ALS Research Forum e-Newsletter Vol. 193 **March 28, 2018**

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Research News

Massive ALS GWAS Cements Cytoskeletal Link to Disease

A traffic tie-up in motor neurons may contribute to at least one form of ALS. The study, led by University of Massachusetts' **John Landers** in Worcester and National Institute on Aging's **Bryan Traynor** in Bethesda, Maryland, found that mutations in the gene encoding the microtubule motor protein Kif5A is associated with ALS and segregates with the disease. The intracellular delivery vehicle transports key cargo including mitochondria and RNA granules along axons in motor neurons. The findings add to growing evidence, which suggest that the disruption of axonal transport in motor neurons may contribute to motor neuron toxicity in ALS (see March 2017; October 2017 news). The study is published on March 21 in *Neuron*.

To learn more about the gene and the collaborations that made this discovery possible, check out a *Traffic Tie-Up May Lead to ALS, Scientists Say*.

New RNA CRISPR Tool Normalizes Tau Splicing

A new CRISPR editing technique opens the door to the development of potential therapies for ALS and FTD. The approach, introduced by research teams led by Salk Institute's **Patrick Hsu** in San Diego, California and Arbor Biotechnologies' **David Scott** in Cambridge, Massachusetts, reduces levels of target RNAs and manipulates RNA splicing. The strategy, which involves the use of the compact RNA-guided, RNA-selective nuclease Cas13d (CasRx), can be packaged into AAV gene delivery vehicles, a key first step in developing gene therapies for these diseases. The approach is one of a growing number of strategies that aims to reduce neurotoxicity in ALS and FTD by destroying potentially toxic RNAs (see October 2017 news). The results appeared on March 15 in *Cell* and *Molecular Cell*.

To learn more about how scientists are using CRISPR to target ALS, check out *A New CRISPR Technique Fries C9orf72 RNAs*.

CRISPR Screen Pulls Down Fresh Targets for C9ORF72 ALS

Researchers may be one step closer to understanding how dipeptide repeat proteins (DPRs) may make motor neurons more vulnerable to C9orf72 ALS according to a March 5 report in *Nature Genetics*. The study, led by **Aaron Gitler** and **Michael Bassik** at Stanford University School of Medicine in California, found

that DPRs may contribute to toxicity by inducing ER stress through an Atf4-mediated mechanism - at least in a cellular model of the disease. The findings add to growing evidence that ER stress may play a key role in ALS and therefore may be an important target in the disease (see May 2016, June 2017, January 2018 news; for review, see Parakh and Atkin, 2016).

New TDP-43 Knock-In Mice: A Model for Frontotemporal Dementia?

A new mouse model may help researchers identify new targets for ALS and FTD. The knock-in mouse, developed by University of Cambridge's **Jemeen Sreedharan** in England in collaboration with University of Massachusetts Medical Center's **Robert Brown**, harbors an ALS-linked Q331K mutation in the RNA-binding protein TDP-43. The dysregulation of TDP-43 is thought to play a role in more than 95% of cases of ALS. The mouse is the first knock-in model of TDP43-associated disease. The study appeared on March 19 in *Nature Neuroscience.*

To find out how scientists plan to use this model to discover new targets in ALS, check out *A New Knock-In TDP-43 Mouse Enters The ALS Ring*.

Clinical Trial News

Mexiletine Helps Beat A Charley Horse, ALS Specialists Say

Muscle cramps are a major source of pain for 1 out of 4 people with ALS. Now, a group of physicians, led by Mayo Clinic's **Bjorn Oskarsson** in Jacksonville, Florida, report that mexiletine can help alleviate them. Mexiletine reduced muscle cramps by 33% compared to placebo according to a phase 4 clinical trial analysis. The medication, FDA-approved for the treatment of cardiac arrhythmia, is also emerging as a treatment for muscle stiffness (myotonia) in a growing number of muscle disorders including myotonic dystrophy. The study is published on March 6 in *Muscle and Nerve*.

To learn more about mexiletine, check out *Mexiletine Alleviates Key Source of Muscle Pain in ALS*.

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

Funding Opportunities:

April 2018

Research Grants. Potential ALS Therapies: Preclinical to Phase 1. Fight MND. Application due by **April 1, 2018**.

MRC-NIH Neurodegeneration Partnering Awards. Application due by **April 5, 2018**.

Personalized Medicine. ERA PerMed. Eligibility: AT, BE, CA, DE, EE, ES, FI, FR, HR, HU, IE, IL, IT, LU, LV, NL, NO, PL, RO, SI, SE and TR. Pre-Proposals due by **April 10, 2018**.

Research Grants (Basic Neuroscience). Whitehall Foundation. The focus: neural mechanisms involved in complex behaviors including motor systems. LOIs due by **April 15, 2018**.

Early Career Grants. Brain Canada & Azrieli Foundation. Application due by April 17, 2018.

Ben Barres Early Career Acceleration Awards. Chan-Zuckerberg Initiative Neurodegeneration Challenge Network. Applications due by April 17, 2018.

Collaborative Science Awards. Chan-Zuckerberg Initiative Neurodegeneration Challenge Network. Applications due by April 17, 2018.

NEW! Clinical Validation of a Candidate Biomarker for Neurological Disease. NINDS. Application due by April 17, 2018.

Rapid Response: Canada. FTD. Weston Brain Institute. LOIs due by April 19, 2018.

Rapid Response: Ireland, Netherlands, UK 2018. Biomarkers, including FTD. Weston Brain Institute. LOIs due by April 23, 2018.

Graduate Student Fellowship. AFM-Téléthon. Application due by April 24, 2018.

Teva CNS Target Identification Crowdsourcing Challenge. TEVA and the ALS Association. Proposals due by April 29, 2018.

Identify, Analyze and Evaluate Potential Risk Factors for ALS. CDC. Application due by April 30, 2018.

Breakthrough Prize. Nominate a scientist by April 30, 2018!

May 2018

Graduate Studentships. MND Association. Applications due by May 4, 2018.

Non-Clinical Fellowships. MND Association. Applications due by May 4, 2018.

NEW! Promotion of Translation-Oriented Collaborative Projects in the Field of Rare Diseases. German Federal Ministry of Education and Research (BMBF). Application due by May 8, 2018.

NEW! Harrington Scholar-Innovator Program. Physician Scientists. Discovery or Development of Novel Drugs or Biologics. Application due by May 10, 2018.

June 2018

ALS Canada Project Grant Program. ALS Canada. June 8, 2018.

Check out our updated list of grants and awards.

Job Opportunities:

Full Professor, RNA Biology. University of Vienna. Vienna, Austria.
Faculty, Molecular Pharmacology & Physiology. University of South Florida. Tampa, FL.
Neuropathologist, Tenure-Track. Northwestern University School of Medicine. Chicago, IL.
Senior Research Investigator, Gene Therapy. University of Pennsylvania. Philadelphia, PA.
Postdoctoral Fellow, Da Cruz Lab. Ludwig Institute for Cancer Research. San Diego, CA.
Postdoctoral Fellow, Kalra Lab. University of Alberta. Alberta, Canada.
Postdoctoral Fellow, Miller Lab. University of Oxford. Oxford, England.
Postdoctoral Fellow, Mueller Lab. University of Mass. Medical Center. Worcester, MA.
Postdoctoral Fellow, Yang Lab. Tufts University School of Medicine. Boston, MA.

Research Scientist, Neuroscience. Lilly. Indianapolis, IN.
Research Scientist, Immuno-Neurology. Alector. San Francisco, CA.

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:

Final days to register for ENCALS 2018 in Oxford, England at the early bird rate. Early

registration deadline: April 3, 2018.

April 2018

April 17-21, 2018. Cold Spring Harbor Laboratory. Cold Spring Harbor, NY. Protein Homeostasis in Health and Disease.

April 21-27, 2018. Los Angeles, CA. Annual Meeting of the American Academy of Neurology.

April 30-May 4, 2018. Jackson Laboratory. Bar Harbor, ME. Workshop: Using Mouse Models to Study Neurodegenerative Disease.

May 2018

May 14-17, 2018. EMBL. Heidelberg, Germany. Cellular Mechanisms Driven by Liquid Phase Separation.

June 2018

June 17-21, 2018. Keystone, Colorado. Advances in Neurodegenerative Disease Research and Therapy.

June 20-22, 2018. Oxford, England. ENCALS 2018.

June 22-23, 2018. Oxford, England. TRICALS 2018.

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

STAY CONNECTED: