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

ALS Research Forum e-Newsletter Vol. 180 **September 6, 2017**

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Research News

Breaking Up TDP-43 Inclusions May Be Doable, Scientists Say

Breaking up TDP-43 aggregates may help reduce motor neuron toxicity in ALS. But how to modulate its proteostasis remains unclear. Now, a research team, led by the University of North Carolina's **Todd Cohen,** introduce an assay that reproduces TDP-43 pathology in cultured mammalian cells including neurons, opening the door to discover potential therapies that dissolve these inclusions. In this feature, experts weigh in on targeting TDP-43 aggregates and its potential for people with ALS going forward.

Check out this feature to learn about emerging strategies to tackle proteostasis in ALS, including Orphazyme's arimoclomol.

Stress Relief Helps Neurons in Alzheimer's, ALS

Blocking a key kinase may help protect motor neurons in ALS according to a new study published on August 16 in *Science Translational Medicine*. The study, which took place at Genentech in South San Francisco, CA, found that the deletion of dual leucine zipper kinase (DLK) reduced motor neuron loss (13% vs. 40%) in G93A SOD1 mice and increased their survival by 8 days. The strategy builds, on previous studies, which found that DLK signaling helps refine the connectivity of the developing nervous system by selectively eliminating neurons and pruning axons. Genentech's DLK inhibitor GDC-0134 is now being evaluated as a treatment for ALS at the phase 1 stage.

Newest ALS/FTD Gene Keeps Spotlight on Stress Granules

The buildup of stress granules may play a key role in ALS/FTD according to a new study. The study, led by St Jude's **J. Paul Taylor** in Tennessee and Mayo Clinic's **Rosa Rademakers** in Florida, found that ALS/FTD-linked mutations in the low complexity domain of the stress granule component TIA1 promotes the formation of liquid droplets, suggesting that liquid liquid phase separation contributes to the disease. What's more, these changes lead to a build-up of stress granules and aggregation of TDP-43, potentially contributing to cytotoxicity. The findings add to

growing evidence that key biophysical changes of stress granules may contribute to ALS and ALS/FTD (see March 2017 news). The study is published on August 16 in *Neuron*.

Brain Spheroids Hatch Mature Astrocytes

Researchers are one step closer to generating astrocytes that resemble those in people with ALS. The study, led by Stanford University's **Ben Barres** and **Sergiu Pasca** in California, found that iPSC-derived astrocyte precursors generated from 3D cultures, known as cortical spheroids, mature to an increasingly adult state according to RNAseq analysis. What's more, the cells can perform key astrocytic functions including glutamate uptake, phagocytosis, and the modulation of neuronal calcium signaling. The strategy may enable researchers to study the role of astrocytes in ALS and potentially, develop therapies for the disease. The study is published on August 16 in *Neuron*.

To learn more about astrocytes and ALS, check out our recent feature *Astrocytes in ALS: A Toxic Withdrawl?*

Somatic SNAFU: Can a Few Mutant Microglia Cause Neurodegenerative Disease?

A cadre of rogue microglia is all it takes to orchestrate neurodegeneration- at least in mice, according to a new study published on August 30 in *Nature*. The study, led by Memorial Sloan Kettering Cancer Center's **Frederic Geissmann** in New York and the University of Freiburg's **Marco Prinz** in Germany, found that ERK-activated microglia triggered neuronal loss in the CNS in BRAF V600E mosaic mice, leading to progressive muscle weakness and paralysis. What's more, this loss may occur at least in part, due to inflammation mediated by these microglia. The findings add to growing evidence that inflammation may contribute to the onset of neurodegenerative diseases including ALS and FTD (see February 2017 news). Efforts to target inflammation in ALS are ongoing.

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

Funding Opportunities:

The MND Association in the UK will begin accepting applications for funding ALS research projects beginning September 8, 2017. Click here to learn more.

September 2017

Clinical Research Pilot Grant. Association for Frontotemporal Degeneration. Application due by **September 8, 2017.**

Basic Research Pilot Grant. Association for Frontotemporal Degeneration. Application due by **September 8, 2017.**

Pathfinder 2017. Focus: High-risk High Reward Studies. Network of Centres of Excellence in Neurodegeneration (CoEN). Eligbility includes: Canada, France, Germany, Ireland, Italy, Spain and United Kingdom. Application due by **September 18, 2017.**

High-throughput Screening of Therapeutic Molecules. The French Foundation for Rare Diseases. Application due by **September 19, 2017.**

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

October 2017

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

NEW! 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.

Check out our updated list of grants and awards.

Job Opportunities:

Asst. or Assoc. Professor, Pharmacology & Toxicology. University of Mississippi. Jackson, MS.
Assistant Professor, Neurobiology. Virginia Tech. Blacksburg, VA.
Assistant Professor, Biological Chemistry & Pharmacology. Ohio State University. Columbus, OH.
Physician Scientist, Temple University School of Medicine. Philadelphia, PA.
Principal Investigator, Med. Chem. & Drug Discovery. Southern Research. Birmingham, AL.
Research Scientist, ALS. Stem Cells. University of California. San Diego, CA.
Postdoctoral Fellow, Buchan Lab. University of Arizona. Tucson, AZ.

Associate Scientist III, ALS Target Validation Research. 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:

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

September 2017

September 7-9, 2017. Ottawa, Canada. Ottawa International Conference on Neuromuscular Disease and Biology.

September 16-21, 2017. Kyoto, Japan. World Congress on Neurology.

September 17-19, 2017. Sitges, Spain. Neuro-Immune Axis: Reciprocal Regulation in Development, Health and Disease.

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.

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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