



## EVALUATION OF PATIENT CHARACTERISTICS AS PREDICTORS OF ACUTE TREATMENT TOXICITY

*Andre Rogatko, PhD, Biostatistics, Rollins School of Public Health, Winship Cancer Institute*

**Purpose:** The goal of this initiative is to construct a comprehensive model that integrates clinical, genetic, pharmacokinetic, and pharmacodynamic information to provide guided dose selection. It is expected that the information gathered during this study will allow the customization of dosing regimens, wherein taxane doses are adjusted according to individual patient susceptibilities. Hence, each patient would be maintained at his or her maximum tolerable dose and duration of therapy, thus reducing the number of patients who are underdosed (reduced efficacy), or overdosed (unacceptable toxicity). The Woodruff Fund has been effectively funding pilot studies that create preliminary data for subsequent successful federal research projects. The proposed pilot study would generate preliminary data for an ensuing larger study that will be the first large-scale effort to link genetic, pharmacokinetic, and clinical variables for the prediction of toxicity and response to taxane-based chemotherapy. This project aims to acquire detailed patient information prospectively to identify prognostic factors and patient characteristics predictive of toxic response to taxane-based chemotherapy.

## GENETIC DATABANK FOR CARDIOVASCULAR DISEASE AND STROKE: INVESTIGATION OF THE GENETIC BASIS OF OXIDATIVE STRESS, VASCULAR DYSFUNCTION, CARDIOVASCULAR DISEASE, AND STROKE

*Arshed Quyyumi, MD, A. Azfar Zafari, MD, PhD, Viola Vaccarino, MD, PhD, and David Harrison, MD, Cardiology, School of Medicine*

**Purpose:** Cardiovascular disease (CVD), including stroke, continues to be the principal cause of death in developed countries. The cost of the disease is high in terms of morbidity, mortality, and its financial burden on health care systems. Moreover, ethnicity-based CVD health disparities appear to be common, with the prevalence of diabetes, hypertension, obesity, and CVD events being greater in African Americans compared with their Caucasian counterparts. The aim of this proposal is to establish an adequately powered database of patients who will be phenotyped for both sub-clinical and clinical disease and risk biomarkers, and will be followed up to determine prospective outcomes free of CVD and neurologic events. This database will enable Emory scientists in cardiology, neurology, human genetics, biomarker laboratories, and other departments to compete for independent funding for detailed genomic analyses.

## MAKING A UNIVERSITY HEALTHY BY UNDERSTANDING ITS HEALTH CARE

*Kenneth Thorpe, PhD, Benjamin Druss, MD, PHD, Kimberly Rask, MD, PhD, Health Policy and Management, Rollins School of Public Health*

**Purpose:** A university is a unique form of institution—an employer, a generator of new knowledge, and, for those with academic medical centers, a provider of health care. Although medical and public health researchers commonly study health and health care, there have rarely been systematic efforts to turn the lens back and understand the health and well-being of our own universities. In part, this has reflected limitations shared by all large employer-purchasers, who typically provide insurance through multiple carriers and separate health, mental health, and pharmacy data. Analysis of such data also has been limited by appropriate concerns for maintaining the privacy of university employees. Emory's new Management Service Organization, which merges data across these different insurers and creates a deidentified data base, makes it possible for the first time to track care across those different silos while preserving employee confidentiality. It provides a unique opportunity to advance scientific knowledge, as well as to understand and improve care within the Emory community. This initiative will explore how these data can be used for population-based research at Emory.

## IDENTIFY METHOD OF DETECTION AND CONTROL OF CYTOMEGALOVIRUS CONGENITAL DISEASE

*Edward Mocarski, Microbiology and Immunology, School of Medicine*

**Purpose:** Cytomegalovirus (CMV) remains the major infectious cause of progressive hearing damage in newborns. This project proposes to assemble a working group of investigators to address viral pathogenesis and host immune response determinants that control susceptibility to CMV congenital disease. The aim is to design a program that will investigate natural patterns of infection and protection from disease in order to establish appropriate methods of detection, targets for vaccination, and approaches to therapeutic intervention.

## Projects Affiliated with the Emory/Georgia Tech Predictive Health Initiative\*

### Initiated September 2004

#### STUDY OF BIOMARKERS OF OXIDANT STRESS AS PREDICTORS OF HEALTH AND DISEASE RISK

*Wayne Alexander, MD, PhD, Department of Medicine, School of Medicine*

**Purpose:** To initiate a longitudinal study that examines the relationship between oxidant stress and cardiovascular disease

### Initiated September 2005

#### BEHAVIORAL-GENETIC PREDICTION OF RISK FOR SCHIZOPHRENIA IN CHILDREN

*J. F. Cubells, MD, PhD, Genetics and Psychiatry, School of Medicine*

**Purpose:** This project seeks to develop both molecular genetic and cognitive/behavioral predictors of psychotic illness in children with the 22q11 deletion syndrome (22q11DS). Such children are at statistically very high risk for schizophrenia and other psychotic disorders. A major goal of the work is to generate preliminary data to support competitive applications for federal funding of a large, long-term, longitudinal follow-up of children with 22q11DS.

#### BIOMARKER ASSESSMENT OF METABOLIC AND VASCULAR RISK

*Larry Phillips, MD, Department of Medicine, Endocrinology, School of Medicine*

**Purpose:** Advances in medical science have led to therapies for common disorders such as diabetes, hypertension, and dyslipidemia, which confer major morbidity, mortality, and cost, but current treatment can be provided only once the disorder has been recognized—often after complications have already begun—and cannot restore normal tissue and organ function. In order to improve health, the disorders must be recognized when treatment is more efficacious and more cost-effective; it would be ideal to identify patients at risk earlier in their natural histories, when mechanism-based therapies might be able to prevent loss of function. This predictive health project will test the hypothesis that profiling oxidative stress and inflammatory biomarkers will permit prediction of deterioration of metabolic and vascular function prior to the development of clinical disease.

#### ECONOMIC, EPIDEMIOLOGIC, AND BEHAVIORAL RESEARCH

*Kimberly Rask, MD, PhD, Health Policy and Management, Rollins School of Public Health*

**Purpose:** The purpose of this study is to explore the feasibility of including economic, epidemiologic, and behavioral risk factors in predictive health models, using the specific example of patients with type II diabetes, a common chronic disease. This project will use a national population-based survey and a pilot study at an Emory-affiliated clinical setting to (1) collect a comprehensive set of biologic, behavioral, and environmental risk factors likely to affect an individual's health status and (2) explore the effectiveness of modifying selected risk factors, including health behaviors in persons at high risk of developing a clinical diagnosis of type II diabetes.

The clinical focus of this project has been broadened beyond hypertension to include a constellation of diseases that affect patients with diabetes. These diseases share both behavioral and biologic risk factors and pathways, providing a useful model for evaluating the potential impact of personalized health interventions for chronic health conditions.

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## INFLAMMATION AND PREDICTIVE MEDICINE

*David Stephens, MD, Department of Medicine, Infectious Diseases, School of Medicine*

*Cornelia Weyand, MD, PhD, and J. Goronzy, MD, PhD, Department of Medicine, Lowance Center, School of Medicine*

*Rafi Ahmed, PhD, Microbiology and Immunology, School of Medicine*

**Purpose:** The goal of this project is to identify novel and feasible approaches that integrate exciting new fundamental discoveries at Emory and elsewhere in inflammation and immunity with predictive health. Specifically, the goal is to integrate new quantitative immune methodologies and discoveries into predictive health, to engage multidisciplinary science (genetics, biochemistry, bioinformatics, engineering, microbiology and human immunology, biostatistics and analytical epidemiology, behavioral research, economics, population biology, and clinical medicine) in addressing significant and complex problems in immune dysfunction and to develop strategies for acceptance and use of immunology and immune activation markers in predictive health.

## PREDICTIVE ALGORITHMS OF PARKINSON'S DISEASE

*Gary Miller, PhD, and Scott Bartell, PhD, Environmental and Occupational Health, Rollins School of Public Health*

**Purpose:** The goal of this project is to develop models to predict Parkinson's disease. The strategy includes taking advantage of a wide collection of data, including epidemiologic, basic science, and clinical, to generate algorithms to identify individuals at greater risk of developing Parkinson's disease. Identification of high-risk individuals will allow for early intervention designed to prevent or slow the progression of the disease.

## PREDICTIVE TREATMENT FOR ALS (LOU GEHRIG'S DISEASE)

*Jonathan Glass, MD, Neurology, School of Medicine*

**Purpose:** Approximately 10% of people with ALS inherit the disease directly from their parents. The most common known cause for this familial form of ALS (fALS) is a mutation in the gene superoxide dismutase 1 (SOD1), which accounts for about 20% of familial cases. Animals engineered to carry human SOD1 mutations develop ALS. Therapeutic interventions with a variety of drugs in these animals have shown positive effects on disease onset or progression, but none of these agents has shown efficacy in humans with non-familial forms of ALS. This project proposes to identify the population "at risk" for fALS in order to design a clinical trial to delay the onset or prevent ALS. Specifically, people harboring a mutation in SOD1 have a high likelihood of dying of ALS, and this target population, though small, will be ideal for testing some of the same agents that have been effective in SOD1 mutant animals.

## PROFILING PROTEIN EXPRESSION IN GYNECOLOGIC TUMORS BY PROTEIN ARRAYS

*R. P. Huang, MD, PhD, Gynecology and Obstetrics, School of Medicine*

**Purpose:** Protein arrays have emerged as a technology to study protein expression and protein function in a high-throughput manner. One of the obvious applications of protein arrays is to profile protein expression in a patients' specimen. Through identification of unique biomarkers or biosignatures, antibody arrays may have great impact on predictive and personalized medicine. The purpose of this work is to establish a program for the application of antibody array technology in predictive and personalized medicine using cancer as example.

## Initiated September 2006

### A COMPREHENSIVE MULTIDISCIPLINARY SEARCH FOR BIOLOGIC PREDICTORS OF DISEASE PROGRESSION IN CHRONIC LUNG DISEASE

*Jesse Roman, MD, Dean Jones, PhD, and Ken Brigham, MD, Pulmonary Medicine, School of Medicine*

*Michael Kutner, PhD, Biostatistics, Rollins School of Public Health*

**Purpose:** This initiative will develop tools to assist in predicting which patients with chronic lung disease will show disease progression. This objective is considered important for three reasons. First, once identified, patients predicted to progress can be subjected to aggressive targeted interventions. Second, the identification of patients at risk for progression will help focus limited resources to those who are most likely to need them. Third, it is anticipated that research efforts in this arena will serve to identify novel cellular and molecular mechanisms involved in lung disease development and progression. This, in turn, will unveil new targets for the generation of novel strategies for therapeutic intervention. A multidisciplinary research program has been assembled that includes clinician-investigators, basic scientists, and biostatisticians from several components of the WHSC with the purpose of developing novel tools for predicting disease outcome in patients with lung disease.

## A PHARMACO-METABOLOMIC APPROACH TO PAIN AND SLEEP MANAGEMENT

*Kathy Parker, PhD, Adult and Elder Health, Nell Hodgson Woodruff School of Nursing*

*Marc Bouzyk, PhD, Human Genetics, School of Medicine*

*Raymond Dingleline, PhD, Pharmacology, School of Medicine*

**Purpose:** A variety of factors have been proposed to account for the disturbed nocturnal sleep and daytime sleepiness so often observed in oncology patients. Cancer-related pain, a common and often inadequately treated symptom, is likely a major contributing factor. Although long considered to be the mainstay of pain therapy, opioid analgesics are also known to adversely affect nocturnal sleep quality and cause daytime sleepiness. Nonetheless, optimal treatment of both pain and sleep disturbances is essential for enhancing the functioning and well-being of these patients. The purpose of the proposed study is to help build a statistical model that will predict the best type of opioid, the most appropriate dose, and the optimal timing of opioid administration to maximize pain control and minimize sleep disturbances in an individual—an intervention based on pharmacogenetics and metabolomics.

## BIOMARKERS OF BRAIN PATHOLOGY: IDENTIFYING INCREASED RISKS FOR ALZHEIMER'S DISEASE AND DRUG ADDICTION WITH MASS SPECTROMETRY

*Mark Wilson, PhD, Sarah Pruett, PhD, Leonard Howell, PhD, and Lary Walker, PhD, Yerkes National Primate Research Center*

**Purpose:** Proteomics and metabolomics represent the new frontier for translation research focused on interventional strategies to prevent or treat a number of pathologies affecting the brain, including neurodegeneration and drug addiction. Cutting-edge mass spectrometry is arguably one of the most important applications for protein and small molecular identification and quantification. This collaborative project, aligned to the objectives of the Predictive Health Initiative, will use the analytic power of mass spectrometry to expand two existing research programs to develop new strategies and potential interventions to alleviate neurodegeneration and addiction and, in doing so, will establish proteomics and metabolomics capabilities with the Biomarkers Core at the Yerkes National Primate Research Center.

## BRIDGING IMMUNOLOGY, NEUROSCIENCE, AND IMAGING: A NEW STRATEGY FOR DEVELOPING VACCINES AND THERAPEUTICS AGAINST NEUROLOGIC DISEASES

*Rafi Ahmed, PhD, Emory Vaccine Center, Yerkes National Primate Research Center*

*Stuart Zola, PhD, Yerkes National Primate Research Center*

**Purpose:** The goal of this initiative is to explore the possibility of developing therapeutic vaccines against noninfectious diseases like Alzheimer's disease by applying what is known about immune system function to the development of therapeutics against brain-related neurodegenerative disorders. There is virtually no place else on the globe better suited to undertake this innovative challenge than right here, where there are world-class immunologists, neuroscientists, brain imaging scientists, and the resources of the Emory Vaccine Center/Yerkes National Primate Research Center.

## EARLY INFANCY PREDICTIVE HEALTH MODELING: BIOLOGIC MARKER EXTRACTION, IDENTIFICATION, AND PROJECTION

*Michelle Lampl, MD, PhD, Amanda Thompson, MA, Anthropology, Emory College*

**Purpose:** This project seeks to initiate the development of an Infant Predictive Health Panel to parallel the proposed Adult Predictive Health Profile, with attention to those developmental factors that have been suggested by previous work to predict adult health sequelae. The identification of infant health biomarkers can initiate an evidence-based clinical practice promoting healthy life-ways early on. The research work encompasses: (1) channeling existing extraction and assay methodology to predictive health practice, (2) identifying early risk profiles among healthy infants and contributing to an evidentiary base for health-promoting early life-ways, and (3) promoting collaboration among Emory resources to elevate practical application of existing and potential research to the benefit of the Health Sciences Center and its 2012 goal.

## ESTABLISHING A CANCER RISK PREDICTION AND PREVENTION RESEARCH PROGRAM AT EMORY UNIVERSITY

*Robert Bostick, MD, MPH, Epidemiology, Rollins School of Public Health*

**Purpose:** This project proposes establishing a multidisciplinary Cancer Risk Prediction and Prevention Research Program at Emory that will draw together investigators from public health, medicine, basic science, engineering (at Emory and Georgia Tech), genetics, and biostatistics to work synergistically with the Predictive Health Initiative and the Winship Cancer Institute. The focus of the new program will be on the development, validation, and application of biomarkers of risk for cancer. The development of the Cancer Risk Prediction and Prevention Research Program will begin with research projects on colorectal cancer, the second leading cause of cancer deaths in the U.S. among men and women combined, and on prostate cancer, the second leading cause of cancer deaths in men.