

Health Research Non-Formula Grants - State Fiscal Year 2004-05

The Pennsylvania Department of Health selected five collaborative research projects for funding in response to the Request for Application (RFA) # 03-07-07 for Centers of Excellence for Research on Neurodegenerative Diseases and Centers of Excellence for Research on Tobacco Use and Cessation. All research projects addressed one of the following research priorities established by the Department in conjunction with the Health Research Advisory Committee:

Neurodegenerative Diseases

- Research which develops or employs new technologies (e.g., imaging, biotechnology, nanotechnology, robotics, bioengineering) that leads to etiologic insights and/or early intervention approaches with the goal of preventing, ameliorating, treating, and/or curing Alzheimer's disease, Parkinson's disease, Amyotrophic Lateral Sclerosis, multiple sclerosis or related neurodegenerative diseases (excluding stroke) and providing insight into these conditions. Research may include but is not limited to the development of new cost-effective techniques of imaging and cognitive tests for the early detection of Alzheimer's disease and the identification of specific markers that will improve understanding of the etiology of neurodegenerative diseases. The research must include but is not limited to the testing of a clinical application designed to improve the early detection, amelioration or treatment of persons with neurodegenerative diseases. Research should place emphasis on underserved populations that are at high risk for and disproportionately impacted by neurodegenerative diseases. Applicants must establish a regional Center of Excellence to conduct research that is collaborative across research institutions or organizations. The Center of Excellence should, to the extent practicable, include partners that are smaller colleges and universities, biotechnology and bioengineering companies, and other institutions that are not academic medical centers in addition to the major research institutions. The research should hold the potential for population-based applications that address disparities in health status among vulnerable segments of the population, including rural, urban, or other high-risk Commonwealth populations. At least 50 percent of each grant's funds must be spent on health services and/or clinical research as defined in Act 77 of 2001; no more than 50 percent of each grant's funds may be spent on biomedical research, as defined in Act 77 of 2001. Biomedical research is "comprehensive research pertaining to the application of the natural sciences to the study and clinical practice of medicine at an institution, including biobehavioral research related to tobacco use." As stated in Act 77, biomedical research focuses on the application of the natural sciences and is distinguished from clinical and health services research as defined in Act 77.

Tobacco Use and Cessation

- Research into the underlying causes as well as the prevention and treatment of tobacco use. Research may include but is not limited to one or more of the following areas:
 1. novel approaches to understanding the etiologic mechanisms of tobacco use and addiction, especially among high-risk youth and other high risk populations such as long term 1+pack a day smokers and those with co-morbidities such as cardiovascular disease, pulmonary disease and depression;
 2. testing of new medications to reduce tobacco addiction; and
 3. the development and testing of prevention and treatment strategies to reach African Americans, Latinos or other racial/ethnic populations, persons with low education or income, or other special populations.

The research shall focus on identification of new scientific technologies and approaches at the community level designed to reach a defined high risk population or populations and to address tobacco use and cessation in such populations. Overall, the research should place emphasis on underserved populations or populations that are at high risk for tobacco use and addiction. Applicants must establish a regional Center of Excellence to conduct research that is collaborative across research institutions or organizations. The Center of Excellence should, to the extent practicable, include partners that are

smaller colleges, universities, industry, and other institutions that are not academic medical centers in addition to the major research institutions, including the Commonwealth's ongoing tobacco prevention and cessation programs. These funds shall support research and shall not duplicate the activities of the Commonwealth's tobacco prevention and cessation programs. The research should lead to population-based applications that address disparities in tobacco use among underserved populations including rural, urban, or other high-risk Commonwealth populations. At least 50 percent of a grant's funds must be spent on health services and/or clinical research as defined in Act 77 of 2001; no more than 50 percent of each grant's funds may be spent on biomedical research as defined in Act 77 of 2001. Biomedical research is "comprehensive research pertaining to the application of the natural sciences to the study and clinical practice of medicine at an institution, including biobehavioral research related to tobacco use." As stated in Act 77, biomedical research focuses on the application of the natural sciences and is distinguished from clinical and health services research as defined in Act 77.

The following list of grant awards provides the lead and collaborating institutions, title of the research project, amount of the grant award, grant award period, contact person, and a description of the project.

Centers of Excellence for Research on Neurodegenerative Diseases

- Thomas Jefferson University and the Philadelphia Corporation of Aging - *Modifying Lifestyles and Behavior: Impact on Alzheimer's Disease*, \$3,500,000 for a 48-month project (June 1, 2005 – May 31, 2009)

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The Center of Excellence will address health disparities by: (1) testing innovative screening and in-home skills services for families and persons with dementia from diverse cultural groups, with a specific emphasis on African Americans; (2) advancing an understanding of the scientific underpinnings of the disease process; and (3) educating health and human service professionals and students about state-of-the-art approaches to dementia research and care.

The specific aims of the Center of Excellence are:

(1a) To validate an innovative screening protocol to identify dementia in a racially-diverse community population of older adults. The protocol consists of a brief cognitive test and an informant interview to be administered to 300 nursing home-eligible persons who live at home. This will be validated against a comprehensive dementia evaluation.

(1b) To obtain pilot data on plasma amyloid peptide levels for exploratory analysis of the range of values in an African American population whose plasma amyloid peptide levels have not been studied.

(2) To test (a) the efficacy of a home-based intervention aimed at preventing negative patient outcomes (e.g., nursing home placement) and at improving

life quality of caregivers; and (b) the mitigating effect of the intervention on relevant biomarkers in both the caregiver and the dementia patient. A randomized clinical trial of 278 patient-caregiver dyads will be conducted to determine the efficacy of the home-based intervention to improve patient and caregiver outcomes. Salivary cortisol, a biomarker that has been correlated with stress (including caregiver stress), will be measured before and after standard or experimental intervention.

- The University of Pennsylvania, the Maria de los Santos Health Center, the Philadelphia Veterans Administration Medical Center and the University of the Sciences in Philadelphia (USP) - *Biomarkers of Late Life Dementia: The University of Pennsylvania Center of Excellence for Research on Neurodegenerative Diseases (CERND)*, \$4,972,777 for a 48-month project (June 1, 2005 – May 31, 2009)

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The broad objective is to identify objective cost-effective methods to identify the presence of a neurodegenerative dementing pathology at the earliest stage possible. The project has the following 4 specific aims: 1) to determine the sensitivity, specificity and positive likelihood ratio (PLR) of a variety of candidate biomarkers of late life dementia; 2) in a cross-sectional analysis, to compare the biomarker values in individuals with either mild cognitive impairment (MCI) or Parkinson's disease without dementia (PD) to values found in individuals with Alzheimer's disease (AD), Parkinson's disease with dementia (PDD), and elderly individuals who are cognitively normal (CN); 3) to determine the most cost-effective combination of biomarkers that will detect the presence of a neurodegenerative dementing pathology in individuals with AD and PDD; and 4) to correlate the changes in biomarker values to changes in cognitive function over 2 years.

These aims will be accomplished by recruiting and evaluating 100 individuals with MCI, 100 PD patients without dementia, 50 AD patients, 50 patients with PDD and 50 CN control subjects. All will have a thorough evaluation, including standardized measures of cognition, mood and functional abilities. Biomarkers to be evaluated at baseline and during the observation period include: CSF levels of phospho-tau, beta amyloid and F2-isoprostanes; urine levels of F2-isoprostanes; multiresolution discrete wavelet transform (DWT) analysis of event-related cortical potentials; MRI defined regional atrophy; MRI T1-rho defined macromolecular pathology; PET-FDG imaging of neuronal pathology; and SPECT-IMPY imaging of amyloid deposition. Subjects will complete all biomarker studies at baseline. Longitudinal clinical assessments, blood and urine specimens, and DWT data will be collected annually during the 2-year observation period. The MRI and PET imaging studies will be repeated at the final evaluation.

The USP alliance will foster the ability of this smaller university to generate independently-funded biomedical research, and will facilitate their ability to collaborate with the University of Pennsylvania (UPENN), other academic institutions, and biotech companies in Pennsylvania and elsewhere.

- The University of Pittsburgh, Cellumen, Inc., Carnegie Mellon University, Psychology Software Tools, Inc., the Pennsylvania State University and the Southwestern Pennsylvania Area Agency on Aging - *Detection, Diagnosis, and Intervention in Dementia (DDID)*, \$4,870,114 for a 48-month project (June 1, 2005 – May 31, 2009)

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The primary purpose of the Center is to develop and implement effective ways of screening the elderly population for cognitive impairment using a simple and non-threatening tablet computer for testing. Normal cases and cases with suspected cognitive impairment will be referred to the University of Pittsburgh Alzheimer's Disease Research Center (ADRC) for thorough evaluation to validate the accuracy of the computerized screening technique. Populations targeted for assessment and determination of norms will include subjects from rural areas of southwestern Pennsylvania, African Americans, and a standard volunteer control group in the ADRC. Associated cutting-edge detection and diagnosis techniques will be utilized with these populations, including positron emission tomography (PET) scans of fluorodioxylglucose (FDG) for energy activity in the brain and Pittsburgh Compound B, which labels deposits of beta amyloid, the protein deposited in the brain in Alzheimer's disease (AD). Finally, the MR scans performed as part of the evaluation will undergo analysis by a new Carnegie Mellon University Robotics Institute technique termed future learning. In preliminary studies, this technique appears to classify people into categories of normal, mild cognitive impairment (MCI), or AD by analysis of a single, one-time scan.

The basic research aspects involve development of a high-speed throughput analysis technique to find characteristic diagnostic signatures in alteration of tau protein, a key protein significantly altered in AD and leading to neuronal death. In addition to utilizing these live cell assays to develop diagnostic tests, they will be developed to detect compounds that would interfere with the pathological changes and lead to more effective therapies. High throughput screening of biochemical compounds will also be achieved using the most up-to-date robotic techniques to screen thousands of compounds for diagnostic tests or new lead compounds with which to treat AD. Finally, detection of a biomarker that represents an oxidized lipid will be explored. Biological samples from MCI, AD and normal subjects will be utilized to develop a specific signature for altered lipids in AD with the intention of finding a diagnostic marker or a presymptomatic disease marker in those who would go on to develop AD. These studies will also attempt to replicate other reported oxidized lipid markers to strengthen knowledge in this important area. All of the basic research aims will exchange promising compounds and samples to maximize the ability to detect novel diagnostic tests and potential interventions.

Centers of Excellence for Research on Tobacco Use and Cessation

- The Children's Hospital of Philadelphia, the Children's Hospital of Pittsburgh, Lehigh Valley Hospital, Drexel University College of Medicine and Saint Joseph's University – *Primary Care Network for Adolescent Smoking Cessation*, \$4,968,083 for a 48-month period (June 1, 2005 – May 31, 2009)

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The objectives are to establish a Center of Excellence at Children's Hospital of Philadelphia (CHOP) and create a statewide, collaborative research network to develop and test interventions for reducing adolescent cigarette smoking. This pivotal randomized clinical trial (RCT) will evaluate the effectiveness of Motivational Interviewing (MI) as compared to Structured Brief Advice (SBA) for smoking cessation in adolescents. This RCT will randomize 330 adolescents, ages 14 to 18 (inclusive) to MI or SBA. Reduction of cigarette smoking and smoking abstinence will be evaluated at 8, 12 and 24 weeks. Adolescents who report smoking at least once a week for the past 4 weeks and at least 5 packs in their lifetime will be eligible to participate. Adolescents will be recruited primarily from medical settings. Parents must give informed consent for participants under the age of 18. Participants will be randomized to MI or SBA. Stratification will be by 'readiness to change' smoking behavior. MI consists of three 45-60 minute office sessions and two 45-60 minute office or telephone sessions over 8-12 weeks. MI is a brief client-centered therapeutic style intended to reduce harmful behaviors through advancing stage of readiness to change by developing the discrepancy between current behavior and future goals, values and beliefs. SBA consists of three 15-30 minute office sessions and two 15-30 minute office or telephone sessions over 8-12 weeks. SBA implements Best Practice Guidelines (i.e., 5 A's and 5 R's) and assists participants in accessing resources for smoking cessation. The statewide, collaborative research network consists of Children's Hospital of Philadelphia (CHOP), Lehigh Valley Hospital (LVH), Children's Hospital of Pittsburgh (CHP), Drexel University College of Medicine at St. Christopher's Children's Hospital (DUCOM) and Saint Joseph's University (SJU). The network includes state-funded smoking cessation contractors from each participating county. Network activities include the establishment of multidisciplinary community advisory boards consisting of youth, providers, researchers and community stakeholders. Additionally, the Center will promote educational activities including post-doctoral research fellows, a research assistantship from SJU, and a long-distance training program for health care providers on adolescent tobacco cessation. Additionally, CHOP is developing and evaluating a computer-based screening tool to expand the platform for future tobacco cessation research.

- The University of Pennsylvania, the University of Pittsburgh and Lincoln University – *Improving Tobacco Dependence in Underserved Smokers*, \$1,652,483 for a 48-month project (June 1, 2005 – May 31, 2009)

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This study originally consisted of: (1) a clinical trial to examine the efficacy and safety of modafinil for treating nicotine dependence; and (2) a Training Core to foster the training and career development of minority students and faculty in tobacco control and disparities research. The modafinil trial was stopped when an interim analysis indicated it was not an effective treatment for nicotine dependence. We will continue the Training Core and conduct a new clinical trial to test the effect of alternate recruitment messages on enrollment in a smoking cessation program. The effect of recruitment messages on adherence, retention, and cessation will be examined as well. This trial will also explore mediators and moderators of the effects of recruitment messages on enrollment, adherence, retention, and cessation.

BROAD OBJECTIVES AND AIMS: Initially, the broad objectives of the Pennsylvania (PA) Consortium on Tobacco Disparities (PACTD) were to: (1) Conduct a collaborative research project "Improving Tobacco Dependence Treatment in Underserved Smokers"; and (2) Foster the training and career development of minority students and faculty in tobacco control and disparities research. The specific aims were: (1) To conduct a placebo-controlled randomized trial to test the safety and efficacy of modafinil for tobacco dependence, and (2) To train students and faculty and build research infrastructure at Lincoln University to conduct tobacco control and disparities research. Since the modafinil trial was stopped, we propose a new clinical trial for the remainder of the grant to test the effect of alternate recruitment messages on enrollment in a smoking cessation program.

PROJECT RESEARCH DESIGN: This will be a randomized clinical trial to assess the effect of different recruitment messages (generic message focusing on health threats of smoking vs. enhanced message emphasizing the genetic basis of nicotine dependence) on enrollment in an open-label treatment phase. Potential participants contacting the TTURC about a smoking cessation program from media ads will be screened for eligibility and interest in this study. Those willing to proceed will complete a baseline assessment, will be randomized to a recruitment message arm, and will be scheduled for their initial enrollment visit (week 0). The show-rate at week 0 is the first primary outcome for this study. At week 0, participants will be scheduled for their first smoking cessation program visit (week 1); this program provides 12 weeks of varenicline and 6 in-person behavioral counseling smoking cessation sessions. At Week 1, participants will be evaluated for their enrollment in the cessation program (the second primary outcome variable). At Week 13, all subjects will complete measures of smoking behavior, including measures of continuous abstinence and point prevalence abstinence, which will be biochemically verified (a secondary outcome variable for Aim 1). Adherence to counseling and medication and retention will be assessed as secondary outcomes for Aim 1 as well.