

Summer 2020

E-Newsletter

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The Mary S. Easton Center for Alzheimer's Disease Research at UCLA has very active teams working on basic research, drug discovery, biomarkers for early diagnosis and clinical activity including clinical trials, cognitive testing, and patient care.

Easton Center Welcomes New Director

We would like to welcome Keith Vossel, MD, MSc as the new Director of the Mary S. Easton Center for Alzheimer's Disease Research at UCLA.



Photo: [Keith Vossel, MD, MSc](#)

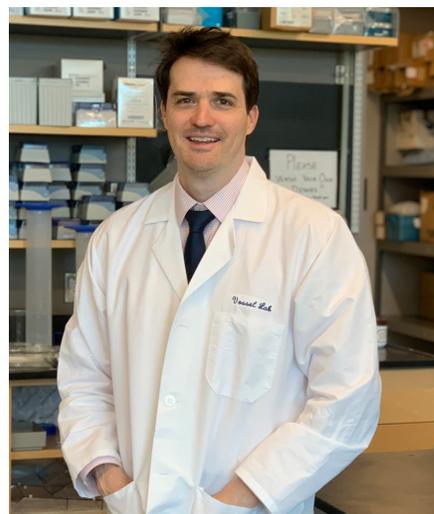
Dr. Vossel received a master's degree in biomedical engineering and medical degree with highest honors from the University of Tennessee, Memphis. He completed neurology residency at Harvard - Massachusetts General and Brigham and Women's Hospitals, where he served as a chief resident. Following residency, Dr. Vossel completed fellowship training in behavioral neurology and postdoctoral training in neurodegenerative disease laboratory research at the University of California, San Francisco (UCSF) and Gladstone Institutes. At UCSF and the University of Minnesota, Dr. Vossel created comprehensive research programs investigating Alzheimer's disease with a focus on brain rhythm abnormalities and translational therapies.

Dr. Vossel has made major contributions to the Alzheimer's field in both basic science and clinical research. He discovered that Alzheimer's disease patients often experience seizures that had previously been unrecognized. Dr. Vossel pioneered the use of extended electroencephalography and magnetoencephalography recordings to study Alzheimer's disease. Using this technology, Dr. Vossel was the first to identify that silent seizure activity, detected during sleep, occurs in over 40% of patients with Alzheimer's disease and accelerates cognitive decline. From this finding, Dr. Vossel initiated, and recently completed, a phase 2 clinical trial of an antiseizure drug to treat silent seizure activity and associated cognitive impairments in Alzheimer's disease. Dr. Vossel also uses brain wave recordings to identify changes in brain rhythms in early-stage Alzheimer's disease, as markers of disease progression as well as response to therapy.

In the laboratory, Dr. Vossel is investigating how the disease protein tau contributes to seizures and associated memory loss in Alzheimer's disease as well as dementia with Lewy bodies. He is currently testing novel tau modifications and antiseizure drugs to prevent seizures and memory loss in scientific models of Alzheimer's disease and related disorders.

With these studies, Dr. Vossel brings a wealth of novel methods for Alzheimer's discovery and therapeutics to the Easton Center. With his unique understanding of basic biology of dementia and experience running clinical trials, Dr. Vossel will enhance the translational goals of the Easton Center.

Dr. Vossel says, "I am excited to join the talented and accomplished team of scientists and clinicians and the great collaborative spirit at UCLA. I look forward to contributing to UCLA's outstanding commitment to excellence in patient care and research. With our large and diverse patient population, world class neurogenetics, modern approaches to biospecimen collection, outstanding neuroimaging facilities, growing clinical program in dementia along with outstanding programs in epilepsy and sleep, brilliant minds in neuroscience, thriving clinical trials program, and established outreach program, I am confident we will make major contributions towards finding a cure for Alzheimer's disease."



We are delighted to have Dr. Vossel as the new Director for the Easton Center. Please join us in giving an enthusiastic welcome to Dr. Vossel.

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Discovery of Dual Inhibitors for the Treatment of Alzheimer's Disease

The Drug Discovery Lab's (DDL) [Tina Bilousova](#), [Jesus Campagna](#), [Barbara Jagodzinska](#), [Patricia Spilman](#), and Professor [Varghese John](#), in collaboration with Professors [Karen Gyllys](#) and Neil K. Garg, had their recent publication highlighted in the May 14, 2020, UCLA Health news about "*the discovery of a novel class of compounds that function as dual inhibitors of the enzymes neutral sphingomyelinase 2 (nSMase2) and acetylcholinesterase (AChE). Inhibition of these enzymes provides a unique strategy to suppress the propagation of tau pathology while supporting cognitive function for the treatment of Alzheimer's disease.*" Aggregation and spread of abnormal forms of the protein tau through multiple brain regions in Alzheimer's disease (AD) are a hallmark of the disease and closely related to decline in cognitive function. Acetylcholinesterase breaks down a molecule important for memory – acetylcholine – and is the target of some currently available therapeutics for the symptoms of AD. nSMase2 is an enzyme which is responsible for control of the release of a subpopulation of small sacs of fluid, called exosomes, which are involved in the spread of tau pathology through the brain. Exosomes are released by brain cells and carry molecules such as proteins or RNA/DNA. The authors describe the key structure-activity relationship elements that control relative nSMase2 / AChE inhibitor potency, and the identification of a lead analog, a drug prototype, that suppresses the release of tau-bearing exosomes *in vitro* and *in vivo*. Identification of these novel dual nSMase2/AChE inhibitors represents a potential new therapeutic approach to AD. The unique combination of pro-cognitive and anti-inflammatory effects with suppression of exosome-mediated tau spread could lead to the development of truly disease-modifying therapeutics. The FDA is currently encouraging the development of combined therapeutics targeting multiple pathways to address the complexity of the AD and the dual inhibitors represent such a combination. Read more in *ACS Chemical Biology*, 2020.

<https://pubs.acs.org/doi/abs/10.1021/acscchembio.0c00311>

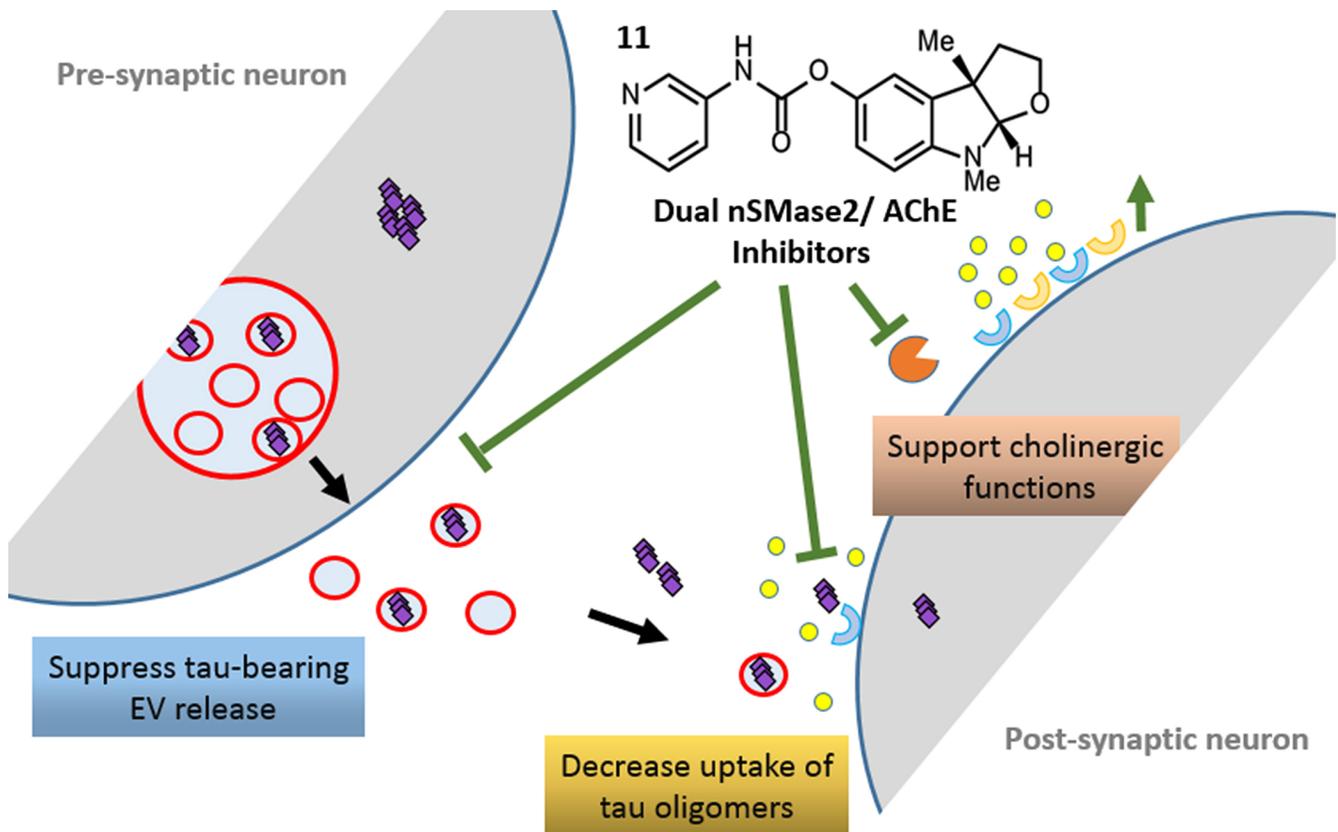


Figure: *Dual nSMase2/AChE inhibitors (structure shown) combine two inhibitory functions in a single molecule.* Inhibition of neutral sphingomyelinase 2 (nSMase2) decreases release of exosomes – small sacs that are released from brain cells that carry proteins, RNA and DNA - from pre-synaptic neurons (the brain cells that transmit information to neighboring cells) and slows the spread of abnormal forms of the protein tau implicated in Alzheimer’s disease. A second function, inhibition of acetylcholinesterase (AChE), increases levels of a key pro-cognitive chemical acetylcholine, which can also block uptake of abnormal tau through the acetylcholine receptors M1 and M3 in post-synaptic neurons (the cells that receive information from pre-synaptic neurons), contributing to the slowing of tau spread.

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New Addition to the Easton Center

Please join us in welcoming a new staff member to the Easton Center.



Photo: [Hannah Bojorquez, BA](#)

Hannah joins the Mary S. Easton Center as a new member of the Neurology Department. She received her Bachelor of Arts degree in Psychology from California State University, Fullerton and is currently working on her Master of Science degree in Evaluation and Applied Research from Claremont Graduate University. During her undergraduate studies, she worked for the Twins Studies Center as a research assistant and worked on various research studies dealing with twin loss bereavement. Before joining the Easton Center, she worked as a clinical research coordinator on pharmaceutical focused research studies in mental health such as ADHD, anxiety, depression, bipolar disorder, and schizophrenia clinical trials. Hannah is excited to work for UCLA’s Alzheimer’s Disease Research Center and looks forward to working on the innovative Alzheimer’s and Dementia related research studies as well as gain research experience as a staff research associate.

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Clinical Research Opportunities

If you would like to advance Alzheimer's disease research, please consider being a study participant. Below are the current recruiting trials. For more information, please visit our website at www.eastonad.ucla.edu or call the **Kagan Clinical Trials** office at **(310) 794-6191**.

BEHAVIORAL NEUROLOGY PROGRAM

- [Early-onset Alzheimer's Disease Phenotypes: Neuropsychology and Neural Networks](#)

OTHER PROGRAMS

- [Curcumin and Yoga Therapy for Those at Risk for Alzheimer's Disease](#)

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For more information on our upcoming lectures and events, please visit the Easton Center [Community Calendar](#).

Memory and Aging

Co-sponsored by UCLA 50 Plus Program

Date: Thursday, September 17, 2020

Time: 10:00 A.M. – 11:30 A.M.

Virtual Forum

For more information and to register, please visit:

<https://connect.uclahealth.org/event/memory-and-aging-1/?date=2020-09-17>

Memory Matters

Co-sponsored by OPICA and Always Best Care Senior Services

Beginning: Thursday, October 1, 2020

Time: 10:00 A.M. – 12:00 P.M.

Virtual Forum

This is an 8-week evidence informed virtual session for people with early memory loss and their care partners. For more information and to register, please contact David Hart, PhD at dHart@abc-seniors.com or at (424) 323-3518.

New Approaches to Treating Alzheimer's Disease
In partnership with Kensington Senior Living

Date: Thursday, October 1, 2020

Time: 3:00 P.M. – 4:30 P.M.

Virtual Forum

In partnership with Kensington Senior Living, the Mary S. Easton Center for Alzheimer's Disease Research at UCLA presents this special educational event. Keith Vossel, MD, MSc, Easton Center Director will discuss the latest in Alzheimer's disease research and Sarah Kremen, MD will discuss current clinical trial research being conducted to treat Alzheimer's disease.

For more information, please contact Monica Moore, MSG at mrmoore@mednet.ucla.edu.

To register, please visit: https://uclahs.zoom.us/webinar/register/WN_jrQOW49gTdOaoBdzC3d05w

Update on Alzheimer's Disease Research
Co-sponsored by Alzheimer's Los Angeles

Date: Wednesday, October 21, 2020

Time: 10:00 A.M. – 11:30 A.M.

Virtual Forum

For more information and to register, please visit:

<https://www.alzheimersla.org/los-angeles-alzheimers-events/alzheimers-research-update-10-21-2020/>

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