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

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Research News

Small Molecule Keeps Mutant SOD1 Out of Trouble

Researchers may be one step closer to creating a small molecule-based therapy for SOD1 ALS. The study, led by University of Liverpool's **Samar Hasnain** in England, found that the blood-brain barrier permeable antibiotic ebselen helps the SOD1 enzyme fold properly by promoting disulfide bond formation and dimerization- at least *in vitro*. The strategy is based in part, on previous studies led by **Peter Lansbury**, now at Lysosomal Therapeutics in Cambridge, MA, which suggest that the formation of these cysteine linkages, may prevent aggregation of the enzyme in the disease (Ray et al., 2004). Ebselen is potentially a key starting point for designing small molecule-based therapies that help reduce motor neuron toxicity. The findings appeared on April 27 in *Nature Communications*.

Large SOD1 Aggregates May Be Protective, ALS Scientists Say

Researchers may be one step closer to identifying the source of motor neuron toxicity in SOD1 ALS. The study, led by University of North Carolina's **Nikolay Dokholyan** in Chapel Hill, found that soluble complexes containing just three molecules of the SOD1 enzyme promoted neurodegeneration - at least in cell culture. What's more, insoluble clumps of the enzyme, known as fibrils, reduced the loss of these motor neuron-like NSC-34 cells by about 50%, suggesting that these inclusions may instead protect these cells against the disease. Together, the findings suggest that small molecules that target small, soluble SOD1 oligomers - not aggregates - may help reduce motor neuron toxicity in the disease. The study appeared on April 16 in the *Proceedings of the National Academy of Sciences*.

Ataxin-2 ASOs May Clear More Obstacles In ALS

Targeting ataxin-2 in ALS may have an added benefit according to a report published on April 2 in *Cell*. The study, led by Johns Hopkins University's **Jeffrey Rothstein** and **Thomas Lloyd** in Baltimore, Maryland, found that

reducing the build up of stress granules, by lowering levels of ataxin-2, also cleared up nuclear traffic tie-ups- at least in iPS-derived C9orf72 ALS motor neurons. The results build on studies that suggest that in ALS, key proteins needed to transport cargo in and out of the nucleus in motor neurons are sequestered in stress granules leading to a toxic build up of proteins in the cytoplasm (see January 2018, April 2018 news; Zhang et al., 2018). Efforts to further evaluate ataxin-2 ASOs as a treatment for ALS is underway (see May 2017 news).

To learn more about ataxin-2 and its potential for sporadic ALS, check out *Ataxin-2 ASOs Aim to De-stress ALS*.

Reporting Clinical Trial Results Needs to Be More Timely, Neurologists Say

Researchers across the globe are evaluating a growing number of potential therapies for ALS in the clinic. But according to a new analysis published on April 30 in *JAMA Neurology*, the findings of many of these clinical trials are not reported, making it more challenging to efficiently develop more effective treatments for the disease. The analysis, led by neurologist **Kevin Sheth** at Yale University School of Medicine in New Haven, Connecticut, found that researchers published the results of only about 1 out of 2 clinical trials [54%; 154 out of 285] registered on ClinicalTrials.gov for neuromuscular diseases. [Keep reading.]

Clinical Trial News

Neuraltus' NP001 Fails In Phase 2B

The immunomodulator NP001 emerged in 2012 as a potential strategy to slow progression of ALS in people with high levels of inflammation (see Miller et al., 2015). But according to results from a phase 2B clinical trial presented on April 26 at the 2018 American Academy of Neurology meeting in Los Angeles, no significant differences in the rate of functional decline (ALS-FRS) or breathing capacity (SVC) could be detected. 138 people with ALS participated.

The randomized, double-blind, placebo-controlled study aimed to confirm whether NP001 could be of benefit to a subset of people with ALS, identified in a previous phase 2 clinical trial by a post-hoc analysis, that exhibited systemic inflammation (see April 2017 news). The approach is being developed by Neuraltus Pharmaceuticals in California.

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

Funding Opportunities:

May 2018

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

ALS Canada-Brain Canada Trainee Program. Postdoctoral and graduate fellowships available. Application due by May 25, 2018.

New Investigator Research Grant, Neurosciences and Mental Health (UK). MRC. Application due by May 30, 2018.

June 2018

MDA Venture Philanthropy Program. LOI due by June 1, 2018.

ALS Canada Project Grant Program. ALS Canada. Application due by June 8, 2018.

NEW! Graduate Student Fellowship. MND Australia/NHMRC. Application due by June 13, 2018.

Research Grants. Muscular Dystrophy Association. Letter of Intent due by June 15, 2018.

NEW! Eppendorf & Science Prize for Neurobiology. Application due by June 15, 2018.

NEW! Innovation Grants to Nurture Initial Translational Efforts (IGNITE): Development and Validation of Model Systems and/or Pharmacodynamic Markers to Facilitate Neurotherapeutic Discovery. NINDS. Application due by June 19, 2018.

Scientific Innovations Award. Brain Research Foundation. LOI due by June 22, 2018.

ALSRP Therapeutic Development Award. Application due by June 22, 2018.

ALSRP Therapeutic Idea Award. Application due by June 22, 2018.

Roger de Spoelberch Prize. Roger de Spoelberch Foundation. Focus: basic and clinical neurodegenerative disease research. Application due before June 30, 2018.

July 2018

NEW! Nonclinical and Early-Phase Clinical Development for Biologics. NINDS. Funding focus: IND-enabling studies and phase 1 clinical trials. Application due by July 18, 2018.

NEW! Harrington Rare Disease Scholar Award. Takeda Pharmaceutical Company.
Application due by July 19, 2018.

The following awards accept applications at any time on a rolling basis.

Early Phase Clinical Trials: Canada. Weston Brain Institute. Funding priorities include FTD.

Wellcome Trust Innovator Award (UK). Funding focus: development of diagnostics and repurposed medicinesfor neurological disorders including rare diseases.

Check out our **updated list** of grants and awards.

Job Opportunities:

Asst. or Associate Professor, Neuroscience Case Western Reserve University. Cleveland, OH.
Asst. Professor, Pathology. University of Manitoba. Winnipeg, Canada.
Neurologist, Centre Hospitalier Universitaire de Nice. Nice, France.
Physician, Physical Medicine & Rehabilitation. VA. St Louis, MO.

Postdoctoral Fellow, Baker Lab. Newcastle University. Newcastle Upon Tyne, England.
Postdoctoral Fellow, Ferraiuolo and El-Khamisy Labs. University of Sheffield. Sheffield, England.
Postdoctoral Fellow, Liachko Lab. VA Hospital. Seattle, WA.
Postdoctoral Fellow, EMBL. Hinxton, England.
Research Associate, Svendsen Lab. Cedars-Sinai. Los Angeles, CA.
Research Technician. Massachusetts General Hospital. Charlestown, MA.

Director, Antibody Discovery. Voyager Therapeutics. Cambridge, MA.
Principal Scientist, Forumulations. Denali Therapeutics. San Francisco, CA.
Senior Scientist, Analytical Development. Voyager Therapeutics. Cambridge, MA.
Senior Scientist, Process Development. Voyager Therapeutics. Cambridge, MA.
Senior Scientist, Discovery Biology. Cytokinetics. San Francisco, CA.
Senior Scientist. Sage Bionetworks. Seattle, WA.
Associate Scientist I, Discovery and Early Development Biomarkers. Biogen. Cambridge, MA.
Postdoctoral Fellow. Novartis. 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:

Last chance to get your abstracts in for the inaugural meeting of Pan-Asian Consortium for Treatment and Research in ALS in Seoul, South Korea. Deadline: May 13, 2018.

April 2018

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.

July 2018

July 6-10, 2018. Vienna, Austria. International Congress on Neuromuscular Diseases.

July 7-11, 2018. Berlin, Germany. FENS Forum of Neuroscience.

July 19-23, 2018. Cold Spring Harbor, NY. Glia In Health And Disease.

July 20-21, 2018. Seoul, South Korea. International Meeting of the Pan-Asian Consortium for Treatment and Research in ALS. Abstracts Due: **May 13, 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

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