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

ALS Research Forum e-Newsletter Vol. 181 **September 20, 2017**

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Research News

Growth Factors: In ALS, The Eyes Have It

Upper and lower motor neurons degenerate in people with ALS, leading in part, to difficulty breathing, speaking and walking. But other motor neurons, including those needed for vision, are spared. A growing number of studies suggest that these oculomotor neurons may resist ALS at least in part, by producing increased levels of key neurotrophic substances. In this feature, experts weigh in on these findings and their implications for treating ALS going forward.

Check out this feature to learn about selective vulnerability, and how scientists are leveraging these mechanisms to develop therapies for ALS.

ALS Motor Neurons, Direct?

Researchers may be one step closer to recreating motor neurons from people with ALS according to a new study led by Washington University's **Andrew Yoo** in St Louis, Missouri. The strategy, which involves the transfection of microRNAs miR-9 and miR-124, and the transcription factors ISL1 and LHX3, enables adult human fibroblasts to be directly reprogrammed into human spinal cord motor neurons. What's more, most of the cells generated by this method appeared to be functional, firing multiple action potentials when depolarized. The strategy is one of a growing number of techniques that aims to streamline the production of human motor neurons in the laboratory to investigate their role in neurodegenerative diseases including ALS. The study is published on September 7 in *Cell Stem Cell*.

From Protector to Instigator, Autophagy Makes About-Face in ALS

Emerging autophagy inducers aim to protect motor neurons in ALS by clearing out protein aggregates (see July 2014, July 2015 news). But according to a new study led by Columbia University's **Tom Maniatis** in New York, this strategy may only be of benefit early in the disease. The study found that autophagy-deficient SOD1 G93A mice exhibited signs of ALS earlier but lived longer. The reason, according to subsequent analysis, is that autophagy may accelerate progression of ALS by promoting inflammation and interneuron pathology late in the disease. The study is

published on September 11 in *Proceedings of the National Academy of Sciences*.

Microglial Kinase RIPK1 Promotes DAM, Blocks Lysosomal Digestion

Blocking RIP1 kinase may reduce inflammation in the CNS in Alzheimer's disease (AD), at least in model mice according to a new study led by Harvard Medical School's **Junying Yuan** in Boston, Massachusetts. The findings, published on September 11 in *Proceedings of the National Academy of Sciences*, build on previous studies from Yuan's team, which found that RIP1 kinase promoted inflammation and neuronal loss in a mouse model of ALS (see February 2017 news; Ito et al, 2016). Together, the findings suggest that blocking RIP1 kinase may be a more general strategy to treat neurodegenerative diseases. The approach is being developed by Denali Therapeutics in San Francisco, California, as a potential therapy for ALS and Alzheimer's disease. A phase 1 clinical trial in healthy adults in Europe is ongoing.

To learn more about the emerging role of RIPK1 in ALS, check out *RIPK1 May Increase Granularity in FTD*.

Clinical Trial News

BrainStorm's NurOwn Launches Phase 3 Clinical Trial in the US

The potential stem cell therapy NurOwn is soon to be evaluated in the ALS clinic at the phase 3 stage. The strategy, developed by BrainStorm Cell Therapeutics in Israel, aims to promote the survival of motor neurons in people with ALS by using mesenchymal stem cells, isolated from their bone marrow, and expanded and differentiated *ex vivo*, to deliver neurotrophic substances including BDNF, GDNF and HGF into the cervical spinal cord. The approach builds on previous work, which suggests that a combination of these substances may be needed to help protect motor neurons against the disease (see April 2017 news; Krakora et al., 2013; Schaller et al. 2017). A total of 200 people with ALS are expected to participate. The double-blind, randomized, placebo-controlled 28-week clinical trial is expected to be completed in April 2019.

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

Funding Opportunities:

The Weston Brain Institute will begin accepting applications for funding for high-risk, high-reward research based in Canada, including FTD, in November 2017. A separate program, focusing on Europe, is expected to begin accepting applications in October 2017.

September 2017

Bench Testing Existing FDA-Approved or Experimental Drugs. National Center for Advancing Translational Sciences. Letter of Intent: **September 30, 2017.**

October 2017

Clinical Research Training Scholarship in ALS. The American Brain Foundation and The ALS Association. Applications due by October 1, 2017.

Research Grants. Frick Foundation for ALS Research. (Deadline extended.) Application due by October 6, 2017.

CReATe Clinical Research Scholarship Program. Application due by October 16, 2017.

November 2017

Biomedical Research Project Grants. MND Association. Applications due by November 3, 2017.

December 2017

NeuroNEXT Clinical Trials. NINDS. Applications due by December 6, 2017.

Check out our updated list of grants and awards.

Job Opportunities:

Director, Center for Neurodegenerative Disorders. University of Maryland. Baltimore, Maryland.
Assistant Director, Aging Brain Initiative. MIT. Cambridge, MA
Junior or Senior Group Leader, Grenoble Institute of Neurosciences. Grenoble, France.
Assistant Professor, Mechanisms of Neurological Disease. Emory University. Atlanta, GA.
Assistant Professor, Biological Chemistry & Pharmacology. Ohio State University. Columbus, OH.
Assistant Professor, Neurobiology and Behavior. University of California. Irvine, CA.
Postdoctoral Fellow, Guo Lab. Yale University School of Medicine. New Haven, CT.
Postdoctoral Fellow, Hu Lab. Cornell University. Ithaca, NY.
Postdoctoral Fellow, Fitzpatrick Lab. Columbia University. New York, NY.
Postdoctoral Fellow, Centre for Systems Neurobiology. Linköping University. Linköping, Sweden.
Graduate Studentship, Kadener Lab. Hebrew University. Jerusalem, Israel.

Scientist I, ALS. Biogen. Cambridge, MA.
Scientist or Senior Scientist. Verge Genomics. San Francisco, CA.
Scientist, Discovery Biology. Prevail Therapeutics. New York, NY.

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 is now open for the 2018 Australasian Motor Neurone Disease Symposium in Melbourne, Australia. Abstracts due: December 18, 2017.

October 2017

October 3-5, 2017. Clearwater Beach, Florida. The 16th Northeast ALS Consortium Meeting.

November 2017

November 11-15, 2017. Washington, D.C. Society for Neuroscience Annual Meeting.

December 2017

December 7, 2017. Boston, MA. ALS/MND Allied Professionals Forum.

December 8-10, 2017. Boston, MA. International Symposium on ALS/MND.

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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