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Conference News

Prion-like Properties of SOD1 and Tau Featured at ALS/MND Meeting
The symptoms of ALS often emerge in one limb or the throat, and then progressively spread to other body regions to more widely affect function. Researchers hypothesize that a prion-like transmission of toxic proteins between adjacent motor neurons may underlie the characteristic spreading of weakness in ALS. At the International Symposium of ALS/MND in Orlando, Florida, researchers discussed findings on prion-like seeding of toxicity between different structural variants of superoxide dismutase (SOD1), as well as between tau proteins associated with frontotemporal dementia and other tauopathies. Click here to read the full report.

Research News

Structure of TDP-43 Prion-like Domain Reveals Membrane Interactions
Researchers from the National University of Singapore have successfully determined the structure, or lack thereof, of the prion-like C terminal domain of TDP-43. This region is found in many RNA-binding proteins, and also harbors the majority of the ALS-causing mutations. In the January 6 PLoS Biology online, researchers report this domain to be structurally disordered and prone to oligomerization. In contrast, ALS-causing mutant variants of TDP-43 promote formation of insoluble aggregates. Interestingly, the researchers have identified a novel membrane-interacting subdomain within this region, which may further promote aggregation and toxicity.

Exceptional Properties of Human Astrocytes Revealed
Seminal studies have revealed that astrocytes are a critical player in driving motor neuron death in ALS (see Feb 2014 news). However, a comprehensive understanding of how mature human astrocytes differ from those of the mouse has been lacking. In the January 6 Neuron, researchers from Stanford University tackle this issue by

purifying and conducting microarray gene expression analysis of mature human astrocytes. Intriguingly, one third of genes enriched in human astrocytes were not expressed in mouse astrocytes. Human astrocytes also exhibit different responses in culture, in particular to glutamate signaling. The researchers expanded the expression analysis to include astrocyte precursor cells as well as astrocytes from diseased tissue, and have made this data publicly available here.

Do Strenuous Workouts Increase ALS Risk in Women?
Although exercise is generally considered beneficial to promote overall health, a new study suggests that in postmenopausal women it could increase the risk of ALS. Previous epidemiological studies in men or mixed gender cohorts have yielded mixed results, but a study reported January 19 inJAMA Neurology online is the first to focus exclusively on women. Researchers from the University of Pittsburgh analyzed baseline physical activity and mortality data over a 10-year period from over 150 thousand postmenopausal women enrolled in the Women's Health Initiative (WHI) study. The analysis revealed that strenuous workouts three or more times a week increased the risk of death from ALS by more than 50 percent. However, the low percent of physically active women in the WHI study, combined with only 0.1 percent of the cohort having ALS reduced the power of the study to link the two, and further studies are needed to confirm these results.

Stress Granules Need Pur-alpha to Come Together
Pur-alpha is a DNA and RNA-binding protein was recently shown to bind C9ORF72 repeat expansions and potentially contribute to the pathogenesis of ALS (Xu et. al., 2013, Sareen et. al., 2013). In a paper published Jan 4 in *Acta Neuropathologica* online, researchers from Louisiana State University and University of Pittsburgh report that Pur-alpha is also an important player in ALS due to mutant fused in sarcoma (FUS). In lymphoblastoid cells from FUS-ALS patients, Pur-alpha colocalized with mutant FUS in cytoplasmic stress granules (SG) after a stress insult, while in human cell lines, Pur-alpha knockdown prevented SGs from forming. In primary motor neurons, overexpression of Pur-alpha was sufficient to restore nuclear localization of mutant FUS and alleviate FUS toxicity. These findings point to Pur-alpha as a regulator of SG dynamics and potential therapeutic target in ALS.

Deals and Partnerships

Gladstone and Biogen Team Up to Identify Novel Candidate ALS Drugs
The biotechnology company Biogen is teaming up with Steven Finkbeiner's laboratory at the Gladstone Institutes in San Francisco to try to identify new candidate ALS drugs. Novel ALS targets identified at Biogen through genetic screens in Drosophila ALS models will be further tested and validated in mammalian neurons at the academic center. The studies will leverage the "Brain Bot," a robotic microscope invented in the Finkbeiner laboratory, which enables longitudinal tracking of individual, cultured cells. Through the collaboration, scientists will develop a high-throughput, streamlined system to screen potential therapies that prevent neurotoxicity and attenuate degeneration in mammalian cells, ultimately aiming to accelerate identification of promising ALS therapies.

New Initiative ALS ONE Sets Four Year Goal to an ALS Therapy

A team of distinguished ALS experts in Massachusetts have joined forces in a new collaborative effort called ALS ONE. ALS ONE strives to accelerate progress towards a therapy for ALS by leveraging the expertise of four outstanding research and patient care organizations in Massachusetts, and promoting data sharing and coordination of efforts among them. Founded by entrepreneur and person living with ALS, Kevin Gosnell, ALS ONE has set the ambitious goal of developing an ALS therapy within four years. The ALS Therapy Development Institute, University of Massachusetts Medical School, Compassionate Care ALS, and Massachusetts General Hospital/Harvard Medical School are leading the efforts, with the ALS Association and ALS Finding a Cure Foundation synergizing their funded initiatives too.

Funding Opportunities:

Department of Defense ALS Research Program (CDMRP) Funding Opportunities. Pre-announcement.

California Institute of Regeneration Medicine (CIRM) Quest 2.0 Awards. Applications due March 15, 2016.

NIH Therapeutics for Rare and Neglected Diseases (TRND) Program and NIH Bridging Interventional Development Gaps (BrIDGs). Now accepting rolling applications.

Click here to view all funding opportunities

Upcoming Meetings:

February 2016

Feb 25-26, 2016: Manchester, UK: 11th Annual Biomarkers Congress.

March 2016

March 6-8, 2016: Miami, FL: Annual Drug Discovery for Neurodegeneration Conference.

March 20-23, 2016: Arlington, VA: MDA Clinical Conference.

March 21-22, 2016: San Francisco, CA: AMIA Joint Summits on Translational Science.

Click here to view the full list of upcoming meetings

Resources:

ALS Drugs in Development Database

ALSGene

The PRO-ACT Database

NEALS Biofluid Repository Available to Researchers

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TargetALS Cores

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