ALS Research Forum e-Newsletter Vol. 152 **May 27, 2016**

Visit the ALS Research Forum to read the complete stories featured in this e-newsletter. Friends and colleagues can sign up for the newsletter here. Follow us on Facebook and Twitter for the latest updates.

We just launched our free Job Opportunities bulletin board for positions in the field of ALS and FTD. Check it out ***here.*** ***Please let us know if you have any open positions in your lab or company!***

FDA Guidance Document - Open Comment Period Ends May 30

The ALS research community is encouraged to review and comment on the Draft FDA Guidance Document on ALS Drug Development. **The deadline for submitting comments is May 30, 2016.** For more information about the FDA guidance document and its importance, click here. To download the draft guidance, click here.

Conference News

Highlights of the American Academy of Neurology Meeting

New discoveries on ALS risk factors and biomarkers were among the highlights on ALS presented at the Annual American Academy of Neurology Meeting, held April 15-21 in Vancouver, British Columbia. Researchers presented findings on dipeptide repeat proteins as potential biomarkers of C9ORF72 ALS, as well as on clinical features associated with the C9ORF72 and the TBK1 mutations (see Feb 2015 news). Also featured were presentations on APOE2 as a risk factor for dementia in ALS (see Mar 2016 news), and on the utility of slow vital capacity (SVC) as an outcome measure in drug trials.

Research News

Environmental Exposure to Pesticides Raises Risk of ALS

In the May 9 *JAMA Neurology*, researchers report that people with ALS have elevated blood levels of long-lasting environmental toxins, and the exposure is associated with a 2 to 5-fold increase in risk of developing ALS. These conclusions were derived from analysis of survey data in combination with objective measurements of toxic chemical levels in the blood. The researchers focused on 122 stable pollutants that are

detectable in blood even decades following exposure, however, larger studies are needed to determine whether these specific chemicals increase the risk of development ALS or rather are general markers of high rates of exposure to pesticides. An accompanying editorial discusses the strengths of this study, as well as challenges with interpretation of case-controlled epidemiological studies.

In ALS Astrocytes, Upregulated Connexins Contribute to Motor Neuron Death
Connexin 43 is the primary astrocyte connexin, a family of proteins that form gap junctions, which enable direct flow of ions and metabolites between cells. According to a new study published in the April 16 *Glia* online, expression of Cx43 is elevated in spinal cord astrocytes of SOD1-G93A mice, as well as in postmortem tissue from sporadic ALS patients and in astrocytes derived from iPSCs from ALS patients. In co-cultures of SOD1-astrocytes with motor neurons, selective blockade of Cx43 hemichannels or gap junctions prolonged motor neuron survival as compared to motor neurons with untreated astrocytes. The results point to elevated expression of astrocytic gap junctions or their component hemichannels as a potential mediator of astrocyte toxicity in ALS.

RNA-Binding Proteins of Stress Granules Exacerbate Tau Toxicity
In times of stress, complexes of RNA and proteins form in the soma and dendrites to enable regulation of translation during the cellular stress response. Dysfunction of these stress granules is associated with many neurodegenerative diseases, including ALS and frontotemporal dementia (see Nov 2015 news). In the May 17 Cell Reports, researchers report that the microtubule associated protein tau interacts with the RNA-binding protein TIA1, a component of stress granules, and regulates its distribution and stress granule assembly. Conversely, TIA1 regulates tau misfolding and toxicity. These studies identify an intricate relationship between tau and the RNA-binding proteins of stress granules and reveal a potential function for the somato-dendritic mislocalization of tau typical of tauopathies.

SP110 is a Modifier Gene of Canine ALS-like Disease
Canine degenerative myelopathy (DM) is a neurodegenerative disease in dogs with similarities to some forms of ALS in humans. In 2008, DM was linked to mutations in SOD1, which underlies approximately 20% of familial ALS cases (see Nov 2008 news). In the May 16 PNAS, report that SP110 variants affect both age of onset and penetrance of DM, based on a results of a genome-wide association study in SOD1-homozygous dogs that either exhibited the disease phenotype or were unaffected. SP110 regulates gene transcription in leukocytes, and the identified variants modify its expression in blood cells. These findings providing a genetic link between immune system dysfunction and the pathogenesis of ALS, and raise further questions about how SP110 modifies the course of disease in dogs, and potentially in humans.

Deals and Partnerships

ViroMed's VM202 is Granted FDA Fast-Track Designation
VM202, a gene therapy developed by ViroMed (dba VM BioPharma in the U.S.), has

been granted fast-track designation by the US FDA as a candidate therapy for ALS. A Phase I/II clinical trial is ongoing to test the safety and tolerability of intramuscular injections of VM202, and the results are slated to be published later this year. VM202 increases production of hepatocyte growth factor (HGF), which induces angiogenesis and acts as neurotrophic factor. In rodent models of ALS, overexpression of HGF has been shown to prolong survival and ameliorate disease (Sun et al., 2002; Ishigaki et al., 2007) . VM202 is also being tested for other indications, including diabetic neuropathy and ischemic cardiovascular disease in Korea, China, and the U.S.

Nanologica and Alcyone Lifesciences Collaborate to Develop ALS Therapy
Two companies developing specialized drug delivery systems have signed a license agreement to develop a combination therapy to treat motor neuron disorders. Nanologica is a materials technology company developing specialized nanoporous silica particles, called NLAB Silica, which can be loaded with a drug of interest to optimize drug stability and delivery. In collaboration with Elena Kozlova of Upsalla University, the company is developing an ALS therapy that combines embryonic stem cell-derived cells with trophic factors encapsulated in the NLAB Silica particles (Garcia-Bennett et al., 2013, Garcia-Bennet et al., 2014). In the new effort, Nanologica is teaming up with medical device company Alcyone Lifesciences to improve CNS delivery of the trophic factors using their specialized CNS infusion systems, and develop a combination drug/stem cell therapy targeting motor neuron disorders.

Funding Opportunities:

June 2016

CIRM Partnering Opportunity for Translational Research Projects. Applications due July 15, 2016.

NINDS Clinical Trial Readiness for Rare Neurological and Neuromuscular Diseases. LOI due July 18, 2016.

July 2016

NEW! The Paulo Gontijo Institute (PGI) International Medicine PG Award. Applications due July 1, 2016.

September 2016

NEW! Frick Foundation for ALS Research Grants. Applications due September 30, 2016.

Full List of Funding Opportunities >>

Job Opportunities:

Research Coordinator, Senior.
University of Pennsylvania
Philadelphia, PA.

Postdoctoral Position in Neurodegeneration Research and RNA Biology
Johns Hopkins University School of Medicine.
Baltimore, MD.
Full List of Job Opportunities >>

Upcoming Meetings:

July 2016

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

July 10-14, 2016: Arlington, VA: RESNA Annual Conference.

August 2016

August 7-12, 2016: Girona, Spain: Gordon Research Conference on Neurobiology of Brain Disorders.

Full List of Upcoming Meetings>>

Resources:

ALS Drugs in Development Database

ALSGene

Alzforum ALS Mouse Model Database

The PRO-ACT Database

NEALS Biofluid Repository Available to Researchers

VABBB ALS CNS Tissue Request Information Site

TargetALS Core Facilities