónoma de San Luis Potosi identified elevated levels of phosphorylated tau aggregates in samples from Alzheimer's and Parkinson's disease patients, but not healthy controls (see Feb 2015 news). More research is needed, but skin samples could provide a rich resource for identifying biomarkers of neurodegenerative disease. Click here to read more.

Diabetes and ALS - A Relationship That's Hard to Understand

Is there an association between diabetes and the risk of developing ALS? Identifying the link between the two diseases

Webinars:

ALSA/NEALS ALS Clinical Trial Pipeline Webinar. Dr. Merit Cudkowicz. June 15, 2015: 1:00-2:00PM EST.

Upcoming Meetings:

June 2015

June 14-17, 2015: Heidelberg, Germany:EMBO Symposium on Mechanisms of Neurodegeneration.

June 14-18, 2015: San Diego, CA: 19th International Congress of Parkinson's Disease and Movement Disorders.

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

June 20-23, 2015: Berlin, Germany: 1st Congress of the European Academy of Neurology.

June 24-27, 2015: Stockholm, Sweden:International Society for Stem Cell Research Meeting.

July 2015

July 6-7, 2015: San Francisco, CA: Neurological Disorders Summit.

July 15-18, 2015: Bilbao, Spain: XII European Meeting on Glial Cells in Health and Disease.

July 27-29, 2015: Rome, Italy: 4th International Conference and Exhibition on Neurology and Therapeutics.

September 2015

could shed light on new pathways involved in ALS and potential therapeutic targets. However, scientists attempting to address this question are reporting conflicting results. In the June 1 *JAMA Neurology*, senior author Marc Weisskopf and colleagues from the Harvard T.H. Chan School of Public Health in Boston found that in Denmark, diabetics had a 39% lower risk of developing ALS. A separate study in the Swedish Population confirmed this association (Mariosa et. al., 2015). However, according to a publication in the May 2 *Journal of Epidemiology,* the opposite association exists *in* the Taiwanese population. Researchers led by senior author Chung-Yi Li of National Cheng Kung University in Tainan City, Taiwan, reported that in Taiwan, ALS patients under the age of 65 had a 67% higher risk of ALS. Nevertheless, once a patient has been diagnosed with ALS, diabetes does not significantly shape their prognosis, according to a paper in the April 21 *Muscle & Nerve* led by senior author Timothy Miller of the Washington University School of Medicine in St. Louis. To read more about the debate, click here.

A MicroRNA that May Prevent Motor Neuron Death

In people with ALS, the limb-innervating lateral motor column (LMC) neurons are among the most vulnerable to degeneration. The cause of this increased vulnerability remains a mystery, but recent studies suggest that regulation of apoptosis by microRNAs (miRNAs) may play a key role: when Dicer, a miRNA-processing enzyme, is knocked-out in mouse embryos, LMC motor neurons degenerate (Chen and Wichterle, 2012). In the May 21 *Cell Reports* online, a research team led by senior author Jun-An Chen from the Academia Sinica in Taipei, Taiwan, identified a cluster of miRNAs known as miR-17~92, which are highly expressed in LMC motor neurons and are capable of preventing apoptosis. Accordingly, limb-innervating neurons began to perish when miR-17~92 was knocked out of mouse embryos. In order to identify the miRNA targets, joint first authors Ying-Tsen Tung and Ya-Lin Lu examined gene expression in the neurons and identified the tumor suppressor phosphatase and tensin homolog (PTEN) as a key target of the miRNAs. What is the role of PTEN and miR-17~92 in ALS? The researchers plan to examine their function in detail in ALS mouse models and patient cells. Clickhere to read more.

Activin Generates Hope for Axon Regeneration

The myelin sheath that engulfs axons ensures rapid neuro-transmission along the length of the axon. But in the central nervous system (CNS), the myelin sheath also secretes growth-inhibiting factors that stunt regeneration. As reported in the May 21 *Neuron*, researchers led by Clifford Woolf and Michael Costigan from the Boston Children's Hospital, together with collaborators from the University of California, Los Angeles, embarked on a quest for new genes that promote axonal

Sept 3-6, 2015: Prague, Czech Republic: 2nd World Congress on Neurotherapeutics.

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

Sept 27-29, 2015: Chicago, IL: American Neurological Association Annual Meeting.

Sept 30 - Oct 4, 2015: Brighton, UK: 20th International World Muscle Society Congress.

October 2015

Oct 15-16, 2015: Chicago, Illinois: 10th Brain Research Conference RNA Metabolism in Health and Disease.

Oct 17-21, 2015: Chicago, Illinois: The Society for Neuroscience Annual Meeting.

Oct 31 - Nov 5, 2015: Santiago, Chile. World Congress of Neurology.

December 2015

Dec 11-13, 2015: Orlando, FL: International Symposium on ALS/MND.

2016

January 2016

Jan 24-27, 2016: Santa Fe, New Mexico: Keystone Symposium on Molecular and Cellular Biology: Axons: From Cell Biology to Pathology.

April 2016

Apr 2-6, 2016: Solden, Austria: 18th International

regeneration. First author Takao Omura cultured dorsal root ganglion (DRG) neurons onto CNS myelin derived from nine, genetically diverse mouse strains, searching for one strain that fairs better than other. One strain stood out - the CAST/Ei strain. These mice, descendants of wild mice in Thailand, express high levels of Activin, a protein in the TGF-β signaling pathway. When this protein was added to the DRG neuronal cultures derived from the common mouse strain C57BL/6 mice, axonal sprouting increased. Could pro-Activin therapy be beneficial in ALS? Clickhere to read more.

Drug News

Eisai Submits New Drug Application for Ultra-high Dose Mecobalamin for ALS

The Japanese pharmaceutical company Eisai has submitted a new drug application (NDA) in Japan for approval of ultra-high dose mecobalamin for treatment of ALS. Mecobalamin, one of the coenzyme forms of the vitamin B12, is already approved for treatment of other indications, such as peripheral neuropathies. In 2004, Eisai initiated a double-blind, placebo-controlled Phase II/III clinical trial of ultra-high dose mecobalamin in ALS, using time to event (ventilation or death) and change in the Japanese ALSFRS-R as primary endpoints. The results of the study suggested a trend toward a beneficial effect, but the difference in the primary endpoints between treated and untreated patients was not statistically significant. However, based on the pronounced treatment effect in two patient subgroups and the dire unmet need for therapies in ALS, Eisai has decided to move forward with the NDA submission in Japan. The results of the late stage clinical trial were presented at the this year's American Academy of Neurology Annual Meeting meeting in Washington, DC in April. Click here to read more.

Q-Therapeutics Cleared to Initiate Clinical Trials in ALS

Salt Lake City, Utah-based Q-Therapeutics has obtained FDA clearance of its Investigational New Drug (IND) application to initiate a Phase I/II trials of their proprietary stem cell therapy in ALS patients. The stem cells, called Q-cells, are purified human glial-restricted progenitor cells, which generate two essential cell types for neuronal protection and repair, astrocytes and oligodendrocytes. Preclinical studies have shown that *Q-Cells*localize to motor neurons in the spinal cord after transplantation and improve survival and motor function in ALS rat models. Q-cells have also been shown to survive longer in the central nervous system than transplanted mesenchymal stem cells. The FDA has already granted *Q-Cells* orphan drug designation (see April 2014 news), and the Phase I/II study will

Neuroscience Winter Conference.

April 16-23, 2016: Vancouver, Canada:American Academy of Neurology (AAN) Annual Meeting.

July 2016

July 2-6, 2016: Copenhagen, Denmark:10th FENS Forum of Neuroscience

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begin upon securing funding and institutional review board (IRB) approval. Click here to read more.

Cytokinetics and the ALS Association Expand Partnership

Cytokinetics and the ALS Association (ALSA) have announced an expanded partnership to advance support services for ALS patients and caregivers and to increase disease awareness. The partnership, which spans both national and regional levels, will include increased sponsorship of the National Walks to Defeat ALS®, initiatives of the ALSA Golden West Chapter, and a challenge grant for care services for ALS patients in the San Francisco Bay Area. Cytokinetics is the developer of tirasemtiv, an activator of the fast skeletal muscle troponin complex, as a therapy for ALS, and is planning a Phase III trial in ALS based on results from the Phase II trial suggesting the drug improves respiratory muscle function. The partnership with ALSA is an opportunity for the company to expand its support of patient services in parallel to advancing its clinical program.
Click here to read more.

InVivo Therapeutics Enrolls Third Patient in Trial of Biodegradable Scaffold for Spinal Cord Injury

A third spinal cord injury patient has been enrolled in InVivo Therapeutics' pilot clinical trial testing a novel biodegradable scaffold as a therapeutic device for spinal cord injury. The surgery was performed at the Carolinas Medical Center in Charlotte, North Carolina only 3.5 days after the injury. The Neuro-Spinal Scaffold is based on a technology co-invented by Robert Langer from the Massachusetts Institute of Technology in Cambridge, MA and Joseph Vacanti now at the Massachusetts General Hospital in Boston, MA, and is designed to form a substrate for nerve sprouting at the epicenter of the wound. In preclinical studies, the device has helped decrease cyst formation and damage to spinal cord tissue following injury. The current trial aims to test safety and efficacy of the Scaffold in five patients with acute spinal cord injury as a prelude to a future pivotal study. Although the company's focus at this stage is spinal cord injury, the platform holds promise for promoting neuronal repair in neurodegenerative diseases, such as ALS and multiple sclerosis.
Click here to read more.

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