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

ALS Forum e-Newsletter Volume 121 **February 13, 2015**

The ALS Drugs in Development Database has been updated! Please take a look and let us know if you would like to submit any new information!

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:

ALS Drugs in Development Database

The ALSGene tool: www.ALSGene.org

The PRO-ACT Database: www.ALSDatabase.org

NEALS Biofluid Repository Available to Researchers

Funding Opportunities:

ALSA Call for Research Proposals: TREAT-ALS Drug Development Contract. Letter of Intent due February 27, 2015.

EU Joint Programme-Neurodegenerative Disease Funding. Pre-proposal due Mar 10, 2015.

CDC Grant: Analyze and Evaluate Potential Risk Factors for ALS. Applications due April 6, 2015.

California Stem Cell Agency (CIRM) 2.0 Awards. Funding for late stage preclinical and

Research News

Two Papers Reveal Mechanisms of Upper Motor Neuron Vulnerability to Degeneration

Upper motor neuron (UMN) degeneration in ALS has typically been viewed as a secondary effect to degeneration of spinal motor neurons, but this paradigm is beginning to shift (see Jan 2015 news story, March 2011 news story). Two new publications in the January 16 *Cerebral Cortex*online provide evidence of how early defects in the function of these neurons can trigger motor disorders. In one study, Hande Özdliner and colleagues from Northwestern University in Chicago demonstrate increased vulnerability of UMN to endoplasmic reticulum (ER) stress in mice lacking UCHL1, a protein, which when mutated in humans leads to motor neuron dysfunction and degeneration. A second study, led by Cristina Zona at the University of Rome, Italy, found that in UMN from ALS mouse models are hyperexcitable and release excessive amounts of potentially detrimental glutamate. Together, these studies show the importance of addressing UMN damage in translational efforts for ALS. Click here to read the full report.

MAP Kinase Signaling Identified as Essential for Axon Degeneration Following Injury

Axonal degeneration during development and following injury is a crucial component of repair and remodeling of connections in the nervous system. However, these same cascades can exacerbate damage to the neural networks in neurodegenerative diseases. A new study from the laboratory of Mark Tessier-Lavigne at Rockefeller University has identified a key early signaling step that triggers axonal degeneration following acute injury and may also play a central role in neurodegenerative diseases. According to the paper, published in the January 15 *Cell*, a protein called Sarm1 triggers activation of the mitogen-activating protein (MAP) kinase pathway (see June 2012 news story), and pathway inactivation can block the cascade that leads to cytoskeletal breakdown and axonal degeneration. These kinases may

clinical stage projects. Due last business day of each month.

Upcoming Meetings:

February 2015

February 23-24, 2015: Manchester, UK: 10th Annual Biomarkers Congress

February 25-26, 2015: La Jolla, CA: Biocom Global Life Sciences Partnering Conference

March 2015

March 1-3, 2015: San Diego, CA: 9th Annual Drug Discovery for Neurodegeneration Conference

March 1-6, 2015: Ventura, CA: Glial Biology, Functional Interactions Among Glia and Neurons: Glial Cells in Health and Disease.

March 1-6, 2015: Ventura, CA: Oxidative Stress and Disease: The Redox Biology of Age-Related Diseases.

March 11-14, 2015: Washington, DC: MDA Scientific Conference.

March 18-20, 2015: Newcastle upon Tyne, UK:8th Annual MRC Neuromuscular Translational Research Conference.

March 18-22, 2015: Nice, France: 12th international Conference on Alzheimer's and Parkinson's Diseases.

April 2015

April 7-11, 2015: Soelden, Austria: The 17th

provide new therapeutic targets for spinal cord injury or neurodegenerative diseases, such as ALS. Click here to read more.

Fruit Fly MicroRNAs Protect Against Glutamate Excitotoxicity
Excitotoxicity due to accumulation of synaptic glutamate is thought to be a central contributor to motor neuron degeneration in ALS (see June 2013 news story, April 2010 news story). A report in the February 2 *Nature Neuroscience* online by Stephen Cohen and colleagues at the Institute of Molecular and Cell Biology in Singapore describes a newly-identified microRNA (miRNA) called miR-1000 that suppresses glutamate excitotoxicity. The miRNA adjusts glutamate release presynaptically by regulating glutamate packaging in presynaptic vesicles by the vesicular glutamate transporter VGlut. Fruit flies lacking this miRNA developed motor deficits and early onset neurodegeneration. A similar miRNA in mammals, miR-137, also regulates expression of VGlut. The researchers are now trying to understand whether miR-137 plays a role in regulation of synaptic activity and neuroprotection in humans. If so, this could provide a new therapeutic target for ALS. Click here to read more.

New Model Helps Assess Astrocyte Function and Dysfunction in ALS
Several landmark studies have implicated astrocytes in motor neuron death in ALS (see Feb 2014 news story, Apr 2007 news story, Oct 2003 news story). However, instructive animal models for examining the behavior of human astrocytes in ALS and other adult-onset diseases have been lacking. Researchers led by Su-Chun Zhang at the University of Wisconsin-Madison have now developed a new mouse model for studying the role of human astrocytes in the adult central nervous system. According to the publication in the Feb 2 *Journal of Clinical Investigation*, the researchers transplanted neural progenitors from human embryonic stem cells into the spinal cord of adult mice, and found that over the course of 9 months, the human progenitors differentiated into astrocytes and functionally integrated into the mouse nervous system. What happened when they transplanted neural progenitors derived from induced pluripotent stem cells from ALS patients? Click here to find out!

Drugs News

Sanofi and Voyager Therapeutics Enter into Gene Therapy R&D Partnership
Sanofi's subsidiary Genzyme is showing its faith in gene therapy for neurodegenerative diseases in an $845 million deal with biotechnology startup Voyager Therapeutics. Under the partnership, Genzyme has the option to license several of Voyager's therapeutic programs once the proof-of-concept clinical trials are complete. Voyager's ALS program (seeFeb 2014 news story) is outside the scope of this partnership, but the investment from Genzyme will help the startup advance its clinical stage adeno-associated virus (AAV) based therapy for Parkinson's disease through Phase I and give a boost to preclinical studies in other therapeutic areas. Click here to read more.

ORIG3N Secures Funding for iPSC-based Personalized Medicine Platform, includes ALS

International Neuroscience Winter Conference.

April 7-8, 2015: San Francisco, CA: The 10th Annual Neurotech Investing and Partnering Conference.

April 18-25, 2015: Washington, DC: The American Academy of Neurology (AAN) Annual Meeting.

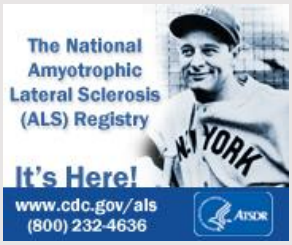
April 21-23, 2015: Boston, MA: BioIT World Conference & Expo.

April 27-29, 2015: Boston, MA: Stem Cell Summit '15.

May 2015

May 5-7, 2015: Philadelphia, PA:Biomarker & Diagnostics World Congress 2015

May 21-23, 2015: Verbania, Italy: European Network for the Cure for ALS (ENCALS) Annual Meeting.



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Boston-based personalized medicine startup ORIG3N was launched last year with the aim to develop breakthrough therapies using induced pluripotent stem cells (iPSC). The company has secured $3M in funding to expand its biorepository program, called Life Capsule, which enables patients to donate blood samples to be stored and/or used for developing individualized therapeutics. The company plans to develop iPSCs derived from these samples into a platform for drug screening, tissue engineering and research, focusing on rare genetic and neurodegenerative diseases including ALS. This is an exciting new company that could help increase the pipeline for new candidate ALS therapies! Click here to read more.

Biogen-Idec and Columbia University Collaborate on Genetic Research and ALS

Biogen-Idec has entered into a $30M alliance with Columbia University Medical Center in New York, NY, to collaborate on genetic research that will include studies in ALS. Under the collaboration, a new postdoctoral program and sequencing facility will be established and new large-scale genomic studies into diseases with significant unmet need will be initiated. David Goldstein, who joined Columbia University in January as director of the new Institute for Genomic Medicine, plans to expand the number of ALS-focused genetic studies at the Institute as part of this collaboration. Click here to read more.

JNK2/3-Specific Inhibitors Identified, Block Cell Death in Parkinson's, ALS

Researchers led by Philip LoGrasso from The Scripps Research Institute in Florida have identified new potent and highly selective c-jun-N-terminal kinase (JNK) inhibitors (see March 2012 news story). The JNKs are a class of enzymes that are linked to oxidative stress and cell death in Parkinson's disease. Evidence also exists of their involvement in the pathophysiology of ALS. The compounds are brain penetrant and improve mitochondrial function in cell-based assays, and the researchers are now working on improving the oral bioavailability of these promising new drugs. Click here to read more.

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