

Alzheimer's and Related Diseases Research Award Fund

2009-2010 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. The five grant awards for 2009-2010 are as follows:

VCU Guo-Huang Fan, Ph.D. "Potential therapeutic effect of lupeol on Alzheimer's neuropathology in a transgenic mouse model"

A major histopathological hallmark of AD is the amyloid plaque, composed of β -amyloid ($A\beta$) peptides. Agents that can reduce $A\beta$ accumulation may have therapeutic potential for AD. Epidemiological studies have reported that fruit and vegetable juices may play an important role in slowing the progression of AD, suggesting that some dietary substances could be effective in reducing AD neuropathology. The investigator discovered that lupeol (a triterpene found in fruits, vegetables, and medicinal plants) potently reduced the production of $A\beta$ in primary neuronal cultures. The mechanism of action is most likely accomplished by inhibiting the proteolysis of amyloid precursor protein, a process necessary for the generation of $A\beta$. This study aims to determine whether lupeol attenuates $A\beta$ -associated neuropathology and improves spatial memory deficits when administered to amyloid precursor protein and presenilin 1 (APP/PS1) double transgenic mice. $A\beta$ accumulation, tau hyperphosphorylation, synaptic loss, and spatial memory deficits will be assessed. The outcomes may lead to the identification of novel therapeutic agents for the treatment of AD. *(Dr. Fan may be contacted at 804/828-1674)*

**Alzheimer's Association Ellen Phipps, C.T.R.S., and Barbara Braddock, Ph.D.
Central and Western Virginia "Home-based cognitive intervention program in dementia"**

This preliminary study aims to investigate and promote 'partnered volunteering' by pairing University students with individuals who have dementia to examine the effectiveness of a home-based cognitive intervention. The intervention is designed to provide opportunities for participants to complete activities that were once meaningful in their lives using Montessori-based instruction, errorless learning, therapeutic recreational principles, and environmental modifications. The study has three goals: 1) to provide an opportunity for successful engagement in life for persons with a diagnosis; 2) to provide relief, education, and support to caregivers; and 3) to foster positive inter-generational relationships. This combination approach may translate into more constructive engagement and appropriate communication exchange for persons with dementia when delivered in the home. The findings will have implications for the development of sustainable community programs.

(Ms. Phipps may be contacted at 434/ 973-6122; Dr. Braddock may be contacted at 434/924-4000)

UVA Karen M. Rose, Ph.D., R.N., and Ishan C. Williams, Ph.D. "Family quality of life in dementia"

Because a diagnosis of dementia has implications for the overall functioning and well-being of the family unit involved, a reliable and valid instrument to assess the impact of services and resources that are provided, or not provided, on family quality of life is needed. This study will gather input from content experts on the dementia-related dimensions that are not addressed in an existing family quality of life instrument for families of children with disabilities. A pilot instrument will be developed and group interviews will be conducted with persons who have mild to moderate stage dementia and their family members to gain insights from their unique perspectives regarding family quality of life and pilot-test the instrument. Subsequent mailings of the revised instrument will be sent to family members of persons with dementia to gather additional data from a larger sample from across the Commonwealth of Virginia. Data from a broad-based use of the resulting instrument could result in enhanced legislation and agency policy. *(Dr. Rose may be contacted at 434/ 924-5627; Dr. Williams may be contacted at 434/924-0480)*

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VCU H. Tonie Wright, Ph.D. “Alzheimer’s A β amyloid peptide interactions with inflammatory chaperone molecules”

The causes for the loss of mental function characteristic of Alzheimer's disease (AD) are not unambiguously identified. β -amyloid (A β) peptide exists in a number of different forms, each consisting of a different number of copies of the peptide molecule. Research suggests that certain of these aggregated states are toxic to brain cells and may also disrupt communication between neurons in the brain. If this is the case, then it is important to know which of these peptide forms are toxic and what other molecules promote their formation. The investigator hypothesizes that chaperone-like inflammatory molecules change the relative concentrations and alter the overall biological activity of the A β pool. In this way, they would regulate the pathological activity of A β and implicitly offer new pharmacological targets for the development of novel therapies and, possibly, new prevention efforts. The experiments to be conducted will provide an initial test of the hypothesis that reciprocal interactions between A β and candidate chaperone molecules modulate the activities of both molecular species and thereby make multiple synergistic contributions to the development of AD. They address important unanswered questions at the molecular and cellular level relating to the fundamental causes of AD.

(Dr. Wright may be contacted at 804/828-6139)

UVA J. Julius Zhu, Ph.D., and Lei Zhang, Ph.D. “Mechanisms for Cdk5-mediated synaptic depression.”

Patients with Alzheimer’s disease (AD) exhibit the enhanced activity of a specific cyclin-dependent kinase 5 (Cdk5) due to the overproduction of a truncated form of the Cdk5 activator, p25 protein. The investigators’ preliminary evidence suggests that over-expression of human p25 in hippocampal neurons causes synaptic depression, a critical event that precedes defects in learning and memory in individuals with AD. Moreover, synaptic activity rapidly regulates Cdk5 signaling, which in turns induces a beta-amyloid-independent synaptic depression. The investigators will explore how Cdk5 activity regulates synaptic transmission. They will also test their central hypotheses that Cdk5 is a novel homeostatic regulator of synaptic strength and that aberrant Cdk5 activity leads to synaptic depression. The model may account for the disappointing results of recent high profile clinical trials because blocking beta-amyloid and tau should stimulate compensatory synaptic depression via Cdk5. The findings should suggest additional molecular targets and provide the scientific foundation for new drug designs and clinical trials.

(Dr.Zhu may be contacted at 434/243-9246; Dr. Zhang may be contacted at 434/243-9562)

2009-2010 ARDRAF Awards Committee

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