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American Neurological Association highlights abstracts to be presented at 144th Annual Meeting, Oct. 13–15 in St. Louis

Advances lead to a more complete picture of precision medicine

(MOUNT LAUREL, NJ, September 5, 2019) — Optimizing neuron survival in the stroke-injured brain. Identifying which subjects will benefit from clinical trials for Alzheimer's disease prevention. Testing a CAAR T cell strategy that prevents the devastation of autoimmune disease **—** these are just a few examples of the cutting-edge research that leading neuroscientists will present at the American Neurological Association's 144th Annual Meeting, **October 13–15, 2019** at the Marriott St Louis Grand.

Nearly a thousand of the nation's top academic neurologists as well as students, trainees, and international professionals will convene for three days of research at the vanguard of neurology and neuroscience. **A pre-meeting symposium the evening of October 12 will focus on Brain-Computer Interfaces in Neurological Disease.**

A complete list of abstracts, under embargo until the start of the meeting October 13, will be made available to journalists on **Friday, October 4**.

For the second year, the meeting will feature a **"Highlights of the Meeting" media roundtable on Tuesday, October 15, 2019 from 11:00 am to noon (CT)**, at which presenters of the six plenary sessions will present highlights, discuss the relevance of the work, and answer questions.

Members of the media are welcome to attend the full meeting and **can preview the full advance program here**. **For the meeting schedule at a glance, click here**.

To register and obtain press credentials, please click here.

Until then, below is a sampling of some of the translational science that will be presented:

1. Ryan Schubert, MD, and Michael R. Wilson, MD, University of California, San Francisco. Multimodal Investigation of the Etiology for Acute Flaccid Myelitis (AFM).

AFM is an acute paralysis resembling polio that since at least 2012 has displayed seasonal spikes in occurrence across the United States, typically in children. Enterovirus (EV), specifically EV-D68, has been implicated as the causal organism, but doubts persist because EV infection is common, and EV RNA is rarely detected in spinal fluid and is not detected in non-sterile sites in 50% of children with AFM. In this study, spinal fluid (CSF) samples from 42 children with AFM and 54 non-AFM-afflicted children were incubated with virus particle-encoding peptides representing all known vertebrate virus and arbovirus genomes. Antibodies in the CSF could then bind their targets and be collected for identification by deep sequencing. Separately, sequencing of spinal fluid RNA, both in an unbiased survey and enriching for EV RNAs, was performed. This extensive, pan-viral antibody-dependent search found antibodies to enterovirus in 29 of 42 patients compared to 4 of 58 control subjects. When antibody testing was combined with traditional methods to directly detect EV in the CSF or a non-sterile site such as the mouth, 36 of 42 patients with AFM had evidence of EV. Thus, the study strongly supports the hypothesis that AFM is due to EV infection and not to other viruses. This is an important advance that will require testing in a larger patient population on the way to developing an anti-EV therapeutic to prevent AFM.

2. Eva Feldman, MD, PhD, University of Michigan. Saturated and Monounsaturated Fatty Acids Differentially Regulate Nerve Function in Murine Models of Obesity.

Neuropathy, characterized by a "pins and needles" sensation and reduced touch sensitivity, is the most common complication of type 2 diabetes. It is accompanied by increased saturated fatty acids (SFAs) in blood. Replacing dietary SFAs with monounsaturated fatty acids (MOUFAs) can improve metabolism in pre-diabetic individuals, but whether it can also prevent neuropathy is unknown. This group studied mice fed either a SFA-rich high fat diet or SFA-rich then switched to a MOUFA-rich high fat diet. Both groups developed metabolic dysfunction and weight gain. However, the group that switched to a MOUFA-rich diet showed restored nerve conduction, higher nerve fiber density in limbs and protected mitochondrial function in sensory nerves. The study strongly supports the use of dietary monounsaturated fats in the treatment of neuropathy in pre-diabetic and type 2 diabetic patients.

3. Giuseppe Faraco, MD, PhD, Weill Cornell Medicine. Dietary Salt Induces Cognitive Impairment by Promoting Tau Pathology.

A high salt diet (HSD) has been associated with risk of dementia even when high blood pressure is controlled. These investigators reported last year that high salt intake in animals caused damage to vessels and reductions in blood flow within the brain by reducing the amount of nitric oxide (NO) produced by blood vessel endothelial cells. Pursuing the mechanism further, this team tested whether HSD impairs cognition through NO by increasing phosphorylation of Tau and forming Tau clumps or aggregates, which occur in several forms of clinical dementia. They found that HSD activates a kinase known to phosphorylate Tau and indeed phosphorylated Tau aggregates formed in mice fed excessive salt. In mice that specifically lack Tau either by genetic knockout or Tau depletion using anti-Tau antibody, HSD did not induce dementia, even though it still reduced NO and blood circulation in the brain. This new insight directly connects dietary salt and Tau regulation mediated through specialized cells in blood vessels and strengthens evidence that avoiding excessive salt may protect both brain vascular and cognitive health.

4. Sangwook Oh, PhD, with Aimee S. Payne, MD, PhD, University of Pennsylvania. Antigen-specific B Cell Depletion for Myasthenia Gravis with Chimeric Autoantibody Receptor (CAAR) T Cells.

Myasthenia gravis (MG) is an autoimmune disease in which a patient's own immune system generates autoantibodies against proteins in the neuromuscular junction that enable motor neurons to stimulate muscle contraction, and this antibody attack creates weakness that can be life-threatening. A rare subtype of MG occurs when pathogenic B cells generate autoantibodies against a muscle specific kinase called MuSK, and this subtype of MG is particularly severe. Current MG therapy involves generalized immunosuppression, but this leaves patients vulnerable to fatal infection. Investigators at UPenn have created a chimeric autoantibody receptor (CAAR) T cell strategy that targets only the pathogenic B cells that make anti-MuSK antibodies, leaving alone B cells that are directed against other antigens. Ongoing studies are evaluating animal models of anti-MuSK MG to test this CAAR-T approach to use targeted B cell depletion for treatment of MuSK MG. If this strategy is successful, it may open a new and effective way to treat this and other autoimmune diseases of the nervous system.

5. Suzanne Schindler, MD, PhD, with Randall Bateman, MD, Washington University in St. Louis. Plasma Aβ42/Aβ40 Measured with a High-precision Assay Predicts Current and Future Brain Amyloidosis.

Alzheimer's Disease (AD) is the most common form of dementia in adults 65 years and older. AD is associated with amyloid plaques containing amyloid-β peptides of 40 and 42 peptides (Aβ40 and Aβ42). Currently Aβ42, total Tau (tTau) and phosphorylated Tau 181 (pTau) are well-

established biomarkers of AD, but they require invasive or expensive tests with limited availability. These investigators have developed a blood test that uses highly specific antibodies followed by mass spectrometry to measure the ratio of Aβ42/Aβ40 and compared these results with amyloid PET scans and cerebrospinal fluid pTau/Aβ42 measures in the same subjects. They present data indicating that the Aβ42/Aβ40 ratio, especially in combination with *APOE* ε4 genotype, accurately diagnoses brain amyloidosis and can be used to screen cognitively normal individuals for brain amyloidosis who are at risk for developing AD dementia. Furthermore, individuals with a negative amyloid PET scan and positive plasma Aβ42/Aβ40 are at increased risk for converting to become amyloid PET-positive. This may provide an important tool for selecting appropriate subjects for participation in clinical trials aimed at AD prevention.

6. Jason Hinman, MD, PhD, University of California, Los Angeles, and Jack Wang, MD, PhD, Stanford University. Absence of Sarm1 Promotes Axonal and Neuronal Survival after Stroke.

Neuron survival and regeneration of neuronal axon connections after stroke is limited but essential for improving recovery of neurological function. Investigators from UCLA have identified new molecular pathways to promote post-stroke recovery by studying a mouse model lacking the gene SARM1 with axons that are inherently resistant to Wallerian degeneration or "dying back" after injury. In this study, they report that SARM1-deficient mice display greater preservation of axons after ischemic stroke and that neurons damaged by stroke show greater survival in the absence of SARM1. They also profile the changes in gene expression after stroke, comparing mice with normal levels of SARM1 and those without. This gene expression profile will help to identify a transcriptional "signature" that can be mimicked in drug treatment strategies to optimize neuron survival and connections in the stroke-injured brain.

"This meeting presents the latest insights from translational neuroscience and clinical investigation that are leading contemporary neurology to a more complete vision of precision medicine," said M. Elizabeth Ross, MD, PhD, Director of the Center for Neurogenetics at Weill Cornell Medicine and Chair of the ANA's Scientific Program Advisory Committee.

"Keeping up with the rapid pace of discovery toward deep understanding of brain disorders makes this ANA annual meeting a must for academic neurologists and neuroscientists interested in the translation of their work to the latest breakthroughs in clinical application."

2019 Plenary Sessions include:

- Brain-Computer Interfaces in Neurological Disease, reporting new strategies for device integration to enhance neurological function

- Dominantly Inherited and Late-Onset Alzheimer's Disease: Genetics, Biomarkers, Timecourse, and Treatments, Presidential Symposium **featuring Kim Campbell, widow of the late musician Glen Campbell,** who battled Alzheimer's dementia

- Emerging Role of the Microbiome in Neurological Disease

- Advances in Regenerative Medicine: Cellular Memory Systems in Brain Repair

- Language Disorders Across the Lifespan, their manifestations and treatment

- Optimizing Clinical Trial Design: innovations accelerating the path to more effective treatments

About the American Neurological Association (ANA)

From advances in stroke and dementia to movement disorders and epilepsy, the American Neurological Association has been the vanguard of research since 1875 as the premier professional society of academic neurologists and neuroscientists devoted to understanding and treating diseases of the nervous system. Its monthly *Annals of Neurology* is among the world's most prestigious medical journals, and the ANA's *Annals of Clinical and Translational Neurology* is an online-only, open access journal providing rapid dissemination of high-quality, peer-reviewed research related to all areas of neurology. The acclaimed ANA Annual Meeting draws faculty and trainees from the top academic departments across the U.S. and abroad for groundbreaking research, networking, and career development. For more information, visit www.myana.org or @TheNewANA1

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