

# COMMONWEALTH OF VIRGINIA

## Alzheimer's and Related Diseases Research Award Fund

### 2021-2022 ALZHEIMER'S RESEARCH AWARD FUND RECIPIENTS ANNOUNCED

The Alzheimer's and Related Diseases Research Award Fund (ARDRAF) was established by the Virginia General Assembly in 1982 to stimulate innovative investigations into Alzheimer's disease and related disorders along a variety of avenues, including the causes, epidemiology, diagnosis, and treatment of the disorder; public policy and the financing of care; and the social and psychological impacts of the disease upon the individual, family, and community. The ARDRAF competition is administered by the Virginia Center on Aging in the College of Health Professions at Virginia Commonwealth University. Questions about the projects may be directed to the investigators or the ARDRAF administrator, Dr. Constance Coogle ([ccoogle@vcu.edu](mailto:ccoogle@vcu.edu)).

**GMU**      **Alicia Hong, PhD, Sojung Kim, PhD, and Emily S. Ihara, PhD**  
***Alzheimer's Research Inquiry and Care for Asian Americans (ARICAA): Protocol development of a culturally tailored social media-based program***

Significant racial and ethnic disparities exist in Alzheimer's disease and related diseases (ADRD) health outcomes, but minorities are less likely to participate in ADRD clinical trials. Asian Americans and Pacific Islanders (AAPI), the fastest growing racial group in the U.S., are underrepresented in ADRD research. AAPI constitute a heterogeneous group; about 67% are foreign born immigrants, many have limited English proficiency and poor access to ADRD information and services due to culture, language, and financial barriers. To address this gap, we will develop a culturally tailored, linguistically appropriate, social media-based program for AAPI older adults and their caregivers. This program, called *Alzheimer Research Inquiry and Care for Asian Americans*, will focus on the largest AAPI group of Chinese Americans. The program will be delivered via WeChat, a popular social media app used Chinese Americans. The research team will adapt evidence-based theory-guided multimedia messages to target the multi-level barriers to ADRD research participation. They will work closely with local AAPI community-based organizations, using community-engaged approaches and user-centered designs. The investigators will conduct focus groups, as well as usability and feasibility testing to ensure the program's cultural relevance, ease of navigation, and high user satisfaction levels. At the conclusion of this study, the program will be ready for an efficacy trial with wide dissemination.

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**GMU**      **Nadine Kabbani, PhD, Alessandra Luchini, PhD, and Amarda Shehu, PhD**  
***Mechanisms of Amyloid Interaction and Signaling through the Nicotinic Receptor***

Alzheimer's Disease (AD) is marked by chronic neurodegeneration in areas of the brain that utilize acetylcholine for signaling and transmission. While many of the current medications aim to restore acetylcholine (cholinergic) signaling by inhibiting its breakdown or mimicking its presentation, emerging approaches that target amyloid beta present new strategy options in AD treatment. Transformative drug development, however, is stymied by barrier gaps in understanding the emergence of pathogenicity in amyloid protein systems; a problem that exists in AD and other neurodegenerative disorders such as Parkinson's disease. To this end, the investigative team will use a new approach that combines innovative methods in protein science and structural and cell biology to study mechanisms of beta amyloid (A $\beta$ )-mediated signaling on target nicotinic receptors in human neural cells. Focusing on both the proteins and lipids, they aim to uncover salient mechanisms that bridge cholinergic and amyloid systems in the pathology and potential treatment of AD.

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**VCU Shenandoah Valley Family Practice Residency**      **J. William Kerns, MD, and Jonathan Winter, MD**  
*Clinician perspectives regarding COVID-19's impact on management approaches to dementia symptoms in Virginia nursing homes*

Despite poor evidence for efficacy, unsafe drugs continue to be used in Virginia long-term care facilities (LTCFs) to treat behavioral symptoms of dementia. The investigators have previously shown that although antipsychotic use is decreasing, antiepileptic mood-stabilizer prescribing to residents with dementia, but no diagnosis of epilepsy, now exceeds all antipsychotic prescribing in Virginia LTCFs. These trends are even more pronounced in rural areas, locales with a high proportion of minorities, and those with adverse socioeconomic determinants of health. There is already early regional and national data suggesting that the numerous stressors of the COVID-19 pandemic have caused deterioration of mood and behavior symptoms in LTCF residents, as well as a dilution of LTCF staffing resources. Both outcomes have resulted in an increased reliance on risky psychoactive drugs. The research team will employ both quantitative and qualitative methods and iteratively survey a representative sample of Virginia LTCF prescribers to delineate perceived trends in resident mood and behavior, as well as changes in management strategies of these symptoms during the COVID-19 pandemic. Survey data will be examined for differences based on prescriber, community, and facility characteristics. The study will examine prescriber degree/training, community composition and regional social determinants of health, facility ownership, and perceived facility resources. Data analyses will emphasize not only obstacles and barriers to best care, but also successes and lessons learned. *(Dr. Kerns can be contacted at 540-631-3700, [bkerns@valleyhealthlink.com](mailto:bkerns@valleyhealthlink.com); Dr. Winter can be contacted at 540-631-3700, [jwinter@valleyhealthlink.com](mailto:jwinter@valleyhealthlink.com))*

**VCU**      **Gretchen N. Neigh, PhD**  
*Dietary Choices as Drivers of Mitochondrial Dysfunction in the Brain: Implications for Dementia*

Fructose consumption has increased by at least 25% in the past 30 years due to increases in added sweeteners such as sucrose and high-fructose corn syrup. Adolescents are the highest consumers of fructose which contributes to a global energy imbalance, resulting in a growing epidemic of metabolic syndrome that begins in adolescence and is maintained into adulthood. The epidemic has resulted in over 20% of American adolescents qualifying as obese and 20% meeting criteria for prediabetes. The implications of these early life dietary choices for the aging brain are unknown. Research has shown that metabolic disease is predictive of Alzheimer's Disease and other dementias, but little is known about the mechanisms by which dietary choices across the lifespan may cause neurodegeneration. Because of the ability to control the environment across the short lifespan of the rat, rodent models can provide insight into the mechanisms by which diet choices early in life can fuel neurodegeneration in late life. Mitochondria, the powerhouse of cells, change in function with aging, and neuronal mitochondrial dysfunction has been directly implicated in Alzheimer's disease. The investigative team has established that a diet high in fructose during adolescence disrupts mitochondrial functioning in young adult rats. This study aims to determine the extent to which early life diet interacts with sex to precipitate cognitive impairment and mitochondrial dysfunction. *(Dr. Neigh can be contacted at 804-628-5152, [Gretchen.mccandless@vcuhealth.org](mailto:Gretchen.mccandless@vcuhealth.org))*

**JMU**      **Terrie Rife, PhD**  
*Understanding the Role of Tau Isoform Variants in the Nucleus*

The misfolding of a protein, called tau, into neurofibrillary tangles correlates with the loss of cognition during Alzheimer's Disease (AD). To comprehend the effects of tangle formation, we must realize the normal function of tau. Recently published data illustrates a novel role for tau in the nucleus where it's binding to DNA provides protection and regulating gene transcription. Tangles appear to keep tau from binding to DNA, resulting in increased DNA damage as well as gene expression changes which likely affect cognition and lead to neuronal death. Completely understanding the role of tau in DNA binding is hampered by the fact that multiple types or isoforms of tau are produced from the tau gene, MAPT. Levels of some of these tau isoforms change during the development of AD and moreover, the function of different isoforms vary from one another in regions believed to interact with DNA or affect the nuclear function of tau. Thus, different isoforms likely have varied abilities to bind DNA, protect against DNA damage and control transcription. To study isoform specific effects, human cell culture lines expressing various tau isoforms will be generated and used to quantitate how well each isoform can bind to and protect DNA. Additionally, DNA binding assays will be used to compare DNA binding among the isoforms. Knowing how each isoform performs will help us to better comprehend how changes in tau expression may affect AD development. *(Dr. Rife can be contacted at 540-568-3343, [rifetk@jmu.edu](mailto:rifetk@jmu.edu))*

**ODU Tancy Vandecar-Burdin, PhD, Brian K. Payne, PhD, and Muge Akpinar-Elci, MD, PhD**  
***An Examination of Isolation and Risk of Alzheimer's Caregivers during COVID-19:  
Computer Use as a Security Risk or Effective Coping Tool?***

This study will investigate the impact of the COVID-19 pandemic on the social isolation and potential cybersecurity risks of Alzheimer's and other dementia caregivers. Utilizing surveys, interviews, and/or focus groups this study will examine the isolation and risks of Alzheimer's caregivers relative to their caregiving responsibilities during the COVID-19 pandemic in Virginia. The pandemic has increased social isolation for most segments of society, but this is perhaps especially problematic for older populations and those with caregiving responsibilities who experienced higher rates of social isolation *prior* to the pandemic. Some caregivers may turn to virtual support networks and other resources to help with their caregiving responsibilities, but this may also place them at greater risk of victimization for cybercrime including identity theft and fraud. **(Dr. Vandecar-Burdin can be contacted at 757-683-3802; [tvandeca@odu.edu](mailto:tvandeca@odu.edu); Dr. Payne can be contacted at 757-683-4757; [bpayne@odu.edu](mailto:bpayne@odu.edu); Dr. Akpinar-Elci can be contacted at 757-683-5900; [makpinar@odu.edu](mailto:makpinar@odu.edu))**

**VCU Shijun Zhang, PhD**

***Development of NLRP3 PET Radiotracers for Alzheimer's Disease***

Neuroinflammation has been recognized as an essential contributor to AD. This notion is supported by the evidence of a number of studies showing increased levels of inflammatory proteins and cytokines long before the clinical symptoms of AD. The Nucleotide-binding Oligomerization Domain (NOD)-like receptors (NLRs) are a family of intracellular proteins, which play a pivotal role in host defense. The NOD-like receptor-pyrin-domain containing protein 3 (NLRP3) inflammasome is an essential component of innate immunity that regulates the production of proinflammatory cytokines and promotes inflammatory cell death. Notably, recent studies have indicated roles of the NLRP3 inflammasome in the pathogenesis of AD. Therefore, development of NLRP3 positron emission tomography (PET) radiotracers represents scientific and clinical interests to help early disease diagnosis and support clinical trials. Recently, the investigator developed selective small molecule NLRP3 inhibitors with novel mechanism of action and efficacy in AD animal models. More importantly, pilot PET imaging studies employing one of the [11C]-labeled analogs demonstrated rapid and displaceable brain uptake. With a long-term goal of developing NLRP3 PET radiotracers to facilitate development of AD therapeutics, the objective of the current proposal is to: 1) prepare analogs based on our newly identified NLRP3 lead inhibitors to improve binding affinity and potency and 2) radiolabel the candidate compounds to evaluate the PET radiotracers in mice for their brain uptake, specific binding and duration of labeling. **(Dr. Zhang can be contacted at 804-628-8266; [szhang2@vcu.edu](mailto:szhang2@vcu.edu))**

***2021-2022 ARDRAF Awards Committee***

The Virginia Center on Aging acknowledges the dedicated work of this independent review panel of subject matter experts and gratefully thanks them for contributing their time and expertise.

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