

Alzheimer's and Related Diseases Research Award Fund

2006-2007 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 (AD) and related disorders along a variety of avenues, such as 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 at Virginia Commonwealth University in Richmond. The six grant awards for 2006-2007 are as follows:

VCU Dusan Bratko, D. Sc. (Department of Chemistry) "Computer Screening of Amyloidogenic Protein Variants"

Because of its ability to provide microscopic insights not accessible by experiment, computational chemistry is becoming an important tool in biophysical and biomedical research. This study addresses, through computer simulation, the molecular properties of pathological intra- or extracellular agglomerations of misfolded proteins associated with Alzheimer's and related diseases. The role of mutations that affect peptide aggregation will be inspected as well. If successful, the proposed work will represent a significant step toward the development of high-throughput computational methods to screen amyloidogenic protein variants. This understanding will assist in identifying systems conditions and protein mutations relevant for prediction, treatment, and prevention of debilitating processes involved in neurodegenerative diseases. New insights into these association mechanisms will contribute toward elucidating fundamental biophysical principles of multi-protein assembly, a key element for successful control of disease-related aggregation processes.

(Dr. Bratko can be reached at 804/828-1865)

EVMS Frank J. Castora, Ph.D. (Department of Physiological Sciences) "Effect of T9861C mtDNA Mutation on Cytochrome Oxidase Structure and Function"

Mitochondria, the "powerhouses" of cells, play an important role in the development of Alzheimer's Disease (AD), and researchers are examining the mitochondrial DNA molecule for mutations that may be associated with AD. This investigator has identified a mutation (T9861C) that dramatically reduces the activity of cytochrome oxidase, one of the essential components of the respiratory chain. The current project is designed to extend this preliminary observation by evaluating the activity of cytochrome oxidase in more AD samples that also possess the same mutation. This research will also use a combination of separation techniques to determine if the mutation is changing the structure or assembly of the cytochrome oxidase complex. Evaluating the effect of this mutation on the structure and function of cytochrome oxidase may help identify how disrupting normal mitochondrial function could lead to or accelerate the development of AD. This, in turn, could provide a potential target for slowing down that inevitable progression. *(Dr. Castora can be reached at 757/ 624-2270)*

UVA Paul Freedman, Ph.D., Richard J. Bonnie, LL. B., and Thomas M. Guterbock, Ph.D. (Department of Politics; Government & Foreign Affairs) "Voting and Dementia in Virginia Long-Term Care Facilities"

This group of investigators will study the policies and practices that affect voting by senior citizens in long-term care settings such as nursing homes and assisted living facilities, particularly as they bear on the enfranchisement (or disenfranchisement) of residents with dementia and other cognitive impairments. The first component of the study is a multi-mode survey of staff informants from a representative sample of long-term care facilities in the Commonwealth of Virginia. The survey will be designed to collect data on registration and voting practices, with an emphasis on the measures taken (if any) to assess voting capacity of individuals with diagnoses of dementia, to promote and facilitate voting by those who are capable of doing so, and to prevent fraudulent exploitation of those who lack the capacity to vote. The second component is a vote-validation study, designed to ascertain from public records the registration status and rate of electoral participation of a sample of residents from a sub-sample of the surveyed long-term care facilities. The results will indicate which policies and practices are most effective in facilitating voting by those residents capable of doing so, and provide the foundation for a national study. *(Dr. Freedman can be reached at 434/924-1372; Professor Bonnie can be reached at 434/ 924-3209)*

UVA Ian G. Macara, Ph.D. and Huaye Zhang, Ph.D. (Center for Cell Signaling, School of Medicine) “The Role of Septins in Alzheimer’s Disease”

One of the pathological hallmarks of Alzheimer’s disease (AD) is the formation of neurofibrillary tangles (NFTs), twisted tangles inside the brain’s nerve cells, which contain hyperphosphorylated tau proteins. In healthy cells, tau is attached to long strands called microtubules, which act as the cell’s “skeleton.” However, in the brain cells of AD patients, tau falls off of the microtubules and sticks together to form tangles. In addition to tau, a family of guanosine triphosphate (GTP)-binding proteins, known as septins, is also found in the NFTs. These investigators have found that septins bind with a homologue of tau that is distributed mainly in non-neuronal tissues, microtubule-associated protein 4 (MAP4), and induces dissociation of MAP4 from microtubules. The major goal of this research is to elucidate the role that septins play in regulating tau-microtubule interactions in hippocampal neurons. In addition, the study will test the hypothesis that septins facilitate NFT formation, first in cultured cells, and then eventually *in vivo*. These results will provide new insights into the function of septins in neuronal cells and their role in Alzheimer’s disease. (*Dr. Macara can be reached at 434/924-1236*)

GMU Jeanne Sorrell, Ph.D., R.N. (College of Nursing and Health) and Catherine J. Tompkins, Ph.D. (Department of Social Work) “Ethics of Respect for Spirituality in Persons Living with Alzheimer’s Disease”

This study seeks to answer the question, “How do members of a faith community describe experiences of spiritual connections to Alzheimer’s disease (AD)?” The investigators will implement a grounded theory methodology to explore the concepts that comprise spiritual pathways and identify categories of spiritual connections within the social context of persons with AD and their families living in a faith community. Unstructured interviews with persons diagnosed with AD, family caregivers, and members of five faith communities will elicit in-depth descriptions of participants’ experiences in three primary focus areas: 1) spiritual beliefs related to coping with AD for both persons with AD and caregivers, both in the early and late stages of the disease, 2) ways in which spirituality contributes to the overall concept of quality of life within a faith community, and 3) ways in which members of faith communities facilitate or hinder the development of spiritual connects for persons with AD and their families. Qualitative data will be analyzed to identify codes, concepts, and categories relevant to the spiritual dimensions that characterize participants’ experiences. Implications of an ethics of respect for spirituality in persons living with AD will be discussed in terms of their implications for health care practice, education, research, and policy. (*Dr. Sorrell can be reached at 703/993-1944; Dr. Tompkins can be reached at 703/ 993-2838*)

VCU Jeffrey L. Dupree, Ph.D. (Department of Anatomy and Neurobiology) “Understanding the Role of Sulfatide in Maintaining Viable Neurons in Alzheimer’s Disease”

Since neuronal death is the most prevalent pathology in AD, most research has focused on understanding intra-neuronal processes that regulate survival. This project, however, will investigate a class of cells whose role in maintaining viable adult neurons has been grossly ignored, i.e., the supporting glial cells known as oligodendrocytes (OLGs), best known for their role in the formation of myelin, the insulating wrap that ensures rapid nerve impulse transmission. In addition, they are almost exclusively responsible for the production of a prominent brain lipid, known as sulfatide, which is significantly reduced in the earliest stages of dementia. The investigator has recently used a mouse that is unable to synthesize sulfatide to show that this lipid is required for the maintenance of oligodendrocyte-neuron interactions. The loss of proper OLG-neuron communication induces abnormal tau phosphorylation as seen in AD. In the aged sulfatide null mice, the accumulation of hyperphosphorylated tau results in a collapse of the microtubular network and the formation of neurofibrillary tangles, one of the hallmark features of AD. This investigator is primarily interested in the initial events that alter tau phosphorylation, and hypothesizes that the loss of OLG-neuronal interactions is one of the unknown external insults that activates tau-directed kinases and contributes to AD pathogenesis. The funded study will test this hypothesis by analyzing the accumulation of hyperphosphorylated tau and determining changes in the expression and distribution of specific tau kinases implicated in AD. (*Dr. Dupree can be reached at 804/828-9536*)