

Health Research Grants

Health Research Formula Grants - State Fiscal Year 2003-04

Thirty-nine organizations received health research formula grants for the state fiscal year 2003-04. Grants may support one or more research projects and research infrastructure projects. The following list of grants provides the name of the grantee, amount of the grant award, grant award period, contact person and a list of the research project(s) supported by the grant including the title of the research project, type of research (biomedical, clinical or health services research), focus of the project, and purpose.

Albert Einstein Healthcare Network (\$186,128) - 3 Projects

Grant Award Period: 5/1/04 - 4/30/06

Contact:

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Research Projects:

- Title: *Neurophysiologic Correlates of Attention Deficits and Treatment Response*
Type of Research: Clinical
Focus: Neurosciences
Purpose: After brain injuries, the majority of individuals have difficulty with attention and concentration. The goals of this project are 1) to understand the nature of these difficulties from the perspective of the networks of nerve cells in the brain that support attention and concentration; and 2) to understand the effects of an attention-enhancing medication on the operation of these networks.
- Title: *Assistive Technology for Adults with Acquired Aphasia*
Type of Research: Clinical
Focus: Neurosciences
Purpose: "Aphasia" denotes acquired language loss due to stroke or other neurological injury. A current NIH grant supports research on an assistive device for facilitating spoken language production in aphasia. This project aims to leverage that funding and increase new grants by developing an evaluation protocol that will predict which patients are capable of learning to operate the device and using it to produce speech that is more informative and more grammatically complex than what they can produce spontaneously.
- Title: *Long-Term Effects of Colon Cancer Survivorship*
Type of Research: Health Services
Focus: Health of Populations, Behavioral and Biobehavioral Processes
Purpose: The purpose of this study is to understand the current physical and psychosocial effects experienced by long term survivors of invasive colon cancer, defined as persons who have been disease free for 5 or more years, either from initial diagnosis or from last relapse.

Allegheny-Singer Research Institute (\$264,887) - 3 Projects

Grant Award Period: 5/1/04 - 4/30/08

Contact:

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Research Projects:

- Title: *Mechanisms of Vasodilation During Hypotension Share Features with Those of Acute Stroke*
Type of Research: Biomedical
Focus: Neurosciences
Purpose: We will attempt to show that the brain circulation's response to low blood pressure is similar to its response to acute stroke. If proven correct, this concordance of mechanisms will further our understanding of the pathophysiology during stroke and provide possible methods for improvement of brain blood flow during acute stroke.
- Title: *Nicotine Effects on Stress-Responsive Hormones: Male-Female Differences*
Type of Research: Biomedical
Focus: Endocrine, Metabolism, Nutrition and Reproductive Sciences
Purpose: Cessation from tobacco use has major and immediate health benefits for users of all ages. Nicotine is highly addictive; consequently, the percentage of tobacco users that quit is low, and studies of successful quit rates of men vs. women are lacking. The purpose of the proposed studies is to investigate the role of sex differences and environmental influences in nicotine effects on stress responsive hormones in animals, as a model to better understand the biology of nicotine addiction and withdrawal. The proposed study may have relevance to tobacco cessation treatment plans directed specifically towards men vs. women.
- Title: *Continuing Renovations to Laboratory Animal Resources Facility*
Type of Research: Biomedical
Focus: Research Infrastructure
Purpose: The purpose of this project is to continue upgrading the ASRI's current animal facility in order to obtain Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) certification. This certification would allow ASRI to enhance current and future research endeavors and to attract top researchers nationwide.

American Aging Association (\$1,875) - 1 Project

Grant Award Period: 5/1/04 - 6/30/05

Contact:

Robert G. Allen, Ph.D.
Research Director
American Aging Association
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Media, PA 19063
(610) 565-9784

Research Project:

- Title: *Antioxidant Effects in Normal and Transformed Cells*
Type of Research: Biomedical

Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics

Purpose: The purpose of this project is to understand how the effects of antioxidant compounds are altered by the amount of antioxidant defenses naturally present in cells. We also will try to understand why some virally induced tumors respond to antioxidants differently than do normal cells and whether non-viral tumors respond differently than normal cells to antioxidant treatments.

American Association for Cancer Research (\$115,950) - 1 Project

Grant Award Period: 5/1/04 - 6/30/06

Contact:

Margaret Foti, Ph.D., M.D.
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Research Project:

- Title: *The Role of Progressive Stroma Signaling in Cancer Permissiveness*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: The purpose of this research is to examine the molecular characteristics and signaling mechanisms by which stromal fibroblasts and their extracellular matrix contribute to cancer progression.

American College of Radiology (\$2,156,639) - 5 Projects

Grant Award Period: 5/1/04 - 4/30/07

Contact:

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Research Projects:

- Title: *American College of Radiology Imaging Network (ACRIN) Positron Emission Tomography Clinical Trials Research Component*
Type of Research: Clinical
Focus: Oncological Sciences
Purpose: The PET Clinical Trials Research Component will provide resources to support cancer clinical trials involving PET. The information from PET will provide earlier and more accurate information about the effectiveness of new cancer drugs. In the next year, studies of lung cancer, gastrointestinal stromal tumors, cancers in children and cervical cancer are anticipated. Funding of the PET research component will allow PET research objectives to be incorporated into these clinical trials. ACRIN will collect, process and analyze PET images obtained on patients participating in federally funded cancer trials.

- Title: *Protection from Dose-Limiting Toxicity of Chemoradiation for Head and Neck Cancer*
 Type of Research: Clinical
 Focus: Oncological Sciences
 Purpose: The first purpose is to identify radiation physical factors that are associated with severe unacceptable (dose-limiting) toxicities from chemoradiation for head and neck cancer. The second purpose is to devise a means of delivering more precise radiotherapy that may be expected to decrease these toxicities. The third purpose is to test whether the results from the first two analyses can be seen in a (currently ongoing) Radiation Therapy Oncology Group (RTOG) trial.
- Title: *An Emerging Technology Assessment Mechanism for Radiation Therapy Oncology Group (RTOG) Protocols*
 Type of Research: Clinical
 Focus: Oncological Sciences
 Purpose: The purpose of this project is to develop, test and implement a methodology for evaluating new technologies as they relate to radiation treatment of cancer patients. This methodology will provide quantitative information on the performance of new technologies that are not under direct study by the protocol in which they are employed. The information gathered will be used to demonstrate that the technology itself is not a limiting factor in the final outcome of a study and to benchmark other competing technologies as they appear. One aim of this work is to speed the process of moving emerging technologies into RTOG protocols. Additionally, this work will serve as a model for launching future protocols that directly study the efficacy of new technologies.
- Title: *Economic and Quality-Adjusted Survival Analyses of Radiation Therapy Oncology Group (RTOG) Clinical Trials Involving Patients with Tobacco Related Cancers*
 Type of Research: Clinical
 Focus: Oncological Sciences
 Purpose: The purpose of this project is to determine, using Medicare claims data and quality-adjusted survival, the most cost effective treatments of patients with head and neck and lung cancers, two tobacco related malignancies. This project will also compare and validate two methodologies for determining quality-adjusted survival. These findings will guide further development of treatments providing the greatest quality-adjusted survival with the most efficient utilization of health care resources.
- Title: *The Patterns of Care Study of Diagnostic Evaluation of Breast Cancer Patients in Pennsylvania and Treatment of Cancer Patients in a Nationwide Database*
 Type of Research: Clinical
 Focus: Oncological Sciences
 Purpose: The purpose of this project is to analyze and report results of a study of screening, diagnostic evaluation, and follow-up evaluation for breast cancer patients in Pennsylvania with particular emphasis on subgroups that may be underserved. To analyze and report results of secondary analyses of a nationwide study of patients treated in radiation oncology facilities throughout the USA.

Bryn Mawr College (\$10,932) - 1 Project
Grant Award Period: 5/1/04 - 4/30/05

Contact:

Leslie B. Alexander, Ph.D.
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Bryn Mawr College
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Research Project:

- Title: *The Alliance in Intensive Case Management (ICM): Qualitative Analysis*
Type of Research: Health Services
Focus: Health of Populations, Behavioral and Biobehavioral Processes
Purpose: This project will analyze qualitative responses to open-ended questions, answered by clients with serious mental illness (smi) and their case managers, about their alliance with each other. It is nested within a largely quantitative study of the reliability and predictive validity of two quantitative alliance measures, the WAI and the HAQ-II. All data were gathered during in-person interviews. Quantitative analysis is completed. Qualitative analysis will validate quantitative alliance findings and extend understanding of early alliance development gained solely from numeric data.

Carnegie Mellon University (\$962,758) - 3 Projects

Grant Award Period: 5/1/04 - 4/30/06

Contact:

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Research Projects:

- Title: *New Fluorescent Probe Technology*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: The goal is to develop a new methodology for inserting fluorescent labels into protein molecules of living cells. Such labels will be visible by using fluorescence imaging microscopes. The probes will allow biomedical scientist to learn about the important molecular pathways and networks that regulate the function of living cells. These are the same pathways that in some tissues become diseased. Therefore, understanding these pathways has an important health impact.
- Title: *Imaging Protein-Protein Interactions in Living Cells*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: The goal is to develop a new methodology for detecting the interactions of protein components that regulate the function and health of cells. This imaging method will allow biomedical scientists to learn about the important molecular pathways and networks that regulate the function of living cells. These are the same pathways that in some tissues become diseased. Therefore, understanding these pathways has an important health impact.

- Title: *Applying New Fluorescent Probes to Pathways in Drosophila*
 Type of Research: Biomedical
 Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
 Purpose: We will analyze interactions of fluorescently tagged protein pairs in *Drosophila* cultured cells and tissues. We will use the fluorescent protein labeling technologies from the other research projects in this grant.
Drosophila cells are an excellent model for research to understand cellular regulation. Understanding cell regulatory pathways has an important health impact.

Children's Hospital of Philadelphia (\$3,657,085) - 10 Projects

Grant Award Period: 5/1/04 - 4/30/08

Contact:

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Research Projects:

- Title: *Gene Expression Signatures and Pediatric Disease*
 Type of Research: Biomedical and Clinical
 Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
 Purpose: The purpose of this project is to determine whether there are identifiable "gene expression signatures" in cell lines established from individuals with selected pediatric diseases. Such signatures could become useful tools in diagnosis, especially in individuals who have clinical indications of a disorder but who do not have a mutation. They would also help to guide future research aimed at understanding the pathogenesis and pathways involved in these disorders.
- Title: *Risk Factors for Pediatric Metabolic Syndrome*
 Type of Research: Clinical
 Focus: Endocrine, Metabolism, Nutrition and Reproductive Sciences
 Purpose: The purpose of this project is to understand the extent to which childhood obesity and its sequelae contribute to the development of metabolic syndrome, a harbinger of Type 2 diabetes and cardiovascular disease in adults.
- Title: *Pharmacometric Research: Dosing Guidance for Pediatric Pharmacotherapy*
 Type of Research: Biomedical and Clinical
 Focus: Biology of Development and Aging
 Purpose: The purpose of this project is to develop practical guidance for dosing pediatric populations (neonates, infants, children and adolescents) defined by models built from information about the drugs themselves, clinical experience in adults and data from actual pediatric trials.
- Title: *Research Excellence in Pediatric Acute Myelogenous Leukemia*
 Type of Research: Biomedical
 Focus: Oncological Sciences

Purpose: This project provides funding for four interrelated projects, all addressing different aspects of Acute Myelogenous Leukemia (AML) of childhood. They are designed to understand the causes of the disease, as well as to propose new approaches to preventing, treating and managing AML.

- Title: *Dysfunction of Synaptic Microdomains Underlying Epilepsy*
Type of Research: Biomedical
Focus: Neurosciences
Purpose: The goal of this project is to conduct pilot studies probing the aberrant functioning of excitatory and inhibitory synapses in epilepsy.
- Title: *DNA, Protein and Cellular Vaccines for Cancer and Infectious Diseases, Including Agents of Bioterror*
Type of Research: Biomedical and Clinical
Focus: Immunology
Purpose: The purpose of this project is to design and develop novel vaccines for infectious diseases and cancer, as well as to identify new therapeutic targets for immune modulation.
- Title: *Stem Cell and Gene Therapy for the Muscular Dystrophy Disorders*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: The purpose of this research project is to develop synergistic programs based on the common theme of stem cell directed cellular and gene therapy for the Muscular Dystrophy Disorders. Its goal is to determine whether the correction of the genetic defect will result in a phenotypic correction of most, if not all, Muscular Dystrophies.
- Title: *Transfusion Therapy to Prevent Complications of Sickle Cell Disease*
Type of Research: Clinical
Focus: Hematology
Purpose: For years, blood transfusion has been used to save the lives of people with sickle cell disease (SCD) during acute illness and to prevent the occurrence of major complications. However, the usefulness of this treatment in young children has not been carefully studied. The purpose of this study is to determine whether chronic transfusion treatment can be carried out in young children with SCD and whether such treatment can prevent the severe complications of the disease.
- Title: *Bypassing Genetic Defects of NF κ B Activation to Improve Immune Defenses*
Type of Research: Biomedical
Focus: Immunology
Purpose: Several important diseases result from a defect in the process leading to the activation of one of the master power switches, called NF κ B, contained inside cells. Many of our body's immune functions require NF κ B to respond to danger in the environment in order to protect us. Unfortunately, children with defects in activating NF κ B can suffer from severe, recurrent, and life-ending infections. The studies of this project are aimed at figuring out new ways to activate NF κ B in response to danger in the environment when normal activation process does not function. Our goal to devise more rational treatments for these children.
- Title: *The Epidemiology, Risk Factors, and Outcomes of Fungal Infections in Children*
Type of Research: Health Services

Focus: Health of Populations, Behavioral and Biobehavioral Processes
Purpose: The purpose of this research program is to better understand which children are at risk for developing fungal infections, the risk factors for developing infection, and the outcomes of these infections.

Children's Hospital of Pittsburgh (\$723,892) - 1 Project

Grant Award Period: 5/1/04 - 4/30/07

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Research Project:

- Title: *Start Up: Mechanisms of Pediatric Lung Injury Research Program*
Type of Research: Biomedical
Focus: Respiratory Sciences
Purpose: The program will provide start-up funding for research laboratories that will investigate how infections lead to severe lung disease in infants and children.

Donald Guthrie Foundation for Education and Research (\$46,918) - 1 Project

Grant Award Period: 5/1/04 - 6/30/05

Contact:

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Research Project:

- Title: *Regulation of Rac1 Localization and Adherens Junction Formation*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: The long-term goal of this project is to understand how the Rac1 protein regulates metastasis of cancer cells. Rac1 may inhibit metastasis by promoting the adhesion of cancer cells to one another, thereby diminishing the dissociation of cancer cells from the primary tumor. This study will compare the localization and function of Rac1 in cell lines that have different abilities to form cell junctions. These studies will characterize the participation of Rac1 in cell-cell adhesion and help define the role of Rac1 in metastasis.

Drexel University (\$1,230,826) - 13 Projects

Grant Award Period: 5/1/04 - 10/31/06

Contact:

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Associate Vice Provost

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Research Projects:

- Title: *Molecular and Structural Mechanisms, Detection and Antagonism of Anthrax Toxins*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: This project takes advantage of exciting new knowledge on anthrax pathogenesis in order to develop antagonism and detection strategies for this infectious disease. The bacterium *Bacillus anthracis*, a lethal pathogen that poses an important bioterrorism and biowarfare threat, produces potent protein toxins that are key to anthrax virulence. Anthrolysin O (ALO) is a newly described hemolytic, pore-forming protein toxin secreted by *B. anthracis* and believed to be important in disease progression. Recent unpublished data reveal that the human macrophage receptor of ALO is toll-like receptor 4 (TLR4). A team has been assembled at Drexel to respond to these new findings in order to meet therapeutic and bioweapon detection needs for anthrax.
- Title: *Development of In-Vivo Spinal and Cortical Neuroprostheses Using Fiberoptic Uncaging and Nanoscale Microfabrication Techniques*
Type of Research: Biomedical
Focus: Bioengineering, Surgical Sciences and Technology
Purpose: The goal of this project is to begin to develop and test a tool that can provide focal control of both deep and superficial neural tissues including excitation, inhibition and modulation state in a fashion compatible with the range of neurophysiological recording techniques. No such clinical tool currently exists, but this could help in alleviating symptoms of diseases such as epilepsy and Parkinson's disease.
- Title: *Support for Formation of a Federally Funded Sexually Transmitted Disease Center at Drexel University*
Type of Research: Biomedical, Clinical and Health Services
Focus: Health of Populations, Behavioral and Biobehavioral Processes
Purpose: This project will support the organization of a sexually transmitted disease center structure at Drexel University College of Medicine and Drexel University. The goals are: (1) to organize the center around basic, translational and clinical research, (2) complete designated research projects that address the missions of the center and (3) establish a funded base for the center that will include federal, as well as other funds so that the center can continue the research.
- Title: *In-Vivo Pre-Cancer Detection with Optoelectronically Enhanced Endoscopy*
Type of Research: Biomedical
Focus: Bioengineering, Surgical Sciences and Technology
Purpose: The purpose of this project is to detect early stages of cancer by the optical examination of cellular defects. We propose to develop an on-chip optical spectrometer directly on an optical fiber which can be employed at the tip of a minimally-invasive endoscope for in-vivo optical examination of cancerous and pre-cancerous cells. This endoscopic spectrometer probe will

identify cellular size variations, targeting specific biopsy locations to increase the sensitivity and accuracy of the biopsy procedure.

- Title: *Roles of Nitric Oxide and Lipid Peroxidation in Traumatic Neuronal Damage*
Type of Research: Biomedical
Focus: Neurosciences
Purpose: In the United States, traumatic brain injury is a significant factor in the mortality and morbidity of individuals under the age of 45, comprising 1-2% of deaths from all causes. Because there are no treatment strategies for the head-injured patient in the chronic phase of injury, survivors are faced with debilitating and long-term neurologic dysfunction that has a major impact on quality of life and carries a significant social and economic burden. In this project, the investigators will seek to understand how membranes and proteins within the neuron are altered after a mechanical injury (trauma), and how these changes contribute to the overall damage and death of neurons.
- Title: *Origins and Evolution of Genomic Instability in Cancer*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: The overall goal of this project is to incorporate the recent advances in high throughput computational and experimental methods in developing novel techniques for accurate diagnosis and individualized treatment of breast cancer. The overall thrust of the project is the integration of computational and experimental approaches to understanding cancer biology and developing effective treatments. The model will provide means for simulating optimal therapy options for individualized treatment. It will also yield an automated image processor software for analysis of histology slides.
- Title: *Monitoring State of Healing in Diabetic Chronic Wounds with Near Infrared Spectroscopy*
Type of Research: Clinical
Focus: Bioengineering, Surgical Sciences and Technology
Purpose: The purpose of the project is to determine in a clinical setting the usefulness of a mobile non-invasive device, to monitor quantitatively the progress of healing of a chronic diabetic wound. The proposed device is based on near infrared light.
- Title: *Developing Minimally Invasive Techniques for Transplanting Stem Cells into the Central Nervous System to Facilitate Earlier and Safer Clinical Trials*
Type of Research: Biomedical
Focus: Bioengineering, Surgical Sciences and Technology
Purpose: This project aims to develop a new, safer and cheaper technology for transplanting stem cells into patients suffering from spinal cord injury. This study project will involve research on animal models; no human patients will be involved.
- Title: *Development of Phase Contrast Imaging Modality for Tabletop X-Ray Microscopy with Intracellular and Molecular Imaging in NanobioMedicine*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: X-ray microscope is a powerful tool as it provides nanometer resolution images of whole, hydrated cells. To date, all x-ray microscopes are synchrotron-based and thus have a small user base. Drexel University is currently undertaking the realization of a tabletop biological x-ray microscope

and the phase contrast imaging modality developed by this project will serve as a precursor for the tabletop x-ray microscope project. Furthermore, making available this nano-scale intracellular imaging capability will greatly enhance the region's biomedical research.

- Title: *Proof-of-Concept for Optical Intraocular Pressure Sensor to Detect Glaucoma*
Type of Research: Health Services
Focus: Bioengineering, Surgical Sciences and Technology
Purpose: The goal of this project is to develop a proof-of-concept that an optical pressure sensor composed of flexible reflective gratings can measure the fluctuations present in the eyes of glaucoma patients. The long-term research goal is to implant an optical pressure sensor in the eyes of patients at high risk for glaucoma, thereby preventing optic nerve damage and loss of vision.
- Title: *Systems Biology Approach to the Understanding of Protein – Protein Interactions: Simulation, Control, and Biological Validation*
Type of Research: Biomedical
Focus: Bioengineering, Surgical Sciences and Technology
Purpose: The purpose of this project is to provide a feasibility study in three key areas: Using combined experimental and theoretical approaches for (1) mapping disease related protein interaction networks, (2) using perturbation analysis to provide insight into the causal functioning mechanism of each respective pathway and (3) providing testable targets to control malfunction of each protein interaction network.
- Title: *A Colorimetric Sensor for the Analysis of Exhaled Breath*
Type of Research: Health Services
Focus: Oncological Sciences
Purpose: This project is directed towards the development of a colorimetric, non-invasive breath sensor that will provide a practical and highly valuable tool for medical diagnostics.
- Title: *Nanowire Nanosensors: A Platform for Probing Protein Interactions*
Type of Research: Clinical
Focus: Oncological Sciences
Purpose: The purpose of this project is to develop a novel sensor platform that will sense biomolecules, their interactions and their structural arrangements. This project is expected to provide methods of enhanced sensitivity and selectivity in the detection of markers for cancer and other diseases.

Duquesne University (\$89,848) - 3 Projects

Grant Award Period: 5/1/04 - 4/30/06

Contact:

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Duquesne University
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Research Projects:

- Title: *Improving TENS as a Treatment for Neurogenic Pain*
Type of Research: Biomedical and Health Services
Focus: Neurosciences

Purpose: The purpose of this project is to improve the effectiveness of high-frequency electrical nerve stimulation (HFS) when used to relieve pain that may develop with damage to the peripheral nervous system (neurogenic pain). The experiments will investigate the most effective site for application of the treatment when delivered through the skin (TENS). In addition, the nervous system mechanisms behind the documented variable response of neurogenic pain to TENS will be investigated at the level of the spinal cord. Understanding these mechanisms will help to refine future application of the treatment.

- Title: *Structural Motifs Underlying G Protein-Coupled Receptor Function*
Type of Research: Biomedical
Focus: Neurosciences
Purpose: Using as paradigms the mu opioid receptor and melatonin receptor, two sequence-divergent G protein-coupled receptors (GPCRs), the project will investigate whether specific amino acid residues and sequences (structural motifs) usually present in GPCRs are key for receptor function. Clarification of the roles of GPCR motifs will provide a blueprint for studies on the thousands of receptors in this family. Results should guide rational design of therapeutic drugs that exert their effects at GPCRs, including development of superior drugs for treating opiate addiction.
- Title: *Preventing Anthrax Infection by Controlling Edema Factor-Calmodulin Binding*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: The spores of *Bacillus anthracis* (anthrax) have been used as a biological weapon against the military and the civilian population. Our work focuses upon drug design to prevent the toxic effects of the bacteria, thus allowing time for conventional treatments to eliminate the bacteria. The proposed efforts will bring molecular modeling, drug design and advanced instrumentation to address this problem. The objective of the proposed work is to understand the binding process between the signaling protein calmodulin (CaM) and anthrax edema factor (EF).

Family Planning Council, Inc. (\$18,107) - 1 Project

Grant Award Period: 5/1/04 – 10/31/05

Contact:

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Research Project:

- Title: *A Study of Obesity and Diabetes Risk Factors in Women Attending Family Planning Clinics*
Type of Research: Clinical
Focus: Health of Populations, Behavioral and Biobehavioral Processes
Purpose: The main purpose of the project is to provide information and recommendations for interventions regarding obesity and diabetes among Family Planning clients.

Fox Chase Cancer Center (\$3,818,851) - 19 Projects

Grant Award Period: 5/1/04 - 12/31/06

Contact:

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Research Projects:

- Title: *Developing Bispecific Single-Chain Fv Molecules to Treat Breast Cancer*
Type of Research: Clinical
Focus: Oncological Sciences
Purpose: Patients with aggressive breast cancer have few options. Activation of EGFR proteins are associated with an aggressive phenotype and may be associated with the failure of breast cancer therapy. Development of antibody-based agents that target the EGFR receptor may increase these aggressive cells' susceptibility to chemotherapy and radiation.
- Title: *Novel Biomarkers to Predict Response to Cancer Therapy*
Type of Research: Biomedical
Focus: Oncological Sciences
Purpose: Currently, patient response to novel anti-cancer treatments is generally monitored by crude endpoints such as patient survival, tumor growth and toxicity. These read-outs provide little opportunity to rationally modify an on-going course of treatment or predict response to therapy. The goal of this study is to develop acute measures (biomarkers) of a novel anti-cancer drug's important biological activity. This will allow physicians to rationally optimize an on-going course of treatment and predict patient response to therapy.
- Title: *Data Mining to Identify Risk Factors for Early Mortality in Lung Cancer Patients*
Type of Research: Biomedical and Clinical
Focus: Oncological Sciences
Purpose: Lung cancer is the leading cause of cancer deaths in Pennsylvania. This project will construct an extensive database regarding the molecular pathology of cancer and integrate this information with clinical features that define prognosis and treatment outcomes for lung cancer patients. We will mine these data using state of the art biomedical informatics methods to identify risk factors for mortality/morbidity in lung cancer patients undergoing pneumonectomy or combined modality therapy for locally advanced non-small cell lung cancer.
- Title: *Inhibition of Fibroblast Activation Protein by Boronic Acid Compounds*
Type of Research: Biomedical and Clinical
Focus: Oncological Sciences
Purpose: Fibroblasts are commonly present in normal tissues, and when found near tumor cells, have different characteristics compared to those surrounding normal cells, and may contribute to the growth and invasiveness of tumors. Boronic acid compounds will be tested to determine their inhibiting effect on tumor growth and metastases.
- Title: *Assessing HER-2 Targets in Breast Cancer*
Type of Research: Biomedical and Clinical
Focus: Oncological Sciences

Purpose: HER-2 is an oncogene that is mutated or amplified in about 25% of all breast cancers. HER-2 in turn activates a number of proteins in the cell that signals growth, invasion, or metastasis. The objective of this work is to identify the most relevant signaling proteins activated by HER-2 in breast cancer specimens.

- Title: *Benign Breast Registry to Assess Valid Endpoints (BeBrave)*
Type of Research: Health Services and Clinical
Focus: Oncological Sciences
Purpose: Of all the breast biopsies performed every year for a suspicious lump or an abnormal mammogram, only 20% reveal breast cancer. The remaining 80% are benign, and represent a spectrum of cellular findings ranging from normal changes to severely abnormal cells. Currently, it is extremely difficult to accurately classify these benign biopsy findings into risk categories. The purpose of this study is to use new molecular approaches which search for specific proteins in the cells that are associated with precancerous changes.
- Title: *Gene-Environment Interactions and Cancer in Pennsylvania*
Type of Research: Health Services
Focus: Oncological Sciences
Purpose: This study will determine the feasibility of establishing a Pennsylvania based cohort to evaluate how genes interact with environmental and lifestyle characteristics to determine cancer risk and outcomes.
- Title: *Is HEI10 a Clinical Target and Biomarker for Metastasis?*
Type of Research: Biomedical
Focus: Oncological Sciences
Purpose: The purpose of this project is to evaluate whether the HEI10 protein contributes to abnormal cell proliferation and metastasis in cancer, and whether HEI10 action is generally active in advanced cancers, or specifically required for some types of metastatic cancer.
- Title: *A New Antibiotic Strategy*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: The purpose of this research project is to use our newly discovered hexameric structure for the enzyme porphobilinogen synthase (PBGS) as the basis for the discovery of novel antibiotic drugs. Inhibition of the essential PBGS enzyme is a new strategy for antibiotic development, and is made possible by our deep understanding of the structural and mechanistic differences between bacterial and human PBGS proteins.
- Title: *Genetic Susceptibility to Lead Poisoning*
Type of Research: Biomedical and Health Services
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: Lead is a toxic substance detrimental to the neurologic development of children and proposed to contribute to the development of cancer. The PBGS protein is the part of blood that has the highest tendency to bind lead. Epidemiological studies correlate two common human alleles for human PBGS with a genetic susceptibility to lead poisoning. The purpose of this project is to determine the differential effect of lead on the PBGS proteins encoded by the two alleles. This promises to establish a molecular basis for the epidemiological results.

- Title: *Selenium and Vitamin E: Experimental Basis for Prostate Cancer Prevention*
 Type of Research: Biomedical and Clinical
 Focus: Oncological Sciences
 Purpose: Prostate cancer is the most commonly diagnosed malignancy in men. Vitamin E and selenium are currently the most promising agents under investigation to reduce the risk of prostate cancer. An understanding of the molecular targets and mechanisms of vitamin E and selenium mediated prostate cancer prevention is mandatory for the development of efficient chemopreventive strategies.
- Title: *Development & Evaluation of a Web-Based Tool for Genetic Risk Counseling and Education*
 Type of Research: Health Services
 Focus: Oncological Sciences
 Purpose: Hereditary forms of colorectal, breast, and ovarian cancer are caused by abnormal genes that are passed from generation to generation. The decision of whether to pursue genetic testing requires a careful risk assessment, of potentially affected family members. Unfortunately, families in Pennsylvania are frequently geographically dispersed, with many not having access to appropriate professional expertise in cancer genetics. The purpose of this project is to develop and evaluate an internet-based method for provision of live, on-line cancer risk assessment and education.
- Title: *Polymorphic Variants of p53 in Cancer Risk and Therapy*
 Type of Research: Biomedical and Clinical
 Focus: Oncological Sciences
 Purpose: The normal function of p53 is to respond to abnormal cell division by directing the cancerous cell to commit suicide. There are two forms of p53 that have decreased ability to induce cell death, and will likely also have decreased ability to suppress tumor development; notably, both of these forms are much more common in African Americans. The proposed studies will test the polymorphic changes, with the potential to identify the genetic basis for the differences in cancer risk in African Americans.
- Title: *Protein Folding and Disease: Structural Basis of Amyloid Fibril Formation in Prion Proteins*
 Type of Research: Biomedical
 Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
 Purpose: The goal of the proposed research is to understand the molecular mechanism underlying the conversion of a normal cellular protein, PrP, into infectious prion particles, which are responsible for a number of fatal neurodegenerative diseases in humans and animals.
- Title: *The Role of Gene Promoter Hypermethylation in Sporadic Colorectal Tumorigenesis*
 Type of Research: Biomedical
 Focus: Oncological Sciences
 Purpose: This project seeks to define the role of gene inactivation by methylation in the development of colorectal cancer and its implications in prevention and treatment.
- Title: *Tumor-Induced Apoptosis in T Cells From Renal Cell Carcinoma Patients*
 Type of Research: Biomedical
 Focus: Oncological Sciences

Purpose: Renal cell carcinoma (RCC) represents nearly 85% of newly diagnosed tumors of the kidney, affecting 30,000 Americans per year and causing 12,000 annual deaths. RCC is resistant to conventional antitumor therapies (chemo- and radiotherapy) making this malignancy extremely difficult to treat. Through this project we hope to define the role the tumor plays in inducing suppression of the immune system and to find new approaches to increase the immune response in patients with renal cell carcinoma.

- Title: *Identifying Defects in Lung Cancer Cells that Promote Abnormal Mitosis*
Type of Research: Biomedical
Focus: Oncological Sciences
Purpose: Lung cancer cells exhibit high rates of chromosome abnormalities that strongly suggest fundamental defects in mitosis. This project will test a panel of mitotic biomarkers for their usefulness in predicting whether cells can undergo a normal mitosis, thus help predict how lung cancer cells will respond to chemotherapies. Furthermore, these biomarkers themselves will be tested to see if they can be used to develop novel anti-cancer drugs.
- Title: *Development of Novel Antimitotic Compounds*
Type of Research: Biomedical
Focus: Oncological Sciences
Purpose: Cancer cell resistance to chemotherapy is a major reason for treatment failure. In the case of antimitotic chemotherapy, resistance to cell death is accompanied by chromosome instability that further augments resistance, and the recurrence of more aggressive tumors. Studies have identified new genes that are essential for normal mitosis. These genes represent new targets for the development of new lines of cancer drugs that can overcome resistance to existing chemotherapies.

Immaculata University (\$5,090) - 1 Project

Grant Award Period: 5/1/04 - 4/30/05

Contact:

Laura Frank, Ph.D., R.D.
Chair, Department of Nutrition Education
Immaculata University
P.O. Box 722
1145 King Road
Immaculata, PA 19345-0722
(610) 647-4400, Ext. 3482

Research Project:

- Title: *Health Education to Reduce Obesity and Chronic Disease Risk in Undergraduate University Women*
Type of Research: Health Services
Focus: Health of Populations, Behavioral and Biobehavioral Processes
Purpose: Under earlier funding, an assessment of the nutrition education needs and preferences of Immaculata students was completed by the researchers, providing a basis for the design of appropriate educational programs. The purpose of this research is to apply this information to the implementation of an ongoing nutrition education program for the student population, and conduct an assessment of the efficacy of this program in engaging students and promoting healthy eating behaviors.

Lankenau Institute for Medical Research (\$346,399) - 5 Projects

Grant Award Period: 5/1/04 - 4/30/05

Contact:

George C. Prendergast, Ph.D.
President and CEO
Lankenau Institute for Medical Research
100 Lancaster Avenue
Wynnewood, PA 19096
(610) 645-3475

Research Projects:

- Title: *Molecular Mechanisms Involved in the Increased Calcium Channel Expression in Hypertensive Arteries*
Type of Research: Biomedical
Focus: Cardiovascular Sciences
Purpose: The purpose of this research project is to understand what causes the increase in the amount of protein that forms pathways allowing calcium to enter muscle cells in arteries of hypertensive subjects contributing to the increased blood pressure in this disease. Preventing the increased production of these calcium proteins may be a novel target for the development of medicines to treat high blood pressure.
- Title: *Elevated Histone Acetyltransferase Activity in Prostate Tumors*
Type of Research: Biomedical
Focus: Oncological Sciences
Purpose: The purpose of this project is to characterize an enzymatic activity that is aberrantly high in adenocarcinomas that develop in a mouse model of prostate cancer, and importantly, to determine if this enzymatic activity, which controls gene expression, is also elevated in human prostate tumors.
- Title: *Regulation and Function of hnRNP-K in Smooth Muscle Cell Growth*
Type of Research: Biomedical
Focus: Cardiovascular Sciences
Purpose: The purpose of this research project is to determine how a protein important in cell growth called hnRNP-K is modified during smooth muscle cell growth, and identify the messenger RNAs that hnRNP-K traffics into the cytoplasm during cell growth.
- Title: *Sensitization of Tumor Cells to Paclitaxel through Bin1 Gene Loss*
Type of Research: Biomedical
Focus: Oncological Sciences
Purpose: The Bin1 gene appears to be detrimental to tumor formation and cancer cells often develop ways to keep the Bin1 gene from being expressed. Interestingly, cancer cells that have lost Bin1 are more sensitive to killing by the cancer drug paclitaxel (Taxol). We propose to investigate the molecular basis for this increase in paclitaxel sensitivity. Additionally, we will test whether Bin1 status is predictive of paclitaxel anti-tumor efficacy in a mouse model.
- Title: *The Role of Epithelial Tight Junction Leakiness in Onset of Gastric Cancer*
Type of Research: Biomedical
Focus: Oncological Sciences
Purpose: We seek to characterize the leak that occurs in the stomach lining prior to the onset of stomach cancer. We will investigate if the leak is causal to cancer progression and/or can be used as an early detection of such cancer.

Lehigh University (\$127,442) - 1 Project

Grant Award Period: 5/1/04 - 4/30/05

Contact:

Maria Bykhovskaia, Ph.D.
Assistant Professor
Biological Sciences
Lehigh University
Iacocca Hall, Room B-217
111 Research Drive
Bethlehem, PA 18015
(610) 758-3079

Research Project:

- Title: *Molecular, Cellular, and Behavioral Aspects of Neuronal Plasticity*
Type of Research: Biomedical
Focus: Neurosciences
Purpose: The purpose of the proposed project is to develop a cross-disciplinary collaborative research aiming to understand different aspects of neuronal functioning.

Lincoln University (\$21,977) - 1 Project

Grant Award Period: 5/1/04 - 6/30/06

Contact:

K. Ramachandra Bhat, Ph.D.
Professor
Department of Chemistry
Lincoln University
1570 Baltimore Pike,
Lincoln University, PA 19352
(610) 932-8300, ext. 3501

Research Project:

- Title: *Development of an Assay for Detection and Quantitation of DNA Double Strand Breaks in Cultured Human Fibroblasts*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: The study proposes to detect the presence of activated and phosphorylated DNA ligase I using an immobilized monoclonal DNA ligase I antibody. The assay is potentially useful to study the effectiveness of various cancer drugs in inducing apoptosis in cancer cells under conditions where concurrent competing DNA repair activity is inhibited.

Madlyn and Leonard Abramson Center for Jewish Life (\$ 48,506) - 1 Project

Grant Award Period: 5/1/04 - 10/31/05

Contact:

Nancy A. Hodgson, Ph.D., R.N.
Senior Research Scientist
Polisher Research Institute
Madlyn and Leonard Abramson Center for Jewish Life
1425 Horsham Road
North Wales, PA 19454-1320
(215) 371-1896

Research Project:

- Title: *Palliative Care Services in Pennsylvania Nursing Homes*
Type of Research: Health Services
Focus: Health of Populations, Behavioral and Biobehavioral Processes
Purpose: The purpose of this project is to identify and describe the extent and characteristics of palliative care services in Pennsylvania nursing homes and to classify existing programs by models of care delivery.

Magee-Womens Health Corporation (\$683,748) - 5 Projects**Grant Award Period:** 5/1/04 – 7/31/05**Contact:**

Robert G. France, M.H.A., M.B.A.
Administrative Director
Magee-Womens Research Institute
Magee-Womens Health Corporation
300 Halket Street
Pittsburgh, PA 15213
(412) 641-5268

Research Projects:

- Title: *Mechanisms of Matrix Metalloproteinase-2 Upregulation in Pregnancy and Relaxin-Mediated Renal Vasodilation and Hyperfiltration*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: The purpose of this project is to define the mechanisms underlying maternal renal adaptations to pregnancy. This understanding is not only fundamental to advancing our understanding of maternal physiology, but also may facilitate our investigation of pathologic processes such as preeclampsia and reno-vascular disease.
- Title: *Maternal Endothelial Progenitor Cells and Preeclampsia*
Type of Research: Biomedical
Focus: Cardiovascular Sciences
Purpose: The purpose of this study is to learn more about what causes the pregnancy-specific hypertensive disease called preeclampsia. The overall hypothesis is that dysfunction of endothelial progenitor cells, specialized blood cells that can be mobilized from the bone marrow into the circulation to help maintain blood vessels (arteries and veins) in a healthy state, is an important contributor to the pathogenesis of preeclampsia. The project will also determine whether deficiencies in these cells persist postpartum in some of these women, helping to explain the increased risk of later-life cardiovascular disease in women with a history of preeclampsia.
- Title: *Homocysteine-Mediated Pregnancy Specific Vascular Dysfunction and Future Cardiovascular Disease*
Type of Research: Biomedical
Focus: Cardiovascular Sciences
Purpose: The purpose of this research project is to investigate the mechanism by which increased homocysteine, an independent risk factor of cardiovascular disease, leads to a pronounced and pregnancy specific loss of the maternal vasculature's ability to respond to vasodilators. This loss of ability to normally respond to vasodilators leads to vasoconstriction, increased blood pressure and eventually contributes to cardiovascular disease.

Cardiovascular disease risk factors, such as increased homocysteine, appear to exert their negative effects on the vasculature over several decades. However, these negative effects are amplified during pregnancy and contribute first to the increased risk of maternal vascular complications of pregnancy such as preeclampsia.

- Title: *Fertility After Cancer Treatment*
Type of Research: Biomedical
Focus: Renal and Urological Sciences
Purpose: Prospects for surviving cancer are increasing with improved therapies. As the population of cancer survivors burgeons, quality of life after cancer is a growing concern. Infertility is a common side effect of chemotherapy and radiation treatment. In men this condition potentially can be treated by cryopreservation of germline stem cells prior to treatment and reintroduction of these cells into the testis upon completion of therapy. Thus, through autologous transplantation of germ cells, it may be feasible for male cancer patients to recover natural fertility and father their own genetic offspring. The proof-in-principle for this approach is already established in mice, rats and goats. Development of a non-human primate model for fertility after cancer is an essential step that will enable translation of this cell-based therapy from the laboratory to the bedside.
- Title: *A Transgenic Mouse Model of Hutchinson-Gilford Progeria Syndrome*
Type of Research: Biomedical
Focus: Biology of Development and Aging
Purpose: Hutchinson-Gilford Progeria Syndrome (HGPS, commonly called "Progeria") is a devastating disease that causes young children to undergo accelerated aging. HGPS recapitulates most of the pathologies of normal aging, causing affected children as young as five years to develop widespread atherosclerosis that includes the coronary arteries and aorta, resulting in death by heart attack or stroke in their early teens. Recently, the genetic basis for HGPS was shown to be caused by a mutation in a gene called Lamin A (*LMNA*). Although the genetic basis of HGPS has now been found, the biological pathways that lead from the mutation to the broad manifestations of aging are unknown. We thus propose to develop a mouse model of HGPS so that we can study the pathological changes that occur over time to cells, tissues, and organs in this disease.

Medical Diagnostic Research Foundation (\$62,239) - 1 Project

Grant Award Period: 5/1/04 - 4/30/05

Contact:

Britton Chance, Ph.D., D.Sc.
President
Medical Diagnostic Research Foundation
39 Northwoods Road
Radnor, PA 19087-3759
(610) 688-8952

Research Project:

- Title: *Early Detection of Breast Cancer in Underserved and High-Risk BRCAI, BRCAII Populations*
Type of Research: Clinical
Focus: Oncological Sciences

Purpose: The purpose of this project is to establish a database on a novel method of breast cancer detection in an underserved population and to obtain a higher rate of patient compliance for breast cancer examination.

Mellon Pitts Corporation (MPC) (\$246,020) - 3 Projects

Grant Award Period: 5/1/04 - 4/30/08

Contact:

James V. Maher, Ph.D.
President
MPC Corporation
801 Cathedral of Learning
University of Pittsburgh
Pittsburgh, PA 15260
(412) 624-4223

Research Projects:

- Title: *Multiscale Dynamics of Biomolecular Complexes and Assemblies*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: This research project seeks to develop computational tools for modeling and simulation that can predict molecular motion in complex biological systems. The ability to simulate, meaningfully, the biomolecular machinery will positively affect many researchers' abilities to develop new therapies against a variety of molecular diseases and to identify new molecular targets for drug/inhibitor binding.
- Title: *NMR Research Initiative*
Type of Research: Biomedical
Focus: Bioengineering, Surgical Sciences and Technology
Purpose: This research seeks to advance state-of-the-art applications of *in vivo* magnetic resonance imaging (MRI) and spectroscopy (MRS) in order to understand tissue and organ function and to optimize these new research methods for application by others. Scientists working at the Pittsburgh NMR Center for Biomedical Research (NMR Center) will be conducting the research.
- Title: *Advancing Proteomics Research into Disease Detection*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: Earlier work in this laboratory led to the development of a powerful technique for proteomics called difference gel electrophoresis (DIGE) that allows one to compare the proteomes of two cell populations (treated/untreated, cancer/normal, etc.) on a single gel by making use of simple visual fluorescence techniques. This research will focus on refinements to the method, improved data analysis, and new applications of the technique.

Monell Chemical Senses Center (\$284,558) - 3 Projects

Grant Award Period: 5/1/04 - 4/30/05

Contact:

Gary K. Beauchamp, Ph.D.
Director and President
Monell Chemical Senses Center
3500 Market St.

Philadelphia, PA 19104-3308
(215) 898-8878

Research Projects:

- Title: *Early Learning about the Sensory Properties of Tobacco*
Type of Research: Biomedical and Health Services
Focus: Health of Populations, Behavioral and Biobehavioral Processes
Purpose: The purpose of this project is to determine the impact of early sensory experiences with tobacco smoke in the home and the context of such experience on young children's hedonic response to the odor of tobacco. Early experience may impact upon later smoking habits as the child matures. The information gleaned from this research may enable us to develop new means to educate children about tobacco.
- Title: *Brain Mechanisms for Food and Cocaine Craving*
Type of Research: Biomedical and Health Services
Focus: Neurosciences
Purpose: This research will lead to a better understanding of brain mechanisms for craving for food and for drugs of abuse. It will help us to understand whether food and drug cravings have any similarities and whether drug addiction changes desire for food. This work should lead to improved methods for the treatment of drug addiction.
- Title: *Matching Funds for the Construction of the Molecular Genomics / Proteomics Facility*
Type of Research: Biomedical and Health Services
Focus: Research Infrastructure
Purpose: Adequate design of a multi-user research facility for investigation of the early events in taste and smell is critical to the efficient functioning of such a facility. The design phase interfaces the scientists with the architect to ensure the development of an appropriate and well-organized laboratory. The development phase brings together the architect and building consultants to allow for planning of the construction schedule.

National Disease Research Interchange (\$77,132) - 2 Projects

Grant Award Period: 5/1/04 - 4/30/05

Contact:

John T. Lonsdale, Ph.D.
Research Director
National Disease Research Interchange
Eight Penn Center, 8th Floor
1628 JFK Boulevard
Philadelphia, PA 19103
(215) 557-7361 ext. 271

Research Project:

- Title: *Analysis of Genetic Contribution to Diabetic Retinopathy and Stratification by Phenotype*
Type of Research: Clinical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: This study is designed to test the hypothesis that the age of onset and the severity of retinopathy, as a complication of diabetes, has a genetic basis. This study will focus on further data collection and analysis from the subset of 500 families from the Type I diabetes database for which cell lines and DNA are available. The statistical significance and validity of the study's

conclusions will be increased by the addition of further data. Developments will also be made to the underlying database to improve the generation and testing of hypotheses.

- Title: *NSABP Institute of Molecular Pathology*
Type of Research: Clinical and Biomedical
Focus: Research Infrastructure
Purpose: The Pathology Division of the National Surgical Adjuvant Breast and Bowel Project (NSABP) houses one of the most valuable annotated tumor tissue banks in the world containing over 35,000 cases. Utilization of this resource has resulted in many important studies that dictated changes in routine clinical practice in the treatment of breast and colorectal cancer. In order to create an infrastructure that will enhance its operation and improve support for molecular pathology, construction of a new NSABP Institute of Molecular Pathology within one consolidated laboratory is proposed. The relocation of its present laboratory is expected to result in more efficient operations of the NSABP Tissue Bank and to support molecular pathology studies conducted by both in-house and collaborative investigators.

NSABP Foundation, Inc. (\$2,278,516) - 2 Projects

Grant Award Period: 5/1/04 - 4/30/07

Contact:

Donna Szczepankowski
Director of Finance and Sponsored Projects
NSABP Foundation, Inc.
Four Allegheny Center, 5th Floor
Pittsburgh, PA 15212
(412) 330-4610

Research Project:

- Title: *Discovery and Validation of Predictors of Response to Anthracycline Based Chemotherapy for Breast Cancer*
Type of Research: Biomedical and Clinical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: The study is aimed at discovering of a set of molecular markers that can be used to predict (before administering therapy) who will benefit from a commonly used chemotherapy regimen of 4 cycles of Adriamycin/cyclophosphamide (AC) for breast cancer. It is estimated that only about 10 to 15% of all breast cancer patients actually benefit from this chemotherapy. Having these markers will allow the beginning of custom tailoring of chemotherapy based on prediction of response. If successful, this study will be followed by a series of studies addressing other chemotherapy drugs.
- Title: *NSABP Institute of Molecular Pathology*
Type of Research: Biomedical and Clinical
Focus: Research Infrastructure
Purpose: The Pathology Division of the National Surgical Adjuvant Breast and Bowel Project (NSABP) houses one of the most valuable annotated tumor tissue banks in the world containing over 35,000 cases. Utilization of this resource has resulted in many important studies that dictated changes in routine clinical practice in the treatment of breast and colorectal cancer. In order to create an infrastructure that will enhance its operation and improve support for molecular pathology, construction of a new NSABP Institute of

Molecular Pathology within one consolidated laboratory is proposed. The relocation of its present laboratory is expected to result in more efficient operations of the NSABP Tissue Bank and to support molecular pathology studies conducted by both in-house and collaborative investigators.

Oncology Nursing Society (\$33,420) - 2 Projects

Grant Award Period: 5/1/04 – 6/30/05

Contact:

Gail Mallory, R.N., Ph.D., C.N.A.A.
Director of Research
Oncology Nursing Society
125 Enterprise Drive
RIDC Park West
Pittsburgh, PA 15275-1214
(412) 859-6308

Research Projects:

- Title: *Nurse Assessments of Process and Outcomes for Hospitalized Cancer Patients*
Type of Research: Health Services
Focus: Health of Populations, Behavioral and Biobehavioral Processes
Purpose: This project seeks to understand the role of the process of nursing care on the outcomes for hospitalized cancer patients.
- Title: *Oncology Nurses' Perceptions of Cancer Patients' Outcomes*
Type of Research: Health Services
Focus: Health of Populations, Behavioral and Biobehavioral Processes
Purpose: This survey research project will determine the perception of oncology nurses, nurse administrators, and nurse educators in Pennsylvania and the United States regarding the impact, value, use, and education needs related to oncology nursing sensitive patient outcomes.

Pennsylvania College of Optometry (\$48,971) - 1 Project

Grant Award Period: 5/1/04 - 4/30/05

Contact:

Alexander M. Dizhoor, Ph.D.
Professor
Pennsylvania College of Optometry
8360 Old York Road
Elkins Park, PA 19027
(215) 780-1468

Research Project:

- Title: *Molecular Mechanisms Related to Cone and Rod Degeneration*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: The purpose of this project is to investigate molecular signaling process in the retina related to causes of blindness by creating genetic models of mice that carry mutation in a protein called retGC1, linked to human cone-rod dystrophy (CORD6), and studying their properties. A mutation related to human blindness will be reproduced in mice using transgenic techniques. Potential physiological, biochemical and anatomical changes in the retina caused by the mutation will be investigated in order to better understand the mechanisms for the retinal cell death as a cause of blindness.

Pennsylvania State University (\$9,245,943) - 30 Projects

Grant Award Period: 5/1/04 - 4/30/08

Contact:

Eva J. Pell, Ph.D.
Vice President for Research and Dean of the Graduate School
The Pennsylvania State University
110 Technology Center
University Park, PA 16802-7000
(814) 863-9580

Research Projects:

- Title: *Manipulation of Signaling Pathways for the Treatment of Breast Cancer*
Type of Research: Biomedical
Focus: Oncological Sciences
Purpose: The purpose of this project is to investigate signaling pathways of breast cancer cells that regulate proliferation, survival and metastasis, in order to discover new pharmacological inhibitors of these pathways to provide optimized regimens for therapy.
- Title: *RING Domains as Targets of Cancer Therapy*
Type of Research: Biomedical
Focus: Oncological Sciences
Purpose: The purpose of this research is to examine the potential of a group of human genes as targets for cancer therapy. These genes are chosen for the presence of a sequence motif known as the RING domain, which specify the gene product function as ubiquitin-protein ligases. These ligases work upstream of the target of a new cancer drug known as Velcade. These upstream enzymes may provide more selective targets with fewer side effects and may provide alternative targets for Velcade-refractory patients.
- Title: *Development of Quantitative Analysis Tools for Mapping Cellular Signaling Pathways*
Type of Research: Biomedical and Health Services
Focus: Bioengineering, Surgical Sciences and Technology
Purpose: Attachment of tumor cells to endothelial cells is critical for migration of tumor cells out of the vascular system to establish metastases. However, how these initial cell adhesion events between tumor and endothelial cells signal downstream pathways that directly regulate the integrity of endothelial barrier requires further elucidation. The proposed quantitative analysis tools integrate mathematical modeling and analysis with experimentation for the discovery and mapping of signaling pathways within a living cell.
- Title: *Nuclear Protein Topography and Interactions in Cancer*
Type of Research: Biomedical
Focus: Oncological Sciences
Purpose: The purpose of this work is to understand the protein interaction network that contributes to changes in the nuclear structures associated with chromatin repression in cancer cells and may cause the unregulated cell proliferation in cancer.
- Title: *Molecular and Cellular Changes that Drive Liver Cancer*
Type of Research: Biomedical
Focus: Digestive Sciences
Purpose: The purpose of the supplemental application will be to expand the scope of the previously funded project to novel aims that have arisen from collaborative studies to date and to expand the scope to human tissue.

- Title: *Chip-Based Nanosensors for Early Cancer Diagnosis by RNA Detection*
Type of Research: Biomedical
Focus: Cardiovascular Sciences
Purpose: The purpose of this project is to develop a device capable of providing early cancer detection by sensing RNA from circulating tumor cells in the blood. The device uses nanometer-scale wires that act as tiny tuning forks, changing their resonant frequency when the proper molecule binds to them.
- Title: *Oral Viral Complications of HIV Infection*
Type of Research: Biomedical, Clinical and Health Services
Focus: AIDS and Related Research
Purpose: Our long-term goal is to establish a large nationally recognized center of excellence focused on basic and translational oral viral infection research. In this application we are proposing research that would directly lead to enabling our team of investigators to apply for the NIH initiated RFA.
- Title: *Role of Antizyme and Polyamines in Tumor Development*
Type of Research: Biomedical
Focus: Oncological Sciences
Purpose: The overall objective of this application is to bring together a group of investigators and generate sufficient preliminary information for the submission of a program project grant (PPG) to the National Cancer Institute. This application would be focused on a protein named antizyme (AZ), which is a key negative regulator of polyamine metabolism and which has been shown in the PI's laboratory to be a potential tumor suppressor gene.
- Title: *Biomarker Discovery for Hormonal Resistant Breast Cancer: a Genomic and Proteomic Approach*
Type of Research: Biomedical
Focus: Oncological Sciences
Purpose: The purpose of this project is to identify serum or tissue biomarkers that could be used in the management of patients with hormone-dependent breast cancer.
- Title: *NMR Studies of Protein Structures & Metabolic Pathways*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: This project has two overarching goals 1) to develop methods for determining the structure of medically relevant proteins in structures, and 2) to develop methods for following cellular metabolism in brain, muscle and liver. To accomplish these objectives, the proposal describes plans to acquire a high field Nuclear Magnetic Resonance (NMR) spectrometer in the College of Medicine (COM), which is an essential tool in modern biology.
- Title: *Function of RAD51 and MATS in Cell Division and Cancer*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: Our purpose is to address two important biological processes affected in cancer: control of cell division and control of genome stability, by focusing on two key regulatory molecules Rad51 and Mats.
- Title: *Sphingosine Kinase Inhibitors in Acute Renal Failure*
Type of Research: Biomedical
Focus: Renal and Urological Sciences

Purpose: The objective of this project is to determine the role of sphingosine-1-phosphate and sphingosine kinase in acute renal failure. Our hypothesis is that sphingosine kinase is a critical component of the inflammation cascade, and subsequent injury in acute renal failure. Our rationale for these studies is that an understanding of how sphingosine kinase and sphingosine-1-phosphate contribute to renal injury, along with the availability of inhibitors of this pathway, may lead to novel forms of treatment of this condition.

- Title: *Bioinformatics Consulting Center at University Park and Hershey Medical Center -- Phase II*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: The Bioinformatics Consulting Center (BCC) mission is primarily to provide bioinformatics support to researchers at Penn State for sequence analysis and statistical design and analysis of functional genomics studies, including microarray experiments.
- Title: *Genetic and Environmental Regulation of Bone Quality*
Type of Research: Biomedical
Focus: Musculoskeletal, Oral and Skin Sciences
Purpose: The overall aim of this work is to bring together a team of investigators with diverse expertise to integrate techniques in quantitative genetics, molecular genetics, tissue mechanics, and cell physiology, with the eventual goal of identifying important genetic determinates of bone quality, and the mechanisms through which identified genes interact with each other and with environmental factors to dictate skeletal health across the lifespan, particularly in old age.
- Title: *Retinoid Homeostasis, Oxidative Stress and Breast Carcinogenesis*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: There is mounting evidence linking the high risk for developing breast cancer of women living in the USA to the exposure of their breast tissue to chronic oxidative stress. Such a state is a known cause of mutations that are prerequisites for cells to become cancerous. This research focuses on characterizing how oxidative stress affects one such protective mechanism, the ability of breast cells to produce from vitamin A the retinoic acid that is needed to maintain these cells in a normal, differentiated state.
- Title: *Integrative Functional Imaging of Cognitive Systems in the Developing Brain*
Type of Research: Biomedical
Focus: Neurosciences
Purpose: The purpose of this project is to develop and implement new methods of noninvasive brain imaging for children and adolescents. Functional magnetic resonance imaging (fMRI) provides specific quantitative maps of brain activity while participants undertake cognitive and motor learning tasks. These methods will identify the neural systems that are critically related to cognitive and motor development in healthy children and teens.
- Title: *Effect of Beta Blockade on Neurohormonal Activation, Left Ventricular Remodeling and Function, and Survival in Chronic Mitral Regurgitation (MR): From Hemodynamics to Cellular Biology*
Type of Research: Biomedical
Focus: Cardiovascular Sciences

Purpose: This experimental study will evaluate the beneficial effects of early beta-blockade on neurohormonal activation, LV remodeling, LV function and survival. The data collected from this study will be used as preliminary data to support our on-going clinical investigations in the medical therapy for chronic MR.

- Title: *Microdevices for Measuring Complement Activation*
Type of Research: Biomedical and Clinical
Focus: Bioengineering, Surgical Sciences and Technology
Purpose: Extracorporeal circulation or the "heart-lung machine" (cardiopulmonary bypass, or CPB) is used to support the functions of the body during open-heart surgery. However, it produces a condition termed "whole-body inflammation" or "systemic inflammatory response syndrome (SIRS)" that may delay healing of tissues and recovery from surgery. A complex system of substances in the blood called the "complement cascade" is stimulated during whole body inflammation, and ways of changing the amount of the complement cascade stimulation when the heart-lung machine is used is an important area of study. The purpose of this research is to develop methods for real-time measuring of complements using microfabrication techniques.
- Title: *Age, Sex, Alcohol, and Exercise Interactions on Signaling Pathways in Cardiac Muscle*
Type of Research: Biomedical
Focus: Cardiovascular Sciences
Purpose: The overall goal of the project is to enable a group of investigators to develop a Program Project Grant application to the National Institute of Health. The investigators participating in this effort are presently conducting research projects that focus on the role of gender differences during aging that impact on the growing body of evidence that cardiovascular disease carries a greater mortality and morbidity in females than males. Research projects are focused along the theme that common signaling pathways are important in protecting the heart from injury.
- Title: *MRI Study of Lung Injury in Aging Rats*
Type of Research: Biomedical
Focus: Biology of Development and Aging
Purpose: The primary purpose of this study is to develop magnetic resonance imaging (MRI) methods to evaluate lung injury in rats. These MRI methods will then be used, in conjunction with traditional biochemical and morphological methods, to compare the severity of a common lung injury model in young versus old rats.
- Title: *Research Infrastructure for New Translational Technologies for Neural Prosthetic Devices*
Type of Research: Biomedical, Clinical and Health Services
Focus: Research Infrastructure
Purpose: - The purpose of this project is to renovate lab space, create animal holding rooms, and build the infrastructure to develop a new Penn State Center for Neural Engineering. It will provide unique medical research and educational opportunities in Pennsylvanians and increase the quality of the medical and engineering students attracted to study in the State. The Center will create new technologies for the next generation of smart neural prosthetic devices. It will provide advanced training for resident physicians and junior faculty from the College of Medicine, as well as train Masters and PhD students in engineering. The ultimate goal is to better treat diseases of the

brain, while providing cutting edge trained physicians and scientists who can carry on this work in the future.

- Title: *Research Infrastructure for Renovations in the Huck Institute of Genomics, Proteomics and Bioinformatics*
Type of Research: Biomedical
Focus: Research Infrastructure
Purpose: Two floors of Wartik Laboratory need major renovations to support the activities of the Institute. The majority of the 5th floor was dramatically redesigned and renovated to convert it to a state-of-the-art facility for biocomputing. Several additional rooms (517, 518, 519, 513 and 513B) still need renovations once the Huck Institutes staff relocate to the new Life Sciences building. The 3rd floor needs renovation to foster interaction and handle increased instrumentation.
- Title: *Mutant Retroviral Integrase with Novel Properties*
Type of Research: Biomedical
Focus: Oncological Sciences
Purpose: Retroviruses are a type of virus that can cause certain cancers and other diseases. All retroviruses have an enzyme named integrase that inserts a copy of the genetic information of the virus into the DNA of an infected cell. Although integrase must act differently on viral DNA and cellular DNA, it is not known how it distinguishes between virus and cell DNA to join them together. Thus, the purpose of this project is to understand how integrase distinguishes between viral and cellular DNA.
- Title: *Colorectal Cancer in the TH2 Deficient Stat6 Knockout Mouse*
Type of Research: Biomedical
Focus: Oncological Sciences
Purpose: The purpose of this work is to better understand the development of colorectal cancer in ulcerative colitis.
- Title: *Growth Regulation of Pancreatic Cancer*
Type of Research: Biomedical and Clinical
Focus: Oncological Sciences
Purpose: Growth of pancreatic cancer is regulated in part by certain small proteins or peptides. One peptide in particular, called gastrin, accelerates cancer growth by stimulating a cancer protein called the CCK-C receptor and another, OGF, inhibits growth. The purpose of this project is to allow the investigator time to develop new strategies, such as raising antibodies against the receptor, that block growth and develop protocols for clinical trials. Blood samples will also be examined from human subjects to determine if pancreatic cancer can be diagnosed in earlier stages by using assays designed to identify the receptor in the blood.
- Title: *Tumor Antigen Presentation in Mice Developing Cancer*
Type of Research: Biomedical and Clinical
Focus: Immunology
Purpose: The overall goal of this project is to gain new understanding of the immune system's response to tumor antigen. The general hypothesis proposes that CD8+ T cells exposed to endogenous tumor antigen under steady-state conditions will either self-destruct or remain in an unresponsive state, while those that encounter antigen in the context of an up-regulated APC will produce an effective anti-tumor immune response.
- Title: *Efficacy of Isometric Handgrip Training to Reduce Arterial Blood Pressure in Older Adults with "High Normal" Blood Pressure*
Type of Research: Biomedical and Clinical

Focus: Cardiovascular Sciences

Purpose: The purpose of this project is to determine the effectiveness of isometric handgrip training in reducing arterial blood pressure (BP) in individuals with elevated cardiovascular disease risk (i.e., older adults with "high normal" BP). A secondary purpose of this project is to gain insight into the possible role of several physiological variables (autonomic nervous system and circulating vasoconstrictor/vasodilator substances) in the reduction in BP with isometric handgrip training.

- Title: *Quantitative Proteomics of Human Acute Lung Injury*
Type of Research: Biomedical and Clinical
Focus: Respiratory Sciences
Purpose: The purpose of this research study is to discover the protein changes occurring in human lung tissue with acute lung injury. Acute lung injury (ALI) and the more severe acute respiratory distress syndrome (ARDS) are prevalent causes of mortality and morbidity. Understanding the changes in protein expression that occur in the lung with ALI would create new possibilities for treatment.
- Title: *Contributory Role of Circulating Endothelial Progenitor cells to the renal Functional Recovery after Ischemia*
Type of Research: Biomedical and Clinical
Focus: Renal and Urological Sciences
Purpose: The purpose of this study is to understand mechanisms by which damage to blood vessels in the kidney are repaired to regain their normal function.
- Title: *Research Infrastructure for a Center for the Treatment, Prevention and Cure of Cancer*
Type of Research: Biomedical, Clinical and Health Services
Focus: Research Infrastructure
Purpose: The purpose is to design and construct a new building for the Penn State Cancer Institute that will bring together patient care, basic and translational research under one roof to enhance our ability to provide comprehensive, coordinated cancer care. The new facility will allow top researchers to work together to create new therapies and to bring them quickly into state-of-the-art clinical care for the patients of central Pennsylvania. Formula funds from the 2003, 2004 and 2005 grants will be used for this project because the entire project cost is estimated to be ~\$100 million.

Philadelphia FIGHT (\$62,772) - 1 Project

Grant Award Period: 5/1/04 - 4/30/05

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Research Project:

- Title: *APC and Innate Immunity in HIV Disease*
Type of Research: Clinical
Focus: AIDS and Related Research

Purpose: The purpose of this study is to investigate the way in which HIV-1 infection affects the immune system by focusing on the population of cells that allows an immune response to start. Specifically, the study intends to determine the state and function of certain blood cells (the dendritic cells and natural killer cells) in HIV-infected persons who have never received anti-retroviral therapy, and to determine whether or not these immune functions are improved when the virus replication is suppressed following anti-retroviral treatment.

Philadelphia Health Management Corporation (\$19,349) - 1 Project

Grant Award Period: 5/1/04 - 4/30/05

Contact:

Jennifer L. Lauby, Ph.D.
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Research Project:

- Title: *Assessment of the Effectiveness of HIV Prevention Case Management for Men and Women Who Use Drugs*
Type of Research: Health Services
Focus: AIDS and Related Research
Purpose: This project will evaluate whether an HIV prevention intervention consisting of outreach to drug users on the street and short-term office-based case management is effective in reducing drug use and reducing sexual risk behaviors. We will analyze data collected at enrollment and 6 months post-enrollment from men and women who participated in the intervention and a comparison group of men and women who did not participate.

Pittsburgh Tissue Engineering Initiative (\$22,965) - 1 Project

Grant Award Period: 5/1/04 - 4/30/05

Contact:

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Research Project:

- Title: *Studies to Support the Development of a Lymphoid Tissue Equivalent (LTE)*
Type of Research: Biomedical
Focus: Immunology
Purpose: The present project will consist of a series of preliminary experiments in which dendritic cells (the first cells in the body to be in contact with infectious agents against which an immune response must be mounted) will be cultured upon a bioscaffold made of extracellular matrix (ECM). These preliminary studies will determine the correct conditions for such cell culture work so that the subsequent work can proceed. The purpose of the overall project in our laboratory for which this feasibility work is being conducted, is to develop an artificial immune system for the purpose of developing vaccines

to protect large populations against diseases that presently cause high morbidity and mortality. For example, effective vaccines against HIV, small pox, and hemorrhagic fever are either only partially effective or difficult to generate in large quantities. Successful completion of the proposed project would identify strategies for the large scale manufacture of these vaccines in systems that require no *in vivo* component. This would represent a major advancement for the medical field.

Temple University (\$2,633,223) - 23 Projects

Grant Award Period: 5/1/04 - 4/30/08

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Research Projects:

- Title: *Mechanisms of Platelet Activation*
Type of Research: Biomedical
Focus: Hematology
Purpose: Platelets get activated and clump together. This platelet clump can block blood circulation in the vessels leading to heart attacks and stroke. We propose to understand the mechanisms by which platelets are activated in the body, so that new drugs can be developed that block these mechanisms and hence platelet activation. Three separate interactive projects with the help of a core project will investigate the mechanisms of platelet activation.
- Title: *Tolerance Induction in Type 1 Diabetes and Latent Autoimmune Diabetes in Adults*
Type of Research: Biomedical
Focus: Immunology
Purpose: The purpose of this project is to develop new drugs for the treatment of patients with type 1 diabetes. Type 1 diabetes is caused by aberrant T cells of the body which recognize and destroy pancreatic beta cells, which produce insulin. This will be accomplished by (i) identifying these aberrant cytotoxic T cells of the body; (ii) identifying the molecular entities of the pancreas that these cytotoxic T cells recognize; and (iii) developing molecules ("altered peptide ligands[APL]") which will resemble the molecular entities recognized by cytotoxic T cells. These APL will convert these cytotoxic effector cells that destroy the insulin-producing pancreatic cells to regulatory T cells which, in turn, will not be able to destroy the insulin-producing pancreatic beta cells.
- Title: *CB2 Agonists as Immunomodulating Neuroprotective Agents*
Type of Research: Biomedical
Focus: Cardiovascular Sciences
Purpose: The purpose of this investigation is to determine if activation of a newly identified component of the cell membrane, called the cannabinoid 2 (CB2) receptor, may provide for protection of the brain and spinal cord under a number of pathologic conditions. The potential therapeutic use of selective

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cannabinoid 2 receptor activation will be studied in animal models of multiple sclerosis, stroke, head trauma and spinal cord injury.

- Title: *Interpretations of Health Messages Among North Philadelphia Latinos: A Pilot Study*
Type of Research: Health Services
Focus: Health of Populations, Behavioral and Biobehavioral Processes
Purpose: The purpose of this project is to examine how messages about smoking and tobacco are interpreted by North Philadelphia Latino residents of all ages and, at a broader theoretical and methodological level, to develop and test a model for examining how communications affect health decision-making among members of different social groups, particularly underserved ethnic minorities.
- Title: *Applications of Bioinformatics Data Analysis to Cardiovascular and Cancer Research*
Type of Research: Clinical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: The main purpose of the proposed bioinformatics data analysis is to analyze cardiovascular and cancer-related data to aid discovering the mechanisms by which diseases develop and progress at the molecular level. This will be accomplished by gene expression data analysis, genomic-scale data analysis, and knowledge extraction from biological databases and public web resources.
- Title: *Studies in the Determinants of Choice, Verbal and Social Behavior in Pervasive Developmental Disorders*
Type of Research: Clinical
Focus: Health of Populations, Behavioral and Biobehavioral Processes
Purpose: The function of the proposed studies is to refine basic research procedures and translate them into beneficial treatments. In addition, one of the studies will analyze alternative instructional strategies and techniques for children with autism.
- Title: *Behavioral, Neural, and Genetic Factors of Nicotine Addiction*
Type of Research: Biomedical
Focus: Neurosciences
Purpose: The overall purpose of the project is to understand the influences of nicotine on learning processes and neural, cellular, and genetic substrates in order better understand and develop treatment for nicotine addiction and therapeutic agents for the treatment of cognitive disorders such as Alzheimer's disease that involve altered acetylcholinergic function, the neurotransmitter system that nicotine activates.
- Title: *Examination of Maternal Role Participation, Well-being, Social Support, and Health of Mothers with Disabilities or Chronic Illnesses*
Type of Research: Health Services
Focus: Health of Populations, Behavioral and Biobehavioral Processes
Purpose: The first objective of this study is to gain normative data about maternal role participation and satisfaction, general role participation, and well-being of mothers with or without disabilities. The second objective is to examine the interrelationship of these variables with the mothers' perception of social support. The third objective is to examine the relationship of the perception of health status (mental and physical) to maternal role participation, social support and well-being.
- Title: *Effect of Lipid Raft Cholesterol on Opioid Receptors in Cell Membranes*

Type of Research: Biomedical

Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics

Purpose: The goal of this research is to understand how the functional properties of opioid receptors in cells are affected by the membrane environments in the context of lipid rafts. Lipid rafts are membrane microdomains composed of cholesterol, sphingolipids, and a subset of proteins that serve as platforms for certain cellular activities.

- Title: *DNA Repair in Real Time by DNA Photolyase: Protein and Model Studies*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: Exposure to ultraviolet radiation (UV) is known to cause skin cancer. The initial insult is often a crosslinking of adjacent nucleic acid bases in DNA generating cyclobutylpyrimidine dimers, or CPDs. All organisms use DNA repair proteins to undo this damaging insult. We are particularly interested in one member of this class of repair proteins, DNA photolyase. Photolyase uses blue light to repair the UV-induced crosslinking. A comprehensive analysis of this mechanism will contribute to our understanding of how nature repairs DNA that could otherwise lead to mutations and cancer. In addition, studies of the binding mode of photolyase will contribute to our understanding of how proteins can manipulate DNA, a biologically critical but quite common function.
- Title: *The Role of Periostin-Like-Factor in Vascular Occlusive Disease*
Type of Research: Biomedical
Focus: Cardiovascular Sciences
Purpose: We have identified an isoform of the Periostin family referred to as Periostin-Like-Factor (PLF). We propose to characterize and determine the function of the splice-variants of periostin including PLF, in vascular smooth muscle cells (VSMCs).
- Title: *Better Understanding and Treatment of Upper Gastrointestinal Motility and Functional Gastrointestinal Disorders*
Type of Research: Clinical
Focus: Digestive Sciences
Purpose: The purpose of this project is to provide funding support for a research coordinator who will assist clinical investigators with the implementation, performance, and completion of four clinical studies with the unifying theme of improving our understanding and treatment of upper gastrointestinal motility and functional bowel disorders. The studies will concentrate specifically on oropharyngeal dysphagia, gastroesophageal reflux disease, functional dyspepsia, and gastroparesis.
- Title: *Mechanisms of Impaired Contractility and Functional Reserve in Human Heart Failure*
Type of Research: Clinical
Focus: Cardiovascular Sciences
Purpose: The purpose of this project is to understand the diminished ability of the failing heart to modulate magnitude and kinetics of relaxation during stress, and to examine adrenergic modulation of relaxation reserve in failing human hearts in a manner that accounts for the defects in Ca²⁺ cycling present in these hearts.
- Title: *Neighborhood Correlates of Social Capital in Philadelphia*
Type of Research: Health Services

Focus: Health of Populations, Behavioral and Biobehavioral Processes
Purpose: This project will use the Philadelphia Health Management Corporation's Household Health Survey from 2002 to investigate the association of measured levels of social capital and other neighborhood characteristics.

- Title: *An Experimental Model to Expand the Therapeutic Window for Treatment of Stroke*
Type of Research: Clinical
Focus: Cardiovascular Sciences
Purpose: The purpose of this investigation is to develop a reliable experimental model that will allow for the evaluation of the potential of drugs and other compounds to increase the time period over which reinstatement of blood flow to the brain will still attenuate neuronal damage after stroke.
- Title: *TULA: A Novel Putative Oncogene*
Type of Research: Biomedical
Focus: Oncological Sciences
Purpose: We recently found a novel protein associated with c-Cbl in T cells, which has a rather unusual structure. Functional studies of TULA, as we have named this protein, show that it may negatively regulate c-Cbl. Since c-Cbl is known to suppress cancerous transformation in various types of cells, TULA is likely to be an oncogene. Indeed, we have shown that TULA activates responses of several cell types to extracellular signals in a manner similar to the effect of typical oncogenes. The purpose of this work is to determine whether or not TULA is indeed a novel oncogene.
- Title: *Mechanistic Characterization of Arginase and Peptidylarginine Deiminase*
Type of Research: Biomedical
Focus: Neurosciences
Purpose: Arginase has been implicated in the regulation of nitric oxide production, and is thus an important factor in the immune response and in the sexual response in both males and females. Peptidylarginine deiminase has been implicated in the development of rheumatoid arthritis and multiple sclerosis. A detailed understanding of the catalytic mechanisms of these enzymes will lead to the development of potent inhibitors with potential therapeutic value.
- Title: *Regulation of Osteoactivin (OA) Gene Expression in Osteoblasts*
Type of Research: Biomedical
Focus: Musculoskeletal, Oral and Skin Sciences
Purpose: The purpose of this project is to evaluate the transcriptional regulation of Osteoactivin (OA) gene expression by osteotrophic factors in osteoblasts, and to examine the role of OA as a downstream mediator of osteoblast differentiation induced by BMP-2.
- Title: *Sorcin, Estrogen Receptors, and Taxol Resistance in Breast Cancer*
Type of Research: Clinical
Focus: Oncological Sciences
Purpose: Increased expression of sorcin in estrogen receptor negative breast cancer cells has been demonstrated to induce taxol resistance. In contrast, sorcin overexpression in estrogen receptor positive breast cancer cells does not give rise to taxol resistant tumor cells. This study aims to decipher the possible interactions between sorcin and estrogen receptors (or lack thereof) that would induce the drug resistant phenotype.

- Title: *Studies on the Mechanism of Thermal Regulation through Hot and Cold Receptors*
 Type of Research: Clinical
 Focus: Neurosciences
 Purpose: Capsaicin, the pungent ingredient of hot chili peppers, causes a burning sensation after acute administration but shuts off sensory nerves after prolonged administration so that capsaicin cream is used to treat chronic pain and itch. Capsaicin acts via a protein called VR1 which is the heat sensor on nerves. The chemical icilin produces a cold sensation through the cold detector protein CMR1. We will examine the two pathways and determine whether they work together in pathways of physiological stress. Answers to these questions will lead to better drugs to treat pain and itch.
- Title: *The Role of Cdk4 in the Development of Melanoma and the Proliferation and Development of T Cells*
 Type of Research: Biomedical
 Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
 Purpose: This work utilizes mice that have been engineered to lack Cdk4 protein (Cdk4^{neo/neo}) or express a repressor-insensitive, hence activated, form of Cdk4 (Cdk4^{R24C/R24C}). We will examine the molecular consequences of these mutations as they relate to cellular proliferation and oncogenesis in MEFs and thymocytes. Through interbreeding the Cdk4^{R24C} mouse line with mice carrying the melanocyte-specifically-expressed Tyr-RAS transgene, we address the cooperativity of Rb (through Cdk4 activation) and Ras in the development of melanoma and provide a mouse model for melanoma.
- Title: *Mechanistic Significance of Structure and Protein Movement in Salmonella Typhimurium Orotate Phosphoribosyltransferase (OPRTase)*
 Type of Research: Biomedical
 Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
 Purpose: Enzymes are essential for carrying out biological reactions at high rates. OPRTase catalyzes the synthesis of nucleotides, a component of DNA. This project will examine how the structure and motion within OPRTase contributes to carrying out its reaction. Additionally, OPRTase can serve as a model enzyme to aid our fundamental understanding of how structural changes in protein during catalysis can lead to a favorable enzymatic state for increasing reaction rates.
- Title: *Characterization of p130/p107 Functions Not Inactivated by CDK4-Mediated Phosphorylation*
 Type of Research: Biomedical
 Focus: Oncological Sciences
 Purpose: This study will increase our knowledge of the mechanisms underlying cell cycle regulation, the process by which cells determine when it is appropriate to divide. Specifically, the aim of this project is to identify and characterize novel functions of the tumor suppressors p130 and p107, which negatively regulate the cell cycle. Although it was previously thought that p130 and p107 are inactive when phosphorylated, there is recent evidence to the contrary. Thus, this project will identify and characterize functions of p130 and p107 not inactivated by CDK4 mediated phosphorylation.

Thomas Jefferson University (\$5,488,272) - 11 Projects

Grant Award Period: 5/1/04 - 4/30/08

Contact:

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Research Projects:

- Title: *Clinical Utility of Biomarkers for Stage III Non-Small Cell Lung Carcinoma and Stage IV Head and Neck Cancer*
Type of Research: Clinical
Focus: Oncological Sciences
Purpose: The purpose is to analyze stored tissue samples from patients treated with a combination of chemotherapy and radiation therapy (no surgery) for advanced lung or head and neck cancer and determine if some of the features of the cells in these samples can predict prognosis and indicate future treatment directions.
- Title: *Fragile Genes in Cancer Prevention and Therapy*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: The fragile gene Fhit, when put into a virus such as adenovirus and infected into mouse tumors, can stop tumor growth. This project will identify proteins expressed in tumors before and after Fhit virus infection, determine their structure and explore their usefulness as therapeutic targets.
- Title: *FHIT Function in Normal and Tumor Cells*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: Fhit protein is present in normal and lost in most tumor cells. The purpose is to describe differentially expressed proteins in Fhit negative cells, to identify proteins that bind to Fhit and determine their structure.
- Title: *PET-CT Imaging of Breast Cancer*
Type of Research: Biomedical
Focus: Bioengineering, Surgical Sciences and Technology
Purpose: The purpose of this project is to utilize state-of-the-art imaging equipment to develop a molecular imaging technique that will diagnose early breast cancer and distinguish normal from diseased tissue, thereby reducing the number of unnecessary invasive procedures to diagnose breast cancer.
- Title: *Role of Ca²⁺ Channels and Ca²⁺ Influx in Regulating Synaptic Vesicle Recycling in Neurons*
Type of Research: Biomedical
Focus: Neurosciences
Purpose: The primary purpose of this project is to understand how nerve cells communicate with each other and how such communication can be regulated by Ca²⁺. Nerve cells communicate with each other via release of specific chemicals called neurotransmitters.
- Title: *Role of IL-12 in the Immunopathogenesis of Experimental Autoimmune Neuritis*
Type of Research: Biomedical
Focus: Neurosciences

Purpose: Experimental autoimmune neuritis (EAN) is an experimental model for acute inflammatory demyelinating polyneuropathy (AIDP or Guillain-Barré syndrome; GBS). This model is useful to (1) define mechanisms which are responsible for the development of EAN and (2) identify new therapies for this disease that can be applicable in GBS. This project will evaluate the role of IL-12 in EAN, its production by the peripheral nervous system (PNS) and its contribution to inflammatory demyelination. This information may be helpful if IL-12 is to be considered as a target for therapy in GBS.

- Title: *Completing Phase One Construction of the Center for Translational Medicine*
Type of Research: Biomedical
Focus: Research Infrastructure
Purpose: The goal of this project is to complete Phase One of the newly established Center for Translational Medicine within the Department of Medicine at Thomas Jefferson University. The Center is currently 15,000 square feet and the completion of phase one will add 3,000 square feet of premium lab space.
- Title: *Regulatory Mechanisms of Smooth Muscle Contraction in Hormonal Signals via Myosin Phosphatase*
Type of Research: Biomedical
Focus: Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: The purpose of this project is to understand how hormonal signals are mediated in the regulation of smooth muscle contraction via myosin phosphatase.
- Title: *B Cell Tolerance in the Germinal Center*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: The character of pathological autoantibodies that arise in systemic autoimmune states such as lupus differ from antibodies produced during immune responses to foreign pathogens only in their specificity for autoantigen. This project proposes that removal of pathological autoreactive B cells created during normal immune responses occurs in the lymphoid microenvironment of the germinal center. Dysregulation of this process could represent one of the first steps in the etiology of lupus. This project will test this hypothesis using new strains of antibody transgenic mice, one that has a high frequency of B cells reactive with both a foreign antigen and nuclear autoantigens.
- Title: *Protein-Protein Interaction Antagonist Discovery as a Route to Novel Cancer Chemotherapeutic Agents*
Type of Research: Biomedical
Focus: Immunology
Purpose: The purpose of this project is to develop small molecule antagonists of a variety of protein-protein interactions that have been shown to be critical for the initiation or progression of human cancer. These molecules will serve as a first step toward the development of drugs that target these interactions specifically.
- Title: *Generation of Tumor Antigen Specific T Cells with Natural Selection Method for Adoptive T Cell Therapy*
Type of Research: Clinical
Focus: Immunology

Purpose: The purpose of this project is to generate sufficient quantity of tumor antigen specific T cells with the newly developed Natural T Cell Selection Method. These tumor antigen specific T cells will be evaluated for their anti-malignancy potential.

Treatment Research Institute (\$75,727) - 1 Project

Grant Award Period: 5/1/04 - 4/30/05

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Research Project:

- Title: *Survey of Counselors' Perceptions toward Incentive Programs: Substance Abuse Professionals' Attitudes, Education, and Exposure*
Type of Research: Health Services
Focus: Health of Populations, Behavioral and Biobehavioral Processes
Purpose: The purpose of Study 1 is (a) to complete data entry and cleaning on existing survey data collected from 383 substance abuse professionals regarding their perceptions of the use of incentive programs to promote drug abstinence, (b) to provide descriptive information about treatment providers' attitudes toward incentive programs, and (c) to evaluate and revise an existing measure of attitudes toward incentive programs. The purpose of Study 2 is to collect preliminary data to begin to evaluate the effect that education about and exposure to an incentive program has on counselors' attitudes toward incentive programs.

University of Pennsylvania (\$10,877,580) - 28 Projects

Grant Award Period: 5/1/04 - 4/30/08

Contact:

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Research Projects:

- Title: *The Adaptation of Cellular Stress Responses by DNA Viruses*
Type of Research: Biomedical
Focus: Infectious Diseases and Microbiology
Purpose: In order for mammalian DNA viruses to replicate they must adapt their host cells. In so doing the cells will favor viral production instead of their own well being. These virally-induced adaptations are similar to changes which occur in cells during transformation and oncogenesis. These studies will indicate how mammalian DNA viruses may alter vital cellular processes and how they may increase the potential for cells to become immortalized, transformed or oncogenic.

- Title: *Improving Diagnosis and Prognosis of Breast Cancer Using Gene Expression Profiling and Clinical Data*
 Type of Research: Clinical
 Focus: Oncological Sciences
 Purpose: The research project aims to determine whether biomedical informatics approaches can be used to predict breast cancer metastasis.
- Title: *Effects of Atomoxetine on Cigarette Smoking*
 Type of Research: Clinical
 Focus: Health of Populations, Behavioral and Biobehavioral Processes
 Purpose: The purpose of this study is to evaluate the potential benefits of a novel medication, atomoxetine, for nicotine dependence treatment.
- Title: *Clinical Cell and Vaccine Production Facility: Phase 2 of a Research Infrastructure Project*
 Type of Research: Clinical
 Focus: Research Infrastructure
 Purpose: This is a construction project to renovate laboratory space in the University of Pennsylvania medical complex to house the Clinical Cell and Vaccine Production Facility (CVPF), a facility to produce therapeutic vaccines for cancer clinical research, in compliance with Good Tissue Practices (cGTP), current Good Manufacturing Practices (cGMP), and FDA regulations and guidance.
- Title: *Gene-Gene Interactions in Prostate Cancer*
 Type of Research: Biomedical
 Focus: Oncological Sciences
 Purpose: The purpose of this project is to evaluate the complex interaction of prostate cancer susceptibility genes, including genes identified as hereditary prostate cancer genes, hormone metabolism genes, genes involved in inflammatory cytokine response, and genes involved in carcinogen metabolism.
- Title: *Characterization of Genomic Changes in Breast Cancer Progression*
 Type of Research: Biomedical
 Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
 Purpose: This research project aims to identify genetic changes that may facilitate breast cancer progression, with the ultimate goal of developing new molecular therapeutic targets for cancer prevention and treatment.
- Title: *Phase I Study of Telomerase Peptide Vaccination for Patients with Advanced Breast Cancer*
 Type of Research: Clinical
 Focus: Oncological Sciences
 Purpose: The purpose of this project is to determine: (a) whether telomerase peptide can trigger robust immune responses in patients with breast cancer, (b) whether toxicity is acceptable, and (c) whether vaccination results in clinical tumor response.
- Title: *Enhanced Understanding of Human Genetic Disease through the Development and Application of Genomic-Scale Technologies*
 Type of Research: Biomedical
 Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
 Purpose: The overall goal of this project is to exploit new technologies made available in part through prior support from the Health Research Formula Fund to generate genomic-scale datasets relevant to the nature and

treatment of human disease. Support will be provided for the development of new methodologies, and for the application of these tools in the study of disease processes.

- Title: *Construction of Life Sciences Building (Phase I Year 3)*
Type of Research: Biomedical
Focus: Research Infrastructure
Purpose: The purpose of this infrastructure project is to provide state-of-the-art laboratory space for investigators in the Department of Biology in the School of Arts and Sciences, as well as space for the University-wide Penn Genomics Institute. This badly needed space will help Penn to attract the high-quality faculty, students, and postdoctoral researchers who are the essential critical success factor in modern research in the life sciences.
- Title: *A Pilot Study of the Effectiveness of Interactive, Web-Based Patient-Oriented Research Training for Clinical Researchers*
Type of Research: Health Services
Focus: Health of Populations, Behavioral and Biobehavioral Processes
Purpose: The purpose of this study is to assess knowledge retention after a web-based training program that uses interactive web training and adult learning techniques.
- Title: *Vivarium – Research Infrastructure Phase II*
Type of Research: Biomedical
Focus: Research Infrastructure
Purpose: Recent advances in genomics have created the demand for an increase in mouse facilities that will be used for critical experiments in the cause and therapy of disease.
- Title: *Engineering Progenitors for Efficient T-Cell Reconstitution*
Type of Research: Biomedical
Focus: Hematology
Purpose: The purpose of this research is to explore techniques for maintaining and expanding earliest T lineage progenitors (ETPs) *in vitro* without genetic alterations, while maintaining their ability to function as efficient T lineage progenitors. T cells develop in the thymus and play a critical role in coordinating the immune response to pathogens. Deficiencies in T cell number and function are seen after bone marrow transplantation for cancer therapy, in aging, and HIV infection. It is therefore desirable to devise techniques by which T cell production in the thymus can be therapeutically increased.
- Title: *Plasticity of Mouse and Human Cutaneous Epithelial Stem Cells*
Type of Research: Biomedical
Focus: Musculoskeletal, Oral and Skin Sciences
Purpose: Because the skin is the most accessible organ in the body, it represents an ideal potential source of adult stem cells for therapeutic purposes. Stem cells in the skin are located in a specific area of the hair follicle called the bulge. We will test whether these cells can turn into all components of the skin, as well as other cell types such as nerves. The research is geared toward developing cell-based therapies for cutaneous disorders, such as chronic wound healing and alopecia, as well as neurodegenerative and genetic diseases.
- Title: *Developing Eggs from Mouse Embryonic Stem Cells*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics

Purpose: The eventual development of human embryonic stem cells that can be used to effectively treat human diseases, such as cancer and lung disorders, requires background research using animal model systems. This research project will use a mouse model system to determine how best to develop multi-potent stem cells from embryos. These eggs could later be used for the development of mouse embryonic stem cells that are compatible immunologically with the animal to be treated. The knowledge gained from the mouse system could be applied in the future to human stem cell-based therapies.

- Title: *The Role of Pax5 in Limiting Hematopoietic Lineage Plasticity*
Type of Research: Biomedical
Focus: Immunology
Purpose: The purpose of this project is to understand how cells in the adult bone marrow are regulated to differentiate into different lineages. The majority of bone marrow stem cells will become lymphocytes, and the protein Pax5 prevents developing lymphocytes from converting into other blood cell types, such as macrophages. This study will determine whether certain proteins can temporarily inactivate Pax5 and in doing so allow already committed lymphocytes to switch identities.
- Title: *Effective Glioma Therapy by Neural Stem Cell-Based Interferon-beta Delivery*
Type of Research: Biomedical
Focus: Neurosciences
Purpose: The goal of this project is to understand and exploit neural stem cell migration and differentiation for effective brain tumor therapy.
- Title: *Homing, Differentiation, and Efficacy of Stem Cells for Treatment of Myocardial Infarction Evaluated by Non-invasive In Vivo Imaging*
Type of Research: Biomedical
Focus: Bioengineering, Surgical Sciences and Technology
Purpose: The overall goal of this project is to develop a multi-modality molecular imaging approach that permits evaluation of the survival, differentiation and therapeutic effect of stem cell grafting in a murine model of myocardial infarction. The imaging system takes advantage of high sensitivity provided by PET/SPECT and high spatial resolution by MRI, and allows repetitive *in vivo* detection in a non-invasive way; it also provides a platform for future clinical translation.
- Title: *Telomerase Defects in Oral Squamous Cell Carcinoma*
Type of Research: Clinical
Focus: Oncological Sciences
Purpose: The purpose of this research project is to examine the role of telomerase, an enzyme concerned with the formation, maintenance, and renovation of telomeres (the ends of chromosomes), in oral carcinogenesis. The hypothesis of this research is that defects in telomerase-associated genes may play a role in the development of Oral Squamous Cell Carcinoma (OSCC) in otherwise normal individuals who are smokers and/or drinkers.
- Title: *Models for Hepatocellular Carcinoma*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: Hepatocellular carcinoma is one of the common tumor types world-wide. Its incidence has been linked to hepatitis B and C viruses and the incidence in the industrialized countries is increasing due in part to the spread

of hepatitis C for which there is no current vaccine or treatment. Virus- or alcohol-induced cirrhosis generally precedes cancer and limits surgical treatment options. This research will develop an understanding of the role of cirrhosis in the development and maintenance of cancer.

- Title: *Non-Invasive Molecular Imaging of Inducible Transgenic Mouse Models for Breast Cancer*
Type of Research: Biomedical
Focus: Oncological Sciences
Purpose: The purpose of this project is to understand the mechanisms by which breast cancers progress to more aggressive states such as metastasis, recurrence, and therapeutic resistance. This will be accomplished by applying state-of-the-art non-invasive molecular imaging techniques that are capable of detecting the growth and death of tumor cells in living animals to a novel mouse model for breast cancer that faithfully recapitulates essential aspects of the human disease.
- Title: *Cellular Functions of the PRC17 Proto-oncogene*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: The conversion of a normal cell into a cancerous cell is a complex, multi-step process during which the cell accumulates errors in its DNA. These errors cause the cell to invade their underlying tissue, an essential component of malignant progression. The PRC17 gene is known to be present at high levels in invasive breast and prostate cancer cells. This research will address whether this gene plays a causative role in invasiveness, and determine the mechanism by which it functions.
- Title: *Ras-PI3K-Akt Pathway Activation and Intrinsic Radiation Resistance*
Type of Research: Biomedical
Focus: Oncological Sciences
Purpose: To evaluate the relationship between activation of the Ras-PI3K-Akt pathway and clinical outcome and to develop novel targeted therapies to reverse radiation resistance.
- Title: *From Bench to Bedside: Mitotic Checkpoint Integrity Determines Response to Taxane Treatment in Human Cancers*
Type of Research: Biomedical
Focus: Oncological Sciences
Purpose: To assess whether cell cycle control in cancer cells, particularly control of mitosis (cell-division), is linked to treatment efficacy in women with breast cancer; to investigate factors that determine how effectively taxane-based chemotherapy can control human cancers grown in mice; and to test whether new strategies that interfere with cell-cycle control, and which dramatically improve the killing of cancer cells in the laboratory, will have similarly good results in animal models of human cancer.
- Title: *Development of a Novel Murine Model and Novel Therapies for Oral / Head and Neck Cancer*
Type of Research: Biomedical
Focus: Oncological Sciences
Purpose: To develop a mouse model for oral and head and neck cancer that will allow preclinical testing of newly discovered gene and cancer vaccine therapies that would provide the foundation for subsequent human clinical trials.

- Title: *Concurrent Array-Based Comparative Genomic Hybridization and Expression Array Analysis of Laryngeal Carcinoma*
Type of Research: Clinical
Focus: Oncological Sciences
Purpose: To employ Array Comparative Genomic Hybridization (aCGH) and expression array analysis techniques to increase understanding of the molecular mechanisms that lead to the development and recurrence of head and neck cancers with an ultimate goal of determining what makes the normal cells become cancerous, and what can be done to reverse or halt the process once a patient has developed cancer.
- Title: *Understanding Molecularly Targeted Therapy in Patients with Metastatic Melanoma*
Type of Research: Clinical
Focus: Oncological Sciences
Purpose: To perform correlative laboratory studies on melanoma tumor specimens and surrogate tissues obtained from patients with metastatic melanoma enrolled in clinical trials that are investigating molecularly targeted therapy in order to understand the mechanisms associated with anti-tumor responses.
- Title: *Enhancing Biomedical Research by Providing Access to Genomics Scale Data Analysis*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: The goal of this project is to provide tools, user support and analysis services to researchers using genomics scale technologies such as transcript profiling, proteomics, genotyping and large-scale sequence analysis of genomes.
- Title: *Genetics of Cellular Response to Environmental Challenge: Systems Approach*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: In this project, we will determine how genetic differences influence metabolic response to changes in an environmental agent, in this case, glucose level. These studies have obvious potential relevance to diseases such as diabetes and diabetic complications. Our systems approach to studying this complex biological system is to integrate genetic analysis along with gene expression and metabolic studies. This will allow us to understand how inherited genetic variation affects cellular responses to metabolic challenges.

University of Pittsburgh (\$10,877,580) - 6 Projects

Grant Award Period: 5/1/04 - 4/30/08

Contact:

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Research Projects:

- Title: *Nuclear Magnetic Resonance Imaging of Protein Structure*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: Protein structures provide an essential framework for determining biomolecular functions and for designing novel drugs with high disease specificity and minimal side effects. There is a mismatch between the number of known protein sequences and known protein structures. The purpose of this project is to increase the number of known protein structures, particularly membrane proteins, using high-field nuclear magnetic resonance spectroscopy.
- Title: *Membrane Transport in the Central Nervous System*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: The goal of this research is to develop multiple imaging techniques to study membrane transport in the central nervous system. The techniques will be based on the generation of variants of green fluorescent protein, which allows imaging of biological processes in living cells. These studies are expected to allow for enhanced analysis of the fundamental neuronal process of ion movement across neuronal membranes.
- Title: *Pharmacogenetics and Human Disease*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: The purposes of this project are (1) to investigate the basic mechanism by which the structure of the human genome influences drug response, and (2) to study how a gene can be used as a drug. Achieving these goals will significantly enhance understanding of how drugs can best be used and facilitate the discovery of new, more effective drugs.
- Title: *Polarized Membrane Traffic in Kidney Cells*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: - The goal of this project is to understand the normal role of the enzyme OCRL1 in the distribution of newly synthesized proteins to two distinct cell surfaces in renal epithelial cells, a process known as polarized membrane trafficking. The gene *ocrl*, which encodes the enzyme OCRL1, is defective in patients with Lowe syndrome, a rare genetic condition in males that produces mental and physical handicaps, as well as medical problems including kidney malfunction.
- Title: *Cellular Events in Cancer Initiation and Progression*
Type of Research: Biomedical
Focus: Oncological Sciences
Purpose: The basic research activities defined in this project will focus on understanding the differences between cancer cells and normal cells and will also define new approaches for diagnosis and therapy. The studies will be based on the concept that cancer results from the accumulation of cellular changes. Damage to DNA results in changes that can be passed on each time the cell divides, influencing genotype and protein expression.

- Title: *New Approaches for Cancer Therapy*
Type of Research: Biomedical and Clinical
Focus: Oncological Sciences
Purpose: This study will use a multifaceted approach to identify improved methods for cancer treatment. The projects proposed to reach this goal include: improving drug design to reduce tumor gene inactivation of compounds, finding vaccine strategies to improve the recognition and destruction of tumors by immune cells, identifying targets that inhibit tumor growth and ways of directing therapy to those targets, and using sensitive imaging methods to quantify therapeutic efficacy.

Weis Center for Research - Geisinger Clinic (\$163,358) - 1 Project

Grant Award Period: 5/1/04 - 4/30/06

Contact:

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Research Project:

- Title: *Molecular Profiling of Human Disease*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: The purpose of this study is to use new molecular tools, enabled by advances in knowledge of the structure of genes and novel technologies, to identify patterns of gene expression that are characteristic of disease phenotypes ("molecular profiling"). The information derived from these experiments will provide novel insights into the pathophysiology of these diseases, and identify potential new targets for development of improved therapies.

Wills Eye Hospital (\$11,748) - 1 Project

Grant Award Period: 5/1/04 - 4/30/05

Contact:

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Research Project:

- Title: *Detection of Retinoblastoma, the Most Common Malignant Eye Cancer in Children*
Type of Research: Biomedical
Focus: Oncological Sciences
Purpose: Retinoblastoma (RB) is the most common childhood cancer of the eye. Untreated it can be fatal, and it occurs in both hereditary and nonhereditary forms. The purpose of this study is to improve the health status of children by designing methods to identify changes in the gene

responsible for the eye tumor, which will allow early detection thereby preventing blindness and enhancing the survival rate.

Wistar Institute (\$1,676,669) - 8 Projects

Grant Award Period: 5/1/04 - 6/30/05

Contact:

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Research Projects:

- Title: *The Growth and Regulation of Human Tumors in a Regeneration-Permissive Host, the MRL.RAG-/- mouse*
Type of Research: Biomedical
Focus: Oncological Sciences
Purpose: One of the major problems with studying human cancer is the lack of models. Ideally, one would hope to grow human tumors in an animal model; however one often does not see the type of growth or metastatic potential of that tumor. Because of the immune response and the xenograft situation using human tumors in mice, for example, investigators have used immunodeficient mice that will not reject the tumors. Researchers at The Wistar Institute have been studying a mouse, the MRL mouse, which has been shown to regenerate tissue. The process of regeneration seen in this mouse and not in other mouse strains shares many characteristics with tumor progression. Researchers at The Wistar Institute would like to explore the ability of this mouse to grow human tumors.
- Title: *Multifunctional Antibacterial Peptides*
Type of Research: Biomedical
Focus: Infectious Diseases and Microbiology
Purpose: The purpose of this project is to assess the utility of derivatives of native antibacterial peptides in drug development. On one hand, new molecular entities will be identified that fight bacteria resistant to current antibiotics. On the other hand, a novel vaccination strategy will be developed against viral infections and cancer.
- Title: *A Model System for Investigating Breast Cancer Metastasis to Bone*
Type of Research: Biomedical
Focus: Oncological Sciences
Purpose: The purpose of this project is to investigate the mechanism of human breast tumor metastasis to bone. The approach employs an innovative model system comprised of a special tissue culture bioreactor (*in vitro* component) and immunosuppressed mice (*in vivo* component). Because over 90% of breast tumors selectively metastasize to bone during disease progression, information about the molecular mechanism(s) involved in bone metastasis will guide future therapy of this disease.
- Title: *Postgraduate Research in Cellular and Molecular Basis for Oncogenesis*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics

Purpose: The goal of this project is to fund postgraduate research in order to advance our understanding of oncogenesis and to develop new therapies for cancer.

- Title: *Research Infrastructure: Research Laboratory Renovations*
Type of Research: Biomedical
Focus: Research Infrastructure
Purpose: The Wistar Institute will up-grade approximately 2500 ft² of research laboratory space to accommodate new faculty and the programmatic realignment of existing research teams.
- Title: *Structure-Based Design of Molecules to Reactivate Tumor-Derived P53 Mutations*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: The p53 protein is altered in the majority of human cancers. The purpose of these studies is to use information on the three-dimensional structure of the p53 protein to help design small molecule compounds that will repair altered p53 proteins. Such compounds may have therapeutic value in the treatment of p53-mediated cancers.
- Title: *Development of Diagnostic and Prognostic Markers for Cancer Using Genomic and Proteomic Approaches to Analyze Patient Samples and Mouse Models for Cancer*
Type of Research: Biomedical
Focus: Cell Biology, Biological Chemistry, Macromolecular Biophysics, Genomes and Genetics
Purpose: The focus is on developing new markers that will (1) complement and improve existing technology for early cancer diagnosis, (2) identify patients with poor prognosis, (3) predict responsiveness to therapy, and (4) provide new targets for therapy.
- Title: *Dissect and Characterize the Functions of PTS in Transgenic Embryos*
Type of Research: Biomedical
Focus: Biology of Development and Aging
Purpose: The goal of this project is to investigate the mechanism by which the Hox gene, Abdominal-B is regulated. Abdominal-B is a master regulatory gene that controls the body plan and the identities of individual cells in the posterior region of an animal. When this gene in humans is not properly regulated, a range of diseases would occur including prostate cancer and Wilm's tumor. The PTS is a key control element for the Abdominal-B gene. We propose to study how this element works in a well established genetic system, the fruit fly embryo.