

Health Research Non-Formula Grants - State Fiscal Year 2003-04

The Pennsylvania Department of Health selected five collaborative research projects for funding in response to the Request for Application (RFA) # 02-07-20 for Centers of Excellence for Research on Lung Disease and Centers of Excellence for Research on Pregnancy Outcomes. All research projects addressed one of the following the research priorities established by the Department in conjunction with the Health Research Advisory Committee:

- Research to improve the prevention, diagnosis, and treatment of certain lung disorders that may result from environmental exposures. Research must focus on one or more of the following lung disorders: bronchial asthma, occupational lung diseases, chronic obstructive pulmonary diseases (emphysema and chronic bronchitis), bronchiectasis, and interstitial lung diseases such as idiopathic pulmonary fibrosis, pulmonary vascular disease, and different forms of lung cancer. Research on cystic fibrosis or other lung disorders and interventions designed to modify tobacco use patterns will not be considered. The research must be focused on underserved populations or populations that are at high risk for lung disease. 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 and other institutions that are not academic medical centers in addition to the major research institutions. The research should lead to population-based applications that address disparities in health status among underserved populations including rural, urban, and other high-risk Commonwealth populations.
- Research to improve pregnancy outcomes for mothers and their children. Research may include but is not limited to one or more of the following areas: toxemia; intrauterine effects and prenatal factors related to autism; the effect of infectious diseases on pregnancy outcomes; factors related to endothelial function such as arginine, Vitamin E, and aspirin; factors related to premature labor; gestational diabetes; and detection of risks and causes of developmental abnormalities. The research must be focused on underserved populations or populations that are at high risk for experiencing adverse pregnancy outcomes. 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 and other institutions that are not academic medical centers in addition to the major research institutions. The research should lead to population-based applications that address disparities in health status among underserved populations including rural, urban, and other high-risk Commonwealth populations.

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 Pregnancy Outcomes

- Drexel University, East Stroudsburg University, the Health Federation, Philadelphia Department of Public Health, Temple University and the University of Pennsylvania - *Philadelphia Collaborative Preterm Prevention Project*, \$4,899,644 for a 48-month project (June 1, 2004 – May 31, 2008)

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The long term overall goal is to improve pregnancy outcomes and specifically to reduce adverse outcomes in disadvantaged and minority populations. The broad objective of this project is to transform Drexel's multidisciplinary pregnancy outcome research group into a major Center of Excellence and expand its membership to include scientists from a number of institutions in the Philadelphia area. This multidisciplinary team will undertake a large prospective randomized trial aimed at reducing repeat preterm births in Philadelphia women who just experienced a preterm birth at < 34 weeks gestational age. The project aims to reduce repeat preterm births by targeting a wide variety of risk factors for preterm birth including identification and treatment of infections, smoking, stress, depression, and abnormal weight (too high or too low) and by delaying repeat pregnancy. It is hypothesized that these seemingly disparate yet well-known risk conditions lead to preterm birth through a common physiological mechanism, increase in systemic inflammation. It is believed that the proposed interventions will eliminate or ameliorate these conditions and therefore the associated systemic inflammation in the interconceptional period. The project will test the hypothesis that reducing inflammation prior to pregnancy will reduce the likelihood of a repeat preterm birth. This research is novel because it is focusing on an extremely high-risk group in the interconceptional period, using a multi risk factor reduction approach and because we are testing a novel biological pathway.

- The Pennsylvania State University, Family Health Council of Central Pennsylvania, Franklin and Marshall College and Lock Haven University of Pennsylvania - *Central Pennsylvania Center of Excellence for Research on Pregnancy Outcomes*, \$4,702,613 for a 48 month project (June 1, 2004 – May 31, 2008)

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The overall goal of this project is to reduce disparities in adverse pregnancy outcomes (preterm birth and low birth weight) by improving women's preconceptional health and health care. The project will focus on high-risk, medically underserved populations in Central Pennsylvania, with particular emphasis on rural areas that have received little prior attention. The specific aims are to: (1) characterize the population prevalence of a range of environmental, psychosocial and biological risk factors for preterm birth and low birth weight in reproductive-age women in Central Pennsylvania; (2) identify the relationships among risk factors and race/ethnicity, socioeconomic status, rurality, and health care access; and (3) develop and test a multidimensional intervention to improve women's preconceptional health, health behaviors, and health literacy by addressing prevalent proximal risk factors and barriers to health care in high-risk populations. The methods will include a population-based survey of women and a randomized trial of a biobehavioral group intervention.

- The University of Pennsylvania, Children's Hospital of Philadelphia, Albert Einstein Medical Center and Pennsylvania Hospital - *Center of Excellence for Research in Pregnancy Outcomes*, \$4,779,544 for a 48-month project (June 1, 2004 – May 31, 2008)

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The proposed research project will use a multi-center double-blind, parallel, randomized, controlled clinical trial design to compare the efficacy of dental scaling and root planing compared to control treatment (superficial cleaning) for the prevention of preterm birth in pregnant women with periodontal disease.

The primary outcome measure for this study will be preterm birth at less than 35 weeks. The relationship between treatment and other secondary outcome measures, including preterm birth <37 weeks and <32 weeks, length of gestation (continuously measured), neonatal morbidity, and maternal infectious complications will also be examined.

There will also be a nested molecular-genetic component of this study, in which gingival fluid/cervicovaginal matrix metalloproteinase and interleukin specimens will be stored, as will maternal DNA (to assess polymorphisms in genes plausibly linked to inflammation linked preterm birth). The specimens on all preterm births and a sample of term deliveries will be analyzed in order to better understand the mechanism by which periodontal disease is associated with preterm birth, and whether response to therapy may depend on disease severity and underlying genetic susceptibility.

A prospective randomized, placebo-controlled clinical trial has been selected because it is the most appropriate way to obtain the most valid measure of efficacy, controlling for a large number of variables, whether known or unknown, measurable or unmeasurable, that may confound the association between periodontal disease and preterm birth. A double blind design was chosen to assure an unbiased measure of outcome.

Centers of Excellence for Research on Lung Disease

- Temple University, Lancaster General Hospital, Philadelphia College of Osteopathic Medicine, University of Pittsburgh, and the Western Pennsylvania Hospital – *Pennsylvania Study of Chronic Obstructive Pulmonary Exacerbations (PA-SCOPE)*, \$4,717,877 for a 48-month period (June 1, 2004 – May 31, 2008)

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Chronic obstructive pulmonary disease is a progressive and debilitating disease caused mainly by smoking. In the U.S. in 2000, COPD was responsible for 8 million office visits, 1.5 million emergency room visits, 726,000 hospitalizations, and 119,000 deaths. In Pennsylvania, chronic respiratory lung diseases are the 4th leading cause of death. Pennsylvania spends at least \$400 million per year treating acute episodes of COPD. As the population ages, these costs will still soar even if smoking cessation programs are successful because of the aging COPD patients who are "already in the pipeline." PA-SCOPE focuses on COPD exacerbations. *Phase 1* of PA-SCOPE will evaluate a diverse population of 300 Pennsylvania residents to identify potential risk factors for exacerbations of (COPD) leading to hospitalization. Approximately 200 African American patients and 100 Caucasians will be enrolled. An additional 300 patients without COPD will be recruited to provide a gene pool reference (i.e., blood sampling only) since no normal reference data exists in such a racially diverse patient group. Because data indicate that African American and rural patients have more severe COPD with more frequent hospitalizations, special attention will be paid to geographic residence as a potential risk factor for COPD exacerbations. Genetic predispositions, infections, environmental exposures, and socioeconomic status will also be evaluated. *Phase 2* of PA-SCOPE will test a novel, low-cost system designed to help COPD patients of all races get earlier medical help via a 1-800 phone number. In this randomized 2-year prospective trial in 400 patients with a recent history of exacerbation, the goals will be to reduce hospitalizations and deaths due to COPD exacerbations and to improve patient quality of life, lung function, and everyday activity levels.

- The Wistar Institute, Fox Chase Cancer Center and the University of Pennsylvania – *Identification of Lung Cancer Biomarkers from Blood*, \$3,422,351 for a 48-month project (June 1, 2004 – May 31, 2008)

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The *broad objective* of this project is to use synergistic state-of-the art proteomic and gene profiling methods to identify serum markers of human lung cancer that can be used for early diagnosis of high risk patients. *Aim 1* will use a SELDI mass spectrometry-like approach to analyze protein patterns in patient sera and matched controls to identify protein biomarkers specific for lung cancer. *Aim 2* will use a SCID mouse model system where recently established human lung cancer cell lines are implanted. Serum will be analyzed by novel proteomic protein profiling methods capable of distinguishing human proteins secreted by the human tumor into the mouse serum. *Aim 3* will use microarrays to examine the gene expression profiles in the peripheral blood of lung cancer patients and controls to identify "cancer specific" gene expression patterns. *Aim 4* will select the best putative biomarkers of human lung cancer identified in the above aims, for further testing using patient serum samples. These putative protein biomarkers will be evaluated by producing specific antibodies to these markers and establishing high throughput quantitative immunoassays. Genetic biomarkers will be tested by establishing real time PCR assays. These assays will then be used to screen large numbers of serum samples from patients with early

stage lung cancer and matched controls. Biomarkers will be evaluated for their potential to detect early disease in high risk patients.

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