ALS Forum e-Newsletter Volume 123 **March 13, 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

VABBB ALS CNS Tissue Request Information Site

Funding Opportunities:

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

Department of Defense ALS Research Program. Preannouncement. FY15 RFP Announcements to come in April 2015.

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

Conference News

Keystone Symposium: Neuroinflammation in Diseases of the Central Nervous System

The complex role of microglia in neurodegenerative disease has long baffled researchers. What is the role of this class of resident macrophages in the central nervous system (CNS), and how does it differ from the role of infiltrating macrophages from other regions of the body? Why are microglia neuroprotective under certain circumstances, but detrimental to neurons under other conditions? Is neuroinflammation a cause or effect of neurodegenerative processes? These topics and others were the subject of intense debate at the Keystone symposium on "Neuroinflammation in Diseases of the Central Nervous System (CNS)," held January 25-30 in Taos, New Mexico. Click below to read Jessica Shugart's full report from the Symposium on cutting-edge research and the controversies surrounding neuroinflammation in the CNS.

Part I provides an overview of the range of topics debated surrounding neuroinflammation in the CNS.
Part 2 addresses microglial origins and how their local environment helps seal their fate.
Part 3 describes how the cells change in the diseased brain.

Research News

Galectin 3-TLR4 Signaling Triggers Neuroinflammatory Response in Microglia

Several studies point to the contribution of activated microglia to neurodegeneration in ALS (see March 2014 news story). However the mechanisms that trigger the microglial inflammatory response and how they lead to neuronal demise remain elusive. According to a publication in the March 10 *Cell Reports*, the sugar-binding proteins galectins may play a central role. A research team from the laboratories of Bertrand Joseph at the Karolinska Institute in Stockholm and Tomas Deierborg at Lund University in Sweden

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

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

Upcoming Meetings:

March 2015

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

report that galectin-3 (Gal3) secreted by activated microglia acts as a paracrine ligand for Toll-like receptor 4 (TLR4) on neighboring microglia and exerts pro-inflammatory effects. In brain ischemia models and models of lipopolysaccharide-induced neuroinflammation, disruption of the Gal3-TLR4 interaction is neuroprotective and reduces inflammation. Furthermore, Gal3 is found in postmortem spinal cord of sporadic ALS patients. However, Gal3's role in ALS is still a matter of controversy, since its deletion in mouse models of ALS exacerbates neuroinflammation (Lerman *et. al.*, 2012). How can these discrepancies be resolved? Click here to find out more.

Sage Bionetworks Launches Public Repository of Large-Scale Datasets in AD

Multidimensional, large-scale datasets collected and compiled through international collaborative efforts are valuable resources to generate new insights on disease mechanisms, potential therapeutic targets, and clinical trial design (see *e.g.* Oct 2014 news story). The non-profit biomedical research organizationSage Bionetworks (and its partners DREAM) has spearheaded a variety of projects to improve understanding of disease through predictive modeling and computational challenges (see June 2014 news story), including collaborating with Prize4Life oncomputational challenges based on the PRO-ACT database (see also Nov 2012 news story). The organization has now launched a publicly available repository of AD-related datasets generated as part of a public-private partnership called Accelerating Medicines Partnership's (AMP) Alzheimer's Initiative. These initial datasets were generated from human brain samples, and include data types such as RNA-sequencing, genotyping data, clinical data and more. Sage is in the process of organizing and standardizing the datasets, which are publicly available to researchers worldwide. Lessons learned and new insights from this data initiative can help inform similar data initiatives in ALS.
Click here to read more.

Largest Human Epigenome Dataset Made Publicly Available

A collaborative research effort that spanned 7 years and included 258 researchers has finally come together with the public release of the "largest collection of human epigenomes" yet. In the February 19 *Nature*, Manolis Kellis from MIT and colleagues in the Roadmap Epigenomics Consortium present a detailed description of 111 datasets from human tissue and cell lines profiled for epigenetic modifications, such as histone modifications and DNA methylation, which shape whether a gene is expressed or remains silent. Although the reference dataset was derived from healthy tissue only, the data can yield insights on disease mechanisms too by helping identify expression patterns of

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

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: Berlin, Germany: 1st Congress of the European Academy of Neurology.

September 2015

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.

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

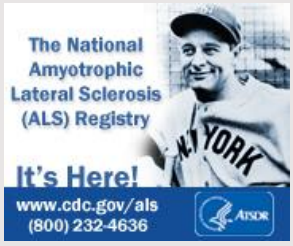
December 2015
Dec 11-13, 2015: Orlando, FL: International Symposium on ALS/MND.

disease genes, as well as putative functions of genetic loci where variants increase risk of disease. In a small set of Alzheimer's disease (AD) samples, high-risk variants were found predominantly in genomic regions that regulate immune function, providing further support for the role of the immune system in the disease. A second paper in the February 19Nature by Kellis, Li-Huei Tsai and colleagues corroborated these findings using epigenome datasets from a mouse model of AD. These studies underscore the merit of analogous studies in ALS to derive insights on the function of genetic variants and the impact of tissue-specific gene expression in ALS (see Sept 2014 news story). Click here to read more.

Drug News

Neuralstem Announces Promising Phase II Clinical Trial Results of NSI-566 in ALS
Neuralstem has announced top line results of its Phase II clinical trial of NSI-566 in ALS (see Nov 2014 news story). The trial enrolled 15 ALS patients who all received injections of Neuralstem's proprietary therapy of human spinal cord-derived neural stem cells. The study safety results were positive, and treatment was well tolerated at the maximal dose examined. On the efficacy front, the results were encouraging as a subset of patients exhibited stabilization of disease progression. However, further confirmation of the positive effect will be necessary in a larger cohort. According to Jonathan Glass, an investigator in the trial and director of the Emory ALS Center "Elucidating which factors define a patient who may have a therapeutic response to the stem cell treatment will be the next key challenge". A larger controlled trial is expected to begin later this year, with a parallel effort to develop approaches to pre-select the patients most likely to respond. Click here to read more.

Whole Exome Sequencing-Based Diagnostic Service Now Available for Rare Neurological Disorders
Quest Diagnostics has announced its first whole exome sequencing service for diagnosis of rare pediatric neurological disorders with suspected genetic causes. The lab-based test called Neurome, which was developed by the diagnostics company Personalis specifically probes genomic regions implicated in nervous system function, both within coding regions of known clinical significance as well as in a limited number non-coding regions. The exome sequencing results are subsequently interpreted by a clinical team in conjunction with a comprehensive clinical evaluation to make the final evaluation of the patient's suspected disorder. Although the Neurome test is currently focused on genes associated with pediatric disorders, this test



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presents another advance in the field of diagnostics that could ultimately lead to an ALS diagnostic test based on analysis of a broad range of ALS genetic risk factors (see July 2014 news story; April 2012 news story) and genetic risk factors to be revealed (*e.g.* through efforts such as Project MinE - see Oct 2014 news story). Click here to read more.

Acapela Group Application Helps ALS Patients Create Their Own Voice

One of the most debilitating aspects of ALS as reported by patients is loss of the ability to speak. Augmentative and Alternative Communication (AAC) solutions developed to synthetically recreating a patients voice before it is lost are a big step forward in maintaining this aspect of patients' identity.Acapela Group announced the launch of a new application called 'my-own-voice', which similarly to ModelTalker (see Feb 2015 news story) helps patients create a synthetic voice based on their own voice, rather than using a generic synthetic one. The app has already been tested on 10 patients (including at least one ALS patient), who have helped the company continue to improve the product. The company is currently establishing partnership with major AAC vendors on the market, and in discussions to collaborate with several major ALS clinics. Click here to read more about the recording process and feedback from an ALS patient.

MDA Hires Two New Scientific Program Officers

The Muscular Dystrophy Association has announced the hire of two new scientific program officers, Amanda Haidet-Phillips and Laura Hagerty, to help lead their efforts to advance translational research for neuromuscular diseases and motor neuron diseases. Haidet-Phillips has made noteworthy contributions to ALS research during her post-doctoral training with Nicholas Marakagis at Johns Hopkins University in Baltimore, and doctoral training with Brian Kaspar at the Center for Gene Therapy at The Research Institute at Nationwide Children's Hospital in Columbus, Ohio (see Aug 2011 news story). Her focus at the MDA will be on ALS, Spinal Muscular Atrophy (SMA) and spinal-bulbar muscular atrophy (SBMA). Hagerty joins MDA from GlaxoSmithKline, where she focused on developing therapies for Duchenne Muscular Dystrophy (DMD). These new hires reflect MDA's aggressive plan to increase its research funding, as well as form new partnerships with pharmaceutical companies and other stakeholders. Clickhere to read more.

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