THE ALS FORUM
Discovering a Common Goal, Discovering a Cure

ALS Forum e-Newsletter Volume 108 **July 25, 2014**

Visit the ALS Forum website to read the complete stories featured in this e-newsletter. Please forward this e-newsletter to friends and colleagues who may be interested in learning more about ALS.

Resources:

The ALSGene tool: www.ALSGene.org

The PRO-ACT Database: www.ALSDatabase.org

NEALS Biofluid Repository Available to Researchers

NINDS Fibroblast Repository

VABBB Tissue Request Information Site

Funding Opportunities:

Blueprint Neurotherapeutics Network (BPN): SBIR Small Molecule Drug Discovery and Development for Disorders of the Nervous System (U44)

Bernice Ramsay Innovation Grants: 2014 Discovery Grant (Deadline August 1, 2014)

Webinars:

July 29th, 2014, 4:00PM EST: ALSA Update on ALS Research

August 8, 2014, 1:00-2:00PM EST: ALSA/NEALS PALS Webinar - ALS Clinical Trial

Research News

Heart-Healthy Fatty Acids May Stave Off ALS

Polyunsaturated fatty acids (PUFAs) derived from omega-3 rich foods such as salmon and walnuts, are thought to be beneficial for cardiac health since they are integrated into cellular members and can modify oxidative and inflammatory processes. Recent evidence suggests they are also important for reducing the risk of developing ALS. The findings, reported July 14in *JAMA Neurology* online by Alberto Ascherio and colleagues at the Harvard School of Public Health, were based on retrospective analysis of longitudinal data from over one million participants in five nutrition-related studies, 995 of whom were eventually diagnosed with ALS. The participants with highest consumption of PUFAs were at 34% lower risk of developing ALS. What might be the basis for this protective effect? PUFAs are integrated into cellular membranes, and may modulate oxidative or inflammatory processes in the brain. Next, the researchers plan to conduct a follow-up study tracking the association between blood-based biomarkers for fatty acids and ALS. Click here to read more about these intriguing findings.

Can Autophagy Protect ALS Cell Models from Mutant TDP-43?

Cells routinely dispose of unwanted and dysfunctional materials in a lysosome-mediated process called autophagy. Recent findings by Steven Finkbeiner and colleagues at the Gladstone Institute of Neurological Disease in San Francisco published June 29 in *Nature Chemical Biology*demonstrate that boosting autophagy can help cells dispose of toxic forms of TDP-43 and improves their survival. The researchers elegantly tracked TDP-43 turnover at a single-cell level (see related August 2013 News), using a sensitive approach they developed that can account for unrelated changes in protein levels, for example due to cell death. By screening for compounds similar in structure to a known booster of autophagy, they identified two approved antipsychotics that significantly accelerated turnover of wild-type and mutant TDP-43. Moreover, the two drugs increased survival of induced pluripotent stem cells (iPSC) derived from an ALS patient carrying a TDP-43 mutation. Click here to read more about these elegant experiments.

Preimplantation Genetic Diagnosis - a Rarely Explored Option for

Pipeline Series - Summer 2014

Upcoming Meetings:

July 2014

July 27 - August 1, 2014: Girona - Costa Brava, Spain: Gordon Research Conference: Neurobiology of Brain Disorders, Neurodegeneration and Aging-related Disorders of the Nervous System

August 2014

August 3-8, 2014: Andover, NH: Gordon Research Conference: Musculoskeletal Biology & Bioengineering, Identifying and Overcoming Barriers to Translation

August 3-8, 2014: Waterville Valley, NH: Gordon Research Conference: Synaptic Transmission, Synapses in Networks

August 10-15, 2014: Newport, RI: Gordon Research Conference: Neural Development, From Stem Cells to Circuits

September 2014

September 8-10, 2014: Philadelphia, PA: 3rd International Conference and Exhibition on Neurology & Therapeutics

September 17-20, 2014: Minneapolis, MN: 1st ALS Research Group Meeting

October 2014

October 12-14, 2014: Baltimore, MD: American Neurological Association's 2014 Annual Meeting

October 23-25, 2014: Vancouver, Canada: The

Preventing Familial ALS

For families with inherited forms of ALS, such as carriers of genetics mutations in SOD1, C9orf72, TDP-43, or FUS, the prospect of transmitting a dominant mutation to the next generation is terrifying. Preimplantation genetic diagnosis (PGD) is a technique for avoiding transmission of fatal heritable diseases, and it is becoming more widely available at fertility clinics worldwide. PGD requires in vitro fertilization (IVF) in combination with selection and implantation of non-mutant embryos only. With the discovery of an increasing number of dominant mutations for neurodegenerative diseases such as Alzheimer's disease, Huntington's disease and ALS, PGD is becoming an attractive- but not yet well known- option for families at high risk for adult onset neurodegenerative diseases. Click here to read more about the technique and the personal perspectives of families (note that this is part I of a two-part article).

Dysregulation of Acetylation at the Presynaptic Density Tied to ALS in Fly Model

We recently reported on new findings in ALS patient-derived iPSCs linking synaptic hyperexcitability to ALS (see April 2014 News). A new study, published July 10 in *Cell Reports* by Patrik Verstreken and colleagues and the VIB Center for the Biology of Disease in Leuven, Belgium, identifies an additional mechanism that might increase synaptic excitability in ALS. The researchers found that a protein called Bruchpilot tethers synaptic vesicles and regulates neurotransmission in the presynaptic density of the*Drosophila* neuromuscular junction. Two proteins, elongator protein 3 (ELP3) and histone deacetylase 6 (HDAC6) regulate activity of Bruchpilot by acetylation and deacetylation, respectively, and TDP-43 regulates HDAC6 expression. Intriguingly, both ELP3 and TDP-43 mutations are associated with ALS. How relevant these pathways are to human ALS is yet to be explored. Click here to read to more.

Drug News

Biomarker Data from Genervon Trial Support ALS Therapeutic Potential

Pasadena, California-based Genervon Biopharmaceuticals,which recently completed a Phase IIa trial for their proprietary drug candidate GM604 in ALS, now announced the results of the biomarker data from its the trial. GM604 is unique in that it targets multiple pathways affected in the disease. The drug is a peptide master regulator that crosses the blood-brain-barrier and regulates several developmental pathways related to inflammation, hypoxia and apoptosis (see Drug News June 2013). The company reports that six of the eight biomarkers monitored during the trial suggest that G604 is modifying disease. These are particularly encouraging data considering that the clinical trial was of short duration - only two weeks of treatment followed by a 10 week observation period. Hopefully these promising biomarker results are also reflected in the patient outcome data, which is expected later this year. Click here to read more.

Amorfix Granted U.S. Patent for ALS Therapies Targeting Misfolded SOD1

Mutations in the gene encoding superoxide dismutase (SOD1) account

9th International Conference on Frontotemporal Dementias

November 2014

November 13-14, 2014: Arlington, VA: 24th Neuropharmacology Conference

November 13-14, 2014: Arlington, VA: 9th Brain Research Conference Neuroprotection: Basic mechanisms and translational potential

November 15-19, 2014: Washington, DC: The Annual Society for Neuroscience Annual Meeting

Download your free copy:

Send the ALS Forum e-Newsletters to your colleagues!

Forward to a Friend

for approximately 20% of familial ALS cases. The disease-causing mutations in SOD1 increase the protein's propensity to misfold and aggregate, although it is not completely understood how exactly the mutant forms cause disease. Work from Neil Cashman's laboratory has shown that SOD1 mutations can affect wild-type SOD1 and trigger misfolding of the native protein, as well as transfer the misfolded state from cell to cell (seeOct 2011 News and Dec 2012 News). The company founded by Dr. Cashman, Amorfix Life Sciences Ltd, has now announced that it has been granted broad patent protection for antibody targeting misfolded SOD1 for treating ALS. Amorfix has previously entered into a licensing deal with Biogen-Idec for developing these monoclonal antibodies to treat ALS (see 2010 company press release) and these are currently in preclinical development. Click here to read more.

Innovative Device Helps ALS Patients Speak with their Eyes

ALS patients suffer from progressive degeneration of motor neurons, which leads to muscle atrophy and loss of motor functions. However, in many cases, oculomotor neurons are preserved, enabling controlled movement of the eyes even when the body is otherwise paralyzed. LusoVU, a Portuguese technology company founded by the son of an ALS patient, has just successfully completed its Kickstarter campaign, raising $128,181 to bring their new product, Eyespeak, to the market within 6 months (click here to read more about the technology from the CEO). The device monitors the user's eye position by integrating a miniature camera, a microphone and a speaker. Users will be able to type words using movement of the eyes, and have them spoken via a synthetic voice. The device is expected to dramatically improve communication for ALS patients whose speak or ability to otherwise communicate are impaired by disease. Click here to read more.

Novartis Announces Trial on Presymptomatic AD Patients

Repeated failures in Phase III clinical trials for ALS and Alzheimer's disease are driving researchers and drug developers to seek approaches to intervene earlier in the course of disease. Significant research efforts are targeted at identifying early diagnostic biomarkers to enable earlier treatment (see June 2014 News). Now, Novartis is trying to succeed where others have failed by testing two new AD therapies in presymptomatic patients. They will begin testing two new AD therapies, an immunotherapy and a beta-secretase (BACE) inhibitor, to prevent buildup of amyloid proteins in patients with two copies of the APoE4 gene, which increases the risk of developing disease. This breakthrough study is slated to begin in early 2015. Click here to read more.

The ALS Forum was developed by Prize4Life, Inc.

Identified content provided through a partnership with Alzforum.

Forward email

Prize4Life | PO Box 425783 | Cambridge | MA | 02142