Compound Assessed in Tau Neurofibrillary Tangles

In a press release issued on February 8, the National Institutes of Health (NIH) highlighted the results of NIH-funded preclinical research on genetically engineered antisense oligonucleotide compounds to address tau build-up in a variety of neurodegenerative disorders. The study, published in the January 25 issue of *Science Translational Medicine* by DeVos et al. from Washington University in St. Louis (MO), Ionis Pharmaceuticals (Carlsbad, CA), and the University of Texas Southwestern Medical Center (Dallas, TX) showed prevention and potential reversal of tau-associated damage in mice and nonhuman primates (NHPs).

"This compound may literally help untangle the brain damage caused by tau," said Timothy Miller, MD, PhD, the study's senior author. Injections of the antisense oligonucleotide compound in a mouse model of tauopathy prevented tau clustering in 6–9-month-old mice and appeared to reverse clustering in older mice. The compound also resulted in longer survival and healthier brains in older mice than in those receiving a placebo. In addition, the compound prevented older mice from losing the ability to build nests. Additional NHP experiments produced similar effects.

"These results open a promising new door," said Margaret Sutherland, PhD, program director at the NIH National Institute of Neurological Disorders and Stroke. "They suggest that antisense oligonucleotides may be effective tools for tackling tau-associated disorders."

National Institute of Neurological Disorders and Stroke

MarkVCID to Address Vascular Disorders and Dementia

The National Institutes of Health announced on February 22 the launch of MarkVCID, a consortium designed to accelerate development of new and existing biomarkers for small vessel vascular-related cognitive impairment and dementia (VCID). The 5-year program, developed by the NIH National Institute of Neurological Disorders and Stroke (NINDS), in collaboration with the National Institute on Aging, includes 7 U.S. research groups working together via a coordinating center based at the Massachusetts General Hospital (MGH; Boston). A kick-off meeting for the consortium was held on February 20 and 21 in Houston, TX, before the International Stroke Conference 2017.

"We have brought together a number of outstanding research groups to further develop and validate candidate biomarkers for cerebral small vessel disease," said Steven M. Greenberg, MD, PhD, director of the Hemorrhagic Stroke Research Program at MGH and project leader for the MarkVCID Coordinating Center. "This will be achieved by identifying and focusing on the most promising biomarkers across the research sites."

Current research on potential biomarkers for early detection of VCID is being conducted by individual groups using noninvasive biomarker candidates based on MR imaging, fluid analysis, or other physiologic metrics. The consortium will work to coordinate, standardize, and validate these biomarkers in an effort to speed the most promising approaches to clinical trials and routine use. "The team-based approach taken by the consortium allows us to study candidate biomarkers across different clinical settings at multiple institutions," said Roderick Corriveau, PhD, program director at NINDS. "Ultimately, we hope to develop a gold standard to identify cerebral small vessel disease early enough to intervene with treatment."

The second phase of the project is expected to begin in about 2 years and involve dissemination to all consortium sites of candidates showing the greatest potential. The goal is to deliver small vessel VCID biomarkers that are ready for phase II and III clinical trials. Projects currently funded through the initiative include: novel imaging and endothelial biomarkers of small vessel cerebrovascular disease (University of California, San Francisco), development of MR imaging microvascular biomarkers in cognitive impairment and dementia (Johns Hopkins University, Baltimore, MD), MR imaging and cerebrospinal fluid biomarkers of white matter injury in VCID (University of New Mexico Health Sciences Center, Albuquerque), multimodal MR imaging biomarkers of small vessel disease for older persons with and without dementia (Rush University Medical Center, Chicago, IL), microglial inflammatory and omics markers of cerebral small vessel disease (Boston University Medical Campus, MA), imaging cerebral and retinal microvasculature in cerebral small vessel disease (University of Southern California, Los Angeles), and small vessel disease biomarkers in a longitudinally followed "stroke belt" cohort (University of Kentucky, Lexington).

National Institutes of Health

NIH to Expand Catalog for Genomics Research

The National Institutes of Health (NIH) plan to expand the Encyclopedia of DNA Elements (ENCODE) Project, a genomics resource used by many scientists to study human health and disease, according to a press release issued on February 2. Funded by the National Human Genome Research Institute (NHGRI), part of NIH, the ENCODE Project is generating a catalog of all genes and regulatory elements in humans and select model organisms. With 4 years of additional support, NHGRI is building on a long-standing commitment to develop freely available genomics resources for use by the scientific community.

"ENCODE has created high-quality and easily accessible sets of data, tools, and analyses that are being used extensively in studies to interpret genome sequences and to understand the

consequence of genomic variation," said Elise Feingold, PhD, a program director in the Division of Genome Sciences at NHGRI. "These awards provide the opportunity to strengthen this foundation by expanding the breadth and depth of the resource."

Since its launch in 2003, ENCODE has funded a network of researchers to develop and apply methods for mapping candidate functional elements in the genome and to analyze the large database of generated genomic information. Data and tools generated by ENCODE are organized by 2 groups: a data coordinating center, which houses the data and provides access to the resource through an open-access portal, and a data analysis center, which synthesizes results into an encyclopedia for use by the research community.

NHGRI plans to commit up to $31.5 million in fiscal year 2017 for these awards. With this funding, ENCODE will expand to include characterization centers, which will study the biologic role that candidate functional elements may play and will develop methods to determine the ways in which these contribute to gene regulation in a variety of cell types and model systems. In addition, the project will enhance the ENCODE catalog by developing a way to incorporate data provided by the research community and will use biologic samples from research participants who have consented to unrestricted sharing of their genomic data.

To date, more than 1,600 scientific publications by the research community have used ENCODE data or tools. "We found that many of the people that are using the ENCODE resource are doing so for disease studies, and this attests to its translational value," said Mike Pazin, PhD, a program director in NHGRI's Division of Genome Sciences. More information about the ENCODE Project is available at: https://www.genome.gov/10005107/encode-project.

National Human Genome Research Institute

Second Round of Comments on USP <797>

The U.S. Pharmacopeial Convention (USP) announced in late January that it will seek a second round of public comments on proposed revisions to USP general chapter <797> Pharmaceutical Compounding—Sterile Preparations. General Chapter <797> provides standards for compounding sterile preparations and describes a range of requirements, including responsibilities of compounding personnel, training, environmental monitoring, storage, and testing of finished preparations. The General Chapter was last revised in the second supplement to USP 31–NF 26, which became official on June 1, 2008, and is the current official standard. Proposed revisions (available at http://www.usp.org/usp-nf/notices/general-chapter-797-proposed-revision) were released in 2015, with a public comment period extending from September 25, 2015, to January 31, 2016. More than 2,500 stakeholders submitted more than 8,000 comments, and the USP notes that its Compounding Expert Committee continues to review and revise the chapter based on the public comments. In early February, USP held 2 roundtable sessions for additional stakeholder input.

Revised General Chapter <797> will be published in the *Pharmacopeial Forum* for another public comment period. At Newsline press time, the USP did not have an anticipated date for the chapter's republication. Stakeholders can follow the status of the chapter by signing up for the USP Healthcare Quality Standards Update at http://www.usp.org/HQS-Signup-Form.

U.S. Pharmacopeial Convention

NIH Pilot Program for Innovative Neurological Research

On January 26, the National Institutes of Health (NIH) announced the first 30 recipients of the new R35 Research Program Award (RPA), a pilot initiative designed to encourage creative research by enhancing funding stability through the National Institute of Neurological Disorders and Stroke (NINDS). NINDS-supported investigators who secure an RPA will have their research funded for a period of 5 years, with the potential for an additional 3-year extension. The funding provides support for a grantee's overall research program rather than individual projects. "NINDS created this pilot program to improve the value of the research it funds by enabling proven investigators to pursue long-range, innovative research instead of continually writing and submitting grant applications," said Walter Koroshetz, MD, NINDS director.

The R01 Research Project Grant continues to be the primary source of NIH funding for many laboratories. R01 awards provide support for up to 5 years for a specific set of experiments, and multiple R01s are often necessary to fund a laboratory's body of work. The R35 RPA mechanism provides longer, consolidated support for a grantee's overall research program and will support the entirety of an investigator's mission-related research through NINDS.

The 30 new awardees include principal investigators at a variety of career stages researching a broad range of topics, several of which have direct relevance to nuclear medicine and molecular imaging. "Our goal with the R35 Research Program Award is to fund the research of both well-established investigators who already have multiple grants, as well as earlier stage researchers with single R01s and a track record of significant impact in their field of study," said Robert Finkelstein, PhD, director of the NINDS Division of Extramural Activities. "These grants are aimed at enabling them to focus their creativity and time on performing groundbreaking research."

National Institute of Neurological Disorders and Stroke