THE ALS RESEARCH FORUM
Discovering a Common Goal, Discovering a Cure
PRIZE4LIFE ALS ASSOCIATION

ALS Research Forum e-Newsletter Vol. 170 **April 11, 2017**

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.

Research News

Neurotrophic Factors in ALS: a Winning Combination?

Researchers first turned to neurotrophic factors (NTFs) as a potential treatment strategy for ALS in the early 1990s in hopes to shield motor neurons from destruction. But the clinical translation of these approaches has proved challenging. Now, a new study suggests that multiple factors may be needed to provide the most therapeutic benefit. The study, led by **Georg Haase** at the Aix-Marseille University in France, found that NTFs promote the survival of distinct classes of motor neurons in the lumbar spinal cord. The findings suggest that a combination of these neuroprotective substances may be needed to protect motor neurons affected by the disease. The study appeared on March 16 in the *Proceedings of the National Academy of Sciences*.

Check out our feature to learn more the study, including its implications for the design and delivery of potential neuroprotective ALS therapies.

A New SARM1s Race in ALS Begins

The axon executioner SARM1 is an enzyme and therefore potentially druggable according to a new study published in March 16 in *Neuron*. The study, led by Washington University St Louis' **Jeffrey Milbrandt** in Missouri, found that SARM1 catalyzed the cleavage of NAD+, a key cofactor needed for ATP synthesis. Milbrandt's team previously demonstrated that SARM1 triggered axon degeneration by depleting its energy by reducing the availability of NAD+. The findings build on studies in 2012 led by **Marc Freeman** at the University of Massachusetts Medical School in Worcester which found that injured axons self destruct through a SARM1-mediated mechanism.

Read more to learn about SARM1 and its potential role in ALS.

Profilin May Act Up at Neuromuscular Junctions In ALS

About 1-3% of cases of familial ALS are due to mutations in profilin, a key regulator of actin dynamics. How changes in the axonal cytoskeleton could contribute to ALS, however, remains unclear. Now, **John Landers** and colleagues at the University of Massachusetts in Worcester report that profilin may help keep muscle fibers and motor neurons connected by promoting the remodeling of neuromuscular junctions.

The findings add to growing evidence that a reduction in axonal actin dynamics may contribute to ALS, including the most common form of the disease. The study is published on April 3 in *Human Molecular Genetics*.

Poly Dipeptide in Cerebrospinal Fluid Marks C9ORF72 Expansion Carriers

An emerging biomarker may facilitate the development of potential therapies for C9orf72 ALS, according to a new study led by Mayo Clinic's **Leonard Petrucelli** in Florida. The study found that patient-derived motor neurons pre-treated with C9orf72 repeat RNA-targeted antisense oligonucleotides (ASOs) exhibited a dose-dependent drop in levels of the C9orf72 dipeptide repeat protein polyGP. What's more, the researchers saw a similar dose-dependent decrease in the C9orf72 ASO-treated brain of a mouse model of the disease. The approach is based on an antibody-based "sandwich" assay previously developed by the Petrucelli lab that rapidly detects polyGP in the CSF. The strategy may help scientists evaluate potential therapies for C9orf72 ALS in the clinic by enabling the monitoring of target engagement. The study is published on March 29 in *Science Translational Medicine*.

Read more about polyGP, including its potential to evaluate emerging therapies including ASOs approaching the clinic.

Clinicians C Potential in the Emerging ALS Prognostic Biomarker CRP

The inflammatory biomarker C-reactive protein (CRP) may help inform the outcomes of patients with ALS according to a study published on April 3 in *JAMA Neurology*. The study, led by NeuroMuscular Omnicentre's **Christian Lunetta** in Italy, found that circulating levels of CRP in the blood inversely correlated with functional impairment (ALS-FRS score) and survival (hazard ratio, 1.129; 95% CI, 1.033-1.234; P = .007). 394 patients with ALS participated. The results confirm that the measurement of this inflammatory substance in the blood may help clinicians prognose ALS by identifying patients with a high progression rate. The approach, which involves a standard blood test which checks for inflammation, may also facilitate the evaluation of potential therapies for ALS by enabling the stratification of patients in clinical trials.

Read more about CRP, including its potential to identify "responders" to anti-inflammatory therapies being evaluated in the clinic including NP001.

Can Immune Gene Expression Predict Pace of Motor Neuron Destruction?

Biomarkers are desperately needed to expedite the diagnosis and inform the prognosis of ALS. But how to prioritize the potential candidates identified to evaluate in the clinic has proved challenging. Now, using an unbiased data-driven approach that combines genomics with ALS pathology, **Johnathan Cooper-Knock** and colleagues at the University of Sheffield in England report that CSF soluble TREM2 may be a potential biomarker of ALS progression. Soluble TREM2, which is produced in microglia and may instigate inflammation, is also emerging as an early biomarker of Alzheimer's Disease. The study is published on March 16 in *Acta Neuropathologica Communications*.

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

Funding Opportunities:

The Judith and Jean Pape Adams Charitable Foundation is now accepting applications from US universities to support ALS research. Check out their website for details.

April 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.

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

May 2017

Bioengineering Research Partnerships. NINDS. Application due by May 18, 2017.

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

June 2017

MDA Venture Philanthropy Program. Muscular Dystrophy Association. LOI due by June 1, 2017.

ALS Canada Project Grant Program. Includes former ALS Discovery, Bridge and Clinical Management grant programs. Application due by June 2, 2017.

Check out our updated list of grants and awards.

Job Opportunities:

Physician Scientist, Tenure Track. Temple University. Philadelphia, PA.
Postdoctoral Fellow, Talbot Lab. University of Oxford. Oxford, England.
Postdoctoral Fellow, Sajjadi Lab. University of California, San Francisco.
Research Specialist, ALS and FTD. University of Pennsylvania. Philadelphia, PA
Research Associate II, Neurodegenerative Diseases. University of California, Los Angeles.
Research Associate I/II, Lutz Group. Jackson Labs. Bar Harbor, ME.
Research Associate, FTD. University of California, San Francisco.

.

Senior Scientist, Neuroinflammation. Merck. Boston, MA
Research Scientist, Novartis. Cambridge, MA.
Scientist, Neuroscience. Genentech. San Francisco, CA.
Senior Associate Scientist, Amgen. Cambridge, MA.
Senior Associate Scientist, Yumanity Therapeutics. Cambridge, MA.
Research Associate, Nuredis. Menlo Park, 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:

Registration opens this week for SfN 2017 in Washington, D.C. Abstracts will begin to be accepted on April 13. Abstracts due: May 4.

April 2017

April 22-28, 2017. Boston, MA. AAN 2017.

May 2017

May 2-3, 2017. Leuven, Belgium. Phase Transitions in Biology and Disease. **Early registration (extended): April 21, 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."

June 2017

June 14-17, 2017. EMBL Heidelberg, Germany. EMBO-EMBL Symposium: Mechanisms of Neurodegeneration. Registration deadline: May 3, 2017.

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

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

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

Full List of Upcoming Meetings>>

STAY CONNECTED: