ALS Research Forum e-Newsletter Vol. 153 **June 10, 2016**

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We just launched our free Job Opportunities bulletin board for positions in the field of ALS and FTD. Check it out ***here.*** ***Please let us know if you have any open positions in your lab or company!***

Research News

High IGF-2 in Oculomotor Neurons May Underlie Disease Resistance in ALS

As motor neurons progressively degenerate during the course of ALS, the oculomotor neurons are relatively spared. A study in the May 16 Scientific Reports points to signaling pathways that may contribute to protection of these neurons. The investigators found that IGF-2 protein expression was elevated in oculomotor neurons in tissue from both healthy controls and ALS patients, and the same was true in ALS mouse models based on mutations in SOD1 (SOD1-G93A). The activated IGF-1R, which mediates IGF-2 signaling, was also preferentially expressed in these protected neurons. Restoring IGF-2 to muscles and motor neurons by viral vector delivery of IGF-2 improved motor neuron survival and prolonged lifespan in SOD1-G93A mice. The finding may revive interest in exploiting the IGF signaling pathway for ALS treatment, despite prior disappointing results from human trials.

GWAS Identifies SNPs Associated with Accelerated ALS Progression

A genome wide association study (GWAS) of over 4,000 sporadic ALS patients has revealed single nucleotide polymorphisms (SNPs) that are associated with up to 8 months shorter survival in ALS patients. As published in the May 31 JAMA Neurology, the SNPs were located in introns of two genes - insulin degrading enzyme (IDE) and calmodulin binding transcription activator 1 (CAMTA1). Their link to mechanisms of pathogenesis of ALS are unclear, but CAMTA1 had previously been linked to ataxia and cerebellar dysfunction. Commentators were both excited by the use of GWAS alone to identify factors affecting survival, but also noted that genetic factors alone may not explain the variation in survival observed in ALS.

NMNAT2 Functions as Chaperone Protein in Complex with HSP90

Many neurodegenerative diseases are associated with accumulation of pathological

protein aggregates, which wreak havoc in the cells, and identification of cellular mechanisms to protect against protein misfolding can yield insight on what goes awry in disease. As reported in the June 2 in PLOS Biology, NMNAT2, an enzyme previously known for its role in synthesis of nicotinamide adenine dinucleotide (NAD) and protection from excitotoxic stress, can also function as a chaperone protein. NMNAT2 forms a complex with heat shock protein 90 (HSP90) that promotes folding of protein aggregates, and can toggle between different functions to protect neurons in a context-dependent manner. NMNAT2 could merit exploration in the context of ALS, as approaches to potentiate the heat shock response are under investigation in the lab and the clinic (see Oct 2011 news, March 2016 news).

Missense Mutation Identified that Causes Multiple Sclerosis
Analysis of exome sequencing data from over 2,000 families across Canada has revealed a missense mutation associated with a 70% risk of developing progressive multiple sclerosis. Although 10-15% of MS cases are estimated to have a hereditary component, identification of genes strongly associated with developing the disease has been challenging. As published in the June 1 of Neuron, the researchers found that carriers of a mutated NR1H3, which encodes the nuclear receptor protein Liver X Receptor alpha (LXRA), had a 70% chance of developing MS. The protein helps regulate transcription of genes involved in immunity and inflammation, and LXRA knock-out mice have decreased myelination. Pre-existing LXRA-targeting drug candidates could hasten the development of therapies for this subset of cases.

Assistive Technology

Mind-Reading Machine Can Voice Your Thoughts
Led by scientists at UC Berkeley, researchers are taking steps toward developing a brain implant that can vocalize imagined words for people with diseases that impair speech, such as ALS. In proof of concept studies published May 11 in Scientific Reports,participants performed tasks involving auditory cues, speech or imagined speech, while electrocorticographic (ECoG) signals were recorded from the temporal lobe, frontal lobe, and sensorimotor cortex, brain regions involved in auditory and speech processing. Analyzing the ECoG signals, the team was able to decode words imagined by participants from a finite list of words with 58% accuracy. They now aim to increase the accuracy of decoding and the vocabulary size they are able to decipher.

Deals and Partnerships

Imstar Therapeutics Secures Funding to Advance IMS-088 for ALS
British Columbia-based biotechnology company ImStar Therapeutics has secured seed financing that will enable the company to advance preclinical testing of its lead candidate, IMS-088, for ALS (see Dec 2013 news). IMS-088 is a therapeutic compound derived from withaferin A, which improves function in TDP-43 and SOD1 mouse models of ALS (see Dec 2011 news, Patel et al., 2015). The drug targets TDP-43-related NF-kB activation, and exerts immunosuppressive effects. Investors in the new round of financing are Accel-Rx, BDC Capital, and AviTx, a company co-founded by

Prize4Life founder Avichai Kremer.

miRagen to Advance Anti-miR-155 Therapy with ALSA Grant
miRagen Therapeutics, a clinical-stage biotechnology company specializing in microRNA-based therapies for rare diseases, has received a grant from the ALS Association to support development of MRG-107 for ALS. MRG-107 is a synthetic microRNA antagonist that targets miR-155, a pro-inflammatory microRNA whose expression is elevated in the spinal cord of both familial and sporadic ALS patients (Nov 2013 news, Feb 2015 news). Ablation of miR-155 is SOD1 models of ALS restored microglial function and prolonged survival (Butovksy et al., 2015). The grant will support IND-enabling studies of MRG-107 in collaboration with Howard Weiner's team from the Brigham and Womens' Hospital in Boston, MA.

Funding Opportunities:

July 2016

The Paulo Gontijo Institute (PGI) International Medicine PG Award. Applications due July 1, 2016

CIRM Partnering Opportunity for Translational Research Projects. Applications due July 15, 2016.

NINDS Clinical Trial Readiness for Rare Neurological and Neuromuscular Diseases. LOI due July 18, 2016.

September 2016

Frick Foundation for ALS Research Grants. Applications due September 30, 2016.

Full List of Funding Opportunities >>

Job Opportunities:

Postdoctoral Position
Gladstone Institutes, Steven Finkbeiner Lab
San Francisco, CA

Director, Neuroscience Research & Drug Discovery
Verge Genomics
San Francisco, CA
Full List of Job Opportunities >>

Upcoming Meetings:

Don't miss the abstract submission deadlines listed below!

July 2016

July 2-6, 2016: Copenhagen, Denmark: FENS Forum of Neuroscience.

July 10-14, 2016: Arlington, VA: RESNA Annual Conference.

August 2016

August 7-12, 2016: Girona, Spain: Gordon Research Conference on Neurobiology of Brain Disorders. **Abstracts due July 10, 2016.**

November 2016

NEW! Nov 10-11, 2016: San Diego, CA: RNA Metabolism in Neurological Disease. **Abstracts due July 17, 2016.**

NEW! Nov 12-16, 2016: San Diego, CA: Society for Neuroscience Meeting.

Full List of Upcoming Meetings>>

Resources:

ALS Drugs in Development Database

ALSGene

Alzforum ALS Mouse Model Database

The PRO-ACT Database

NEALS Biofluid Repository Available to Researchers

VABBB ALS CNS Tissue Request Information Site

TargetALS Core Facilities