ALS Research Forum e-Newsletter Vol. 169 **March 28, 2017**

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Research News

A New Study Fires Up the Debate About Misfolded SOD1 and its Potential Role in Sporadic ALS

Misfolded SOD1 may not play a key role in sporadic ALS according to a new study led by University of California San Diego's **Sandrine da Cruz**, **Don Cleveland** and **John Ravits**. The post-mortem tissue analysis, which involved more than 50 people with sporadic ALS, found no misfolded SOD1 in the brain or spinal cord by immunostaining or immunoprecipitation using seven conformational-specific misfolded antibodies. The study according to **John Ravits**, indicates that reducing levels of misfolded SOD1 is unlikely to be helpful in treating sporadic ALS. The study is published on February 28 in *Acta Neuropathologica.*

Check out our feature to learn more about the study, including its implications for the treatment of non-SOD1 ALS.

Neurofilament Light Chain as Prognostic Biomarker in ALS

NfL continues to show promise as a biomarker for ALS prognosis according to a study published on March 6 in *JAMA Neurology*. The retrospective, longitudinal 3-year study, which involved 94 people with ALS, found that NfL levels in CSF inversely correlated with overall survival time (HR, 2.45; 95% CI, 1.66-3.61; P < .001). The results confirm that the measurement of NfL may inform the outcomes of patients with ALS by helping to predict progression rate. The biomarker, according to experts, may be especially helpful in stratifying patients in clinical trials. The development of an ultra-sensitive single molecule array-based blood test is now underway.

Retrotransposons Jump into the Mix in ALS

The reactivation of retrotransposable elements (RTEs) may contribute to ALS through a TDP-43-mediated mechanism according to a study published on March 16 in *PLOS Genetics*. The study, led by Stonybrook University School of Medicine's **Joshua Dubnau** in New York, found that RNA silencing is impaired in a *Drosophila* model of TDP-43 ALS leading to the reactivation of some RTEs. What's more, silencing one of these elements, the endogenous retrovirus (ERV) gypsy, reduced the loss of cells in the brain suggesting that its activation may contribute to neurotoxicity. The study comes at the heels of previous studies from NINDS' **Avindra Nath** in Maryland which found that human ERV HERV-K may become

reactivated in some people with ALS. The findings add to growing evidence that the breakdown of siRNA-based silencing systems may contribute to neurodegenerative disease.

Read more about RTEs, HERVs and ALS, including emerging HERV-K antibodies.

Changes in Low Complexity Sequences May Lead to a Sticky Situation in ALS

The assembly of stress granules, according to *in vitro* studies, is driven by low-complexity sequence domains (LCDs) of RNA-binding proteins (RNPs) including FUS and hnRNPA1. But in ALS, these sequences can be disrupted, leading to biophysical changes in these granules which may contribute to the disease. Now, a University of Pennsylvania team led by **Erika Holzbaur** report that ALS-linked mutations in the LCD of TDP-43 increase the viscosity of RNA granules and impair their mobility within cultured rat cortical axons. The findings suggest that stress granules are fluid and dynamic. But in ALS, these granules become sticky and therefore, may aggregate, which may lead to RNA dysregulation, toxicity and neurodegenerative disease.

ALS Dipeptides Drive Liquid-Liquid Phase Separation and Stress Granule Formation

Dipeptide repeat proteins (DRPs) may play a role in C9orf72 ALS. But how these proteins may contribute to the disease remains hotly debated. Now, a research team led by University of Leuven's **Ludo van den Bosch** report that arginine-rich DRPs induce stress granules *in vitro* using a phosphorylated eIFα2-dependent mechanism. What's more, these DRPs may recruit TDP-43 to these stress granules because increased levels of this RNA-binding protein are detected. The findings come at the heels of a previous *in vitro* study led by German Center for Neurodegenerative Diseases' **Dieter Edbauer** which found that DRPs blocked the nuclear import of TDP-43 leading to its cytoplasmic mislocalization. Together, the findings suggest that DRPs may contribute to TDP43-mediated cytotoxicity in C9orf72 ALS through a stress granule-mediated mechanism.

Assistive Technology News

A New Intracortical BCI Clocks Faster Typing Speeds Out of the Gate

Emerging brain-computer interfaces (BCIs) aim to help people with ALS communicate by bypassing the central nervous system damaged by the disease. But existing investigational devices are too slow for texting purposes. Now, a research team led by **Jamie Henderson** and **Krishna Shenoy** at Stanford University introduce an intracortical BCI that enabled people with ALS to communicate up to 8 words (39.2 characters) per minute. The study is published on February 21 in *Elife*. The wired device is one of a growing number of neurotechnologies being developed by **BrainGate**, a consortium of neuroscientists, neurosurgeons and bioengineers that aims to restore independence to people with paralysis. In future, the Stanford team aims to introduce a wireless device that includes word completion assistance to increase typing rates.

Check out our website to read more of the latest research advances in ALS.

Funding Opportunities:

March 2017

Transformational Research 2017. FTD. Weston Brain Institute. LOI. **March 31, 2017.**

April 2017

NeuroNext Clinical Trials. National Institute of Neurological Disorders and Stroke (NINDS). Application due: **April 4, 2017.**

Stem Cells. Translational Research Projects. California Institute of Regenerative Medicine. Application due: **April 5, 2017.**

Biomarker Development/Validation. The CReATe Consortium in partnership with the ALS Association. ALS and related diseases. LOI: **April 7, 2017.**

Diagnostic Characterization of Rare Diseases. European Commission (Horizon 2020). Application due: April 11, 2017.

Postdoctoral Scholars 2017. Weston Brain Institute. FTD. Application due: April 11, 2017.

ALS Canada Trainee Program. Clinical, Postdoctoral and Graduate Fellowships. LOI: April 14, 2017.

UK: Novel Biomarkers 2017. FTD. Weston Brain Institute. LOI. April 19, 2017.

Identify and Characterize Potential Environmental Risk Factors for ALS and Evaluate Their Impact on ALS Disease Incidence and Progression. Note the submission date has changed. Applications are due by April 21, 2017.

Clinical Management Grant. ALS Association. Includes funding support for new endpoints in ALS clinical trials. Study outline: April 22, 2017.

NEW! PhD studentships. Motor Neurone Disease Association. Application due by April 28, 2017.

May 2017

NEW! TREAT ALS. Preclinical assessment of potential ALS therapeutics. The ALS Association. LOI due by May 23, 2017.

Check out our updated list of grants and awards.

Job Opportunities:

Asst., Assoc. or Full Professor, Stem Cell Biology. Mount Sinai School of Medicine. New York, NY.
Manager, Stem Cell Phenotypic Screening Facility. University of Oxford. Oxford, England. (This link will become active March 29, 2PM EST due to website maintenance.)
Postdoctoral Fellow, Farese-Walther Lab. Harvard School of Public Health. Boston, MA.
Postdoctoral Fellow, Xu Lab. University of Massachusetts Medical School. Worcester, MA.
Research Associate, Fraenkel Lab. MIT. Cambridge, MA.

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Senior Associate Scientist, Neuroimmunology. Biogen. Cambridge, MA.
Associate Scientist III, Neuroimmunology. Biogen. Cambridge, MA.

Hiring someone onto your team? Contact us to add your listing to our updated job board: ALSjobs@prize4life.org.

Full List of Job Opportunities >>

Upcoming Meetings:

April 2017

April 22-28, 2017. Boston, MA. AAN 2017. **Early registration: March 30, 2017.**

May 2017

NEW! May 2-3, 2017. Leuven, Belgium. Phase Transitions in Biology and Disease. **Early registration: March 31, 2017.**

May 11-13, 2017. Bonn, Germany. 5th Venusberg Meeting on Neuroinflammation.

May 18-20, 2017. Ljubljana, Slovenia. ENCALS 2017.

May 22-24, 2017. Barcelona, Spain. Annual World Congress on NeuroTalk. "New Technologies, New Ideas and New Future." **Abstracts due: March 31, 2017.**

June 2017

June 14-17, 2017. EMBL Heidelberg, Germany. EMBO-EMBL Symposium: Mechanisms of Neurodegeneration. **Abstracts due (extended): April 3, 2017.**

June 19-23, 2017. Keystone Symposium: Neuroinflammation: Concepts, Characteristics, Consequences. Early registration: April 19, 2017.

June 26-27, 2017. Meeting the Challenges of Modelling Neurodegenerative Disease in Mice. Buckinghamshire, England.

Organizing an ALS meeting? Contact us to add your conference to our updated calendar: ALSmeetings@prize4life.org.

Full List of Upcoming Meetings>>

Download the Working with ALS Mice Manual Here

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