

Health Research Formula Grants - State Fiscal Year 2002-03

Thirty-seven organizations received health research formula grants for the state fiscal year 2002-03. 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 the title(s) and purpose(s) of the research project(s) supported by the grant.

Albert Einstein Healthcare Network (\$168,475) - 3 Projects

Grant Award Period: 01/01/03 - 12/31/04

Contact:

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Albert Einstein Healthcare Network
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Research Projects:

- *Action Production and Recognition in Ideomotor Apraxia* - The main purpose of the project is to increase knowledge of subtypes and performance patterns in patients with ideomotor apraxia, a common clinical syndrome affecting approximately 50% of patients with left hemisphere stroke.
- *Role of PTX1 Protein in Prostate Cancer* - The purpose of this project is to study the role of a protein known as PTX1 in the growth of prostate cancer. PTX1 has been shown to suppress the growth of human prostate cancer cells. The results of the project will provide a better understanding of the mechanism of action of this protein, which will lead to the design of a means to combat advanced prostate cancer in the future.
- *Cognition and MRI in Older Adults* - The major aim of this research is to develop an MRI image analysis system and to implement this system by analyzing MRI volumes and associating them to performance on neuropsychological tests including eye blink classical conditioning. Genetic risk factors for Alzheimer's disease (AD) and measures that detect AD early such as MRI brain volumes and eye blink conditioning will be assessed in African Americans, Asians (Koreans) and Caucasians because it is important to determine if these measures are equally useful in different ethnic and minority groups.

Allegheny Singer Research Institute (\$307,259) - 3 Projects

Grant Award Period: 01/01/03 - 12/31/05

Contact:

Alison M. Sylvester, M.P.A.
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Allegheny-Singer Research Institute
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Research Projects:

- *Non-invasive Coronary Artery Imaging by Cardiovascular MRI; a Change in the Yardstick* - Despite improvements in x-ray angiographic techniques and catheters, there remains obligate morbidity and mortality from coronary artery disease (CAD) that has remained virtually unchanged over the last decade. A non-invasive method to obtain diagnostic intraluminal coronary information may be possible. We hypothesize that CV MRI may be able to accurately display anatomic coronary

information in a manner similar to traditional techniques, but without the attendant risk.

- *Rat Brain Infarction by Middle Cerebral Artery Occlusion as a Model of Post Stroke Epilepsy* - The purpose of this project is to establish an animal model of post stroke epilepsy as a means to develop medications that could prevent epileptic seizures that occur in some people after they have experienced a stroke.
- *Pituitary-Adrenal Cortical Responses to Nicotine Challenge in Nicotinic Receptor Knockout Mice* - The purpose of this study is to characterize the role of nicotine in stimulating the pituitary-adrenal gland stress hormone response. Receptors for nicotine exist on neurons in the brain, and these neurons participate in control of the pituitary and adrenal glands. Many stresses activate the pituitary-adrenal hormone system, and these hormones have important effects throughout the body. Smoking also activates this stress hormone system. By studying mice bred to lack subtypes of nicotinic receptors ("knockouts"), we can understand the role of nicotine, acting through nicotinic receptors, in stimulating the pituitary-adrenal hormone stress response.

American Association for Cancer Research (\$142,976) - 2 Projects

Grant Award Period: 01/01/03 - 12/31/04

Contact:

Margaret Foti, Ph.D.
Chief Executive Officer
American Association for Cancer Research
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Research Projects:

- *Functional Identification of Pancreatic Cancer Tumor Suppressor Genes* - The purpose of this research project is to identify tumor suppressor genes that are involved in the development of pancreatic cancer.
- *Identification and Characterization of Candidate Tumor Suppressor Genes for Colorectal and Breast Cancer on Chromosome 22q* - The purpose of this research project is to identify tumor suppressor genes and their germline mutations that can lead to breast and colon cancer.

American College of Radiology (\$2,053,097) - 4 Projects

Grant Award Period: 01/01/03 - 12/31/06

Harvey L. Neiman, M.D.
Executive Director
American College of Radiology
1101 Market Street, 14th Floor
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(215) 574-3150

Research Projects:

- *Patterns of Care Study of Diagnostic Evaluation of Breast Cancer Patients in Pennsylvania: Survey Planning and Data Collection* - The purpose of this project is to assess screening, diagnostic evaluation, and follow-up evaluation for breast cancer with particular emphasis on subgroups that may be underserved.
- *Outcomes Associated with Cancer Therapy in Special Populations and Ethnic Minorities at High-Risk for Poor Outcomes* - The purpose of this project is to identify special populations at risk for poorer outcomes after head and neck, lung and

prostate cancer therapies in large standardized clinical trials. The findings will lead to targeted interventions that will improve quality of life and survival.

- *Biomarkers of Prostate Cancer Response to Radiation and Hormone Therapy* - The goals of this project are to determine if abnormalities in the expression of key proteins in the apoptotic pathway are predictive of prostate cancer response to radiation therapy (RT) ± hormone therapy (HT) and to facilitate the selection of appropriate therapy and the development of novel gene therapy strategies to improve prostate cancer cure rates.
- *New Drug Development Program Core (NDDPC) for the Radiation Therapy Oncology Group (RTOG)* - This project has been created within the RTOG to play a key role in the development of innovative anti-cancer agents and more effective treatment strategies with the ultimate aim of improving the survival and quality of life of all patients with cancer.

Bryn Mawr College (\$8,581) - 1 Project

Grant Award Period: 01/01/03 – 6/30/04

Contact:

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Research Project:

- *A Process Evaluation of Ready, Willing & Able – Philadelphia (RWA-P)* - This project evaluates the start-up and implementation in Philadelphia of Ready, Willing & Able, a long-term, residential, work-based treatment program for substance-abusing homeless men that has other, similar programs in Manhattan, Brooklyn, and Jersey City. Relying on interviews, site observation, program data, and data from the City of Philadelphia's shelter system, the study appraises how well this complex, innovative and controversial program establishes itself in a new political and human services environment, how the program functions, and whom it actually serves in what ways.

Carnegie Mellon University (\$1,081,443) - 3 Projects

Grant Award Period: 01/01/03 - 12/31/05

Contact:

Christina Gabriel, Sc. D.
Vice Provost and Chief Technology Officer
Carnegie Mellon University
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Research Projects:

- *Research Infrastructure for a New Computational BioImaging Center* - This research infrastructure project will renovate space and acquire dedicated computer hardware for a new Computational BioImaging Center within the Carnegie Institute of Technology, the CMU School of Engineering; this will create imaging capabilities that advance biomedical science.
- *Understanding Fundamental Processes of Brain Development and Function* - The purpose of this research project is to investigate fundamental processes of brain

development and function through the use of animal models, especially as they relate to learning and memory.

- *Administrative Infrastructure for Biotechnology Efforts* - The purpose of this infrastructure project is to provide administrative support for the Commonwealth's Health Research Formula Fund reporting requirements as well as other university-based biotechnology efforts.

Children's Hospital of Philadelphia (\$3,727,099) - 3 Projects

Grant Award Period: 01/01/03 - 12/31/06

Contact:

Judith K. Argon, M.T.S., M.A.
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The Joseph Stokes, Jr. Research Institute
The Children's Hospital of Philadelphia
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Research Projects:

- *Using a Molecular Chaperone to Augment Immune Response* - The purpose of this project is to decipher the mode of action of the stress protein GRP94 as a molecular chaperone, in order to develop a peptide delivery technology capable of augmenting immune responses.
- *Activity-guided Synaptic Specification* - The goal of this project is to investigate the molecular machinery that subserves synaptic connections, and to provide insight on the development of the precisely wired connections between nerve cells.
- *Immunology Meets Proteomics: Isolation and Characterization of the Immunological Synapse* - The overall goals of this study are to develop a proteomics-based strategy for isolating and analyzing the protein complexes involved in T cell signaling, and to use this strategy to address questions about T cell function that are unanswerable by more conventional approaches.

Children's Hospital of Pittsburgh (\$720,940) - 2 Projects

Grant Award Period: 01/01/03 - 12/31/06

Contact:

David H. Perlmutter, M.D.
Vira I. Heinz Professor and Chairman
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Children's Hospital of Pittsburgh
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Research Project:

- *Pathogenesis and Treatment of Necrotizing Enterocolitis, A Start-up Program* - This project will use animal models and cell culture model systems to examine the mechanism of intestinal injury in necrotizing enterocolitis as a basis for developing novel therapeutic strategies.
- *Pathogenesis of Diarrhea in Cystic Fibrosis, A Start-up Program* - This project will use an animal model to examine the mechanism by which chloride secretion by intestine is regulated and what factors are involved.

Donald Guthrie Foundation for Education & Research (\$55,570) - 1 Project

Grant Award Period: 01/01/03 - 12/31/04

Contact:

Robert S. Aronstam, Ph.D.
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Research Project:

- *Muscarinic Signaling Pathways Controlling Adenylate Cyclase Activity* - The purpose of the project is to understand how brain molecules work to relay signals from one cell to another. This project looks at a specific signaling pathway in the muscarinic pathway. These pathways play a role in memory, attention and learning, and are disrupted in diseases such as Alzheimer's disease. This work may indicate new targets for drug development in these diseases.

Drexel University (\$197,969) - 3 Projects

Grant Award Period: 01/01/03 - 12/31/04

Contact:

Shortie McKinney, Ph.D.
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Drexel University
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Research Projects:

- *Systems Biology: Theoretical Approaches for Oncogene Detection and Drug Design* - The purpose of this project is to provide a feasibility study in two key areas: (1) A theoretical approach to oncogene detection and drug targeting via signal cascades and (2) A synergistic approach using aptamer libraries to drive computational drug design.
- *Protein Aptamers as Anti-Cancer Therapeutics* - The purpose of this project is to develop novel anti-cancer agents.
- *Automated Histological Grading of Breast Cancer* - The purpose of this project is to develop automated computational methods to determine accurate staging (typing) of cancer from the two-dimensional images of paraffin-fixed histology slides of excised tumor tissue. At present, pathologist-based evaluation (grading) of tissue slides is imprecise and is not necessarily predictive of clinical outcome. The imprecision of the grading of cancer has dramatic consequences, including the excessive use of chemotherapy and hormone therapies for cancers such as the breast cancer. The primary mathematical procedure to be used is geo-statistics, a statistical procedure designed to analyze and model spatial relations that occur in nature.

Drexel University College of Medicine (\$1,445,034) - 10 Projects

Grant Award Period: 01/01/03 - 12/31/05

Contact:

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Research Projects:

- *Memory and Impulse Control in Children Prenatally Exposed to Tobacco* - Maternal tobacco use during pregnancy can affect children's memory and impulse control. The hippocampus, prefrontal cortex, and basal ganglia are centrally involved in these abilities. This study will test whether children exposed to tobacco during pregnancy exhibit less activity in these brain regions during memory and impulse control tasks. This study will increase knowledge of how tobacco exposure affects children's development, which may ultimately enhance the effectiveness of early interventions.
- *Molecular Correlation of Ultrasound Tissue Characterization in Breast Tumors* - The purpose of this study is to correlate findings on a specialized ultrasound test with molecular changes in breast tumors, namely apoptosis and angiogenesis. The ultimate goal is the development of a non-invasive test for the identification of high risk tumors in the breast.
- *Interaction of Bacillus Anthracis with Macrophages* - The purpose of this project is to study the role of a newly characterized anthrax cytotoxin on the ability of B. anthracis to escape from and kill human macrophages in culture.
- *Cellular and Network Mechanisms of Afterdischarges in Neocortex* - During some forms of epilepsy the neocortex generates a type of repetitive activity called afterdischarges that is related to the sudden occurrence of seizures. We have recently found a way to induce afterdischarges in neocortex. This method is proving extremely useful in understanding how afterdischarges are generated. Knowing how they are generated means that therapies can be defined to control them. The aim of the proposal is to further develop our in vitro model of afterdischarges so that in future studies we may decipher how afterdischarges are generated.
- *Reprogramming Adult Stem Cells for Cellular Cardiomyoplasty* - Cellular cardiomyoplasty (CCM) involves the implantation of cells into the muscle of the heart to restore function of the heart that has been lost as a result of injury. CCM has been attempted with many different cell types, but each has significant limitations. Adult human stem cells (hMSC) avoid many of these problems. However, they need to be converted into cardiomyocytes in order for them to function in the heart. The purpose of this project is to determine the best methods of pre-treating adult human stem cells prior to implanting them into the muscle of the injured heart, so that they may produce the greatest improvement in cardiac function.
- *A New Method for Analysis of Axonal Topographies* - The pattern of interconnections between brain regions is critical for the flow of activity from one region to the next. It is difficult to characterize patterns of interconnection between brain regions, which involves extensive neuroanatomical and electrophysiology analyses. To facilitate analysis of patterns of connections between brain cells, a new method for labeling these connections will be developed.
- *Investigation of the Role of IL-23 in Cytotoxic CD8+ T Cell Responses* - Cytotoxic CD8+ T cells are important players in controlling tumors and viral infection as they can kill tumor cells and infected cells. The aim of this proposal is to examine the role the novel cytokine interleukin 23 (IL-23) plays in cytotoxic CD8+ T cell responses. We will examine whether IL-23 is required for such responses in mice and most importantly whether such responses can be enhanced by administration of IL-23 to animals. These studies may lead to novel therapeutic approaches to treat tumors and viral infections.
- *Crystallization of the Cytomegalovirus IE72 Protein* - The purpose of this project is to produce well-diffracting crystals of the IE72 protein. In future work, these crystals will be used to determine the structure of the protein by X-ray crystallography.
- *Reciprocal Interactions Between Stress and Serotonin* - This project will investigate the interactions between acute and chronic exposure to a mild stress and the clinically important relevant hippocampal serotonin_{2A} (5-HT_{2A}) receptors.

- *Cloning and Characterization of Novel Genes Required for Non-Homologous End Joining Repair* - The purpose of this project is to isolate and characterize genes required for NHEJ repair while also exploring their efficacy as new genetic markers for tumor staging. The biochemical characterization of NHEJ gene products may lead to new protein chemotherapeutic targets. Moreover, the ability to use NHEJ gene expression profiles as a diagnostic tool for tumor staging will allow clinicians to more precisely define and use the appropriate modalities for treatment of tumors.

Duquesne University (\$100,115) - 3 Projects

Grant Award Period: 01/01/03 - 12/31/04

Contact:

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Research Projects:

- *Screening Human Breast Cancers for Steryl Sulfatase Status* - The purpose of this project is to evaluate human breast cancer tissue samples for the presence of the enzyme steryl sulfatase. This enzyme may be a useful indicator for determining the course of treatment and the prognosis for individuals with breast cancer.
- *Developing a Model "Chain of Survival" Community in a Predominantly African-American Urban Pennsylvania Neighborhood: Operation Churchbeat* - The purpose of this project is to evaluate the overall effectiveness of a church-based educational program targeted to adult residents of a predominately African-American urban Pennsylvania neighborhood. This program is designed to increase participants' knowledge, skills, and willingness to respond effectively to cardiac emergencies (heart attacks and sudden cardiac arrest).
- *Design and Testing of DNA Bending Agents* - The purpose of this project is to design, synthesize and test drugs which bind to double stranded DNA and induce a bend in the helix. DNA bends have been shown to be important for the regulation of gene expression and thus, DNA bending agents offer the potential to control gene expression. This research hopes to develop sequence selective agents that are capable of regulating the expression of genes associated with diseases such as cancer, sickle cell anemia and heart disease.

Fox Chase Cancer Center (\$4,508,784) - 19 Projects

Grant Award Period: 01/01/03 - 12/31/04

Contact:

Robert C. Young, M.D.
 President
 Fox Chase Cancer Center
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 Philadelphia, PA 19111
 (215) 728-2781

Research Projects:

- *Role of the Mismatch Repair Pathway in Promoting Telomerase-Independent Telomere Maintenance* - The purpose of this project is to characterize the role of two genetic factors, p53 mutation and mismatch repair mutation, in determining the mechanism used by tumors to maintain chromosome ends.
- *Improving Recruitment of Special Populations and Ethnic Minorities in Routine and High-Risk Cancer Screening and Prevention Trials* - The purpose of this project is to

identify barriers and develop strategies to increase the recruitment of families with several cases of cancer, and minorities, in innovative cancer-risk education, screening and research programs.

- *Unique Activation through the KIR2DL4 Receptor on Human Natural Killer Cells* - Natural Killer (NK) cells are a subset of white blood cells that can produce cytokines and kill tumor cells. This project will study the NK receptor, KIR2DL4, which stimulates the release of cytokines.
- *Cellular Response to Retroviral DNA Integration* - This project aims to extend our knowledge of cellular genes that are required for the life cycle of retroviruses such as HIV, and their role in cancer.
- *Prevention of Liver Cancer in East Asian Populations in the Delaware Valley* - The purpose of this project is to study the prevalence of rising hepatitis C virus infection in Asian American hepatitis B carriers, living in Philadelphia, who are seeking screening at the FCCC Liver Cancer Prevention Center.
- *Function of the Gene HEI10 in Cancer Development* - This study addresses a novel gene that promises to reveal unique insights into several different classes of cancer. This information will enable us to identify individual differences that impact disease susceptibility, preferred treatment options, and survival rate.
- *Automated Analysis of Gleevec Treatment of GIST Cells* - Microarrays provide a new high-throughput method of personalizing medicine by identifying reasons for drug treatment response and failure. However to successfully use this data, multiple methods of analysis must be applied. This project will develop high-throughput analysis methods and apply them to a study of drug response in gastro-intestinal stromal tumors (GIST).
- *Optimizing Cancer Treatment to Patient Individual Needs* - The purpose of this project is to tailor dose levels to the individual patient so that each patient will be provided with the best cancer treatment. As an overall result, more Pennsylvanians will receive therapeutic doses and fewer will suffer from the treatment's toxic effects.
- *Prevention of Breast Cancer from Radiation Treatment Exposures* - The purpose of this project is to develop new strategies to prevent breast cancer in young women at high risk due to chest radiation or radio-chemotherapy from prior Hodgkin's disease treatment.
- *Proteomics of Inter-Individual Variability* - People vary in their susceptibility to diseases and responses to standard therapy. The differences originate from the variations among the proteins that make up the systems in each person. This study will examine this variability with a new technology called Proteomics, and explain some of these differences in terms of genetic variations among people.
- *Development of Computational Tools for Sequence Analysis and Molecular Modeling of Proteins Involved in DNA Repair* - The purpose of the project is to understand the structure and function of proteins involved in DNA repair, which serve to prevent cancer in human tissues. We propose to develop software for the automated analysis of protein sequences and structures. This software will help us understand the function of these and other proteins using all sources of information now available from the genome and structural genomics projects.
- *Interactions Among Cells and Natural Surroundings* - The purpose of the project is to understand the structural interactions among cancerous cells and their natural surroundings in order to prevent them from invading other tissue and stop cancer progression at the cellular level.
- *Prostate Cancer Cell Killing with Androgen Deprivation and Radiation* - The purpose of the project is to enhance the cell killing effects of androgen deprivation and radiation and to improve the survival of men with prostate cancer.
- *Cost and Outcomes Comparison of Three Treatment Options for Stage I Nonseminomatous Germ Cell Tumor* - The purpose of the project is to maximize the

quality of life of patients facing treatment decisions for stage I nonseminomatous germ cell tumors while minimizing the costs to society.

- *Assay Validation for the Determination of a Cancer Patient's Response Following CEA Vaccination* - The purpose of the project is to establish a correlative testing procedure that will more accurately define a meaningful immune response following biological therapies such as vaccines.
- *Early Genetic Changes in Colorectal Cancer Development* - The purpose of this project is to identify the earliest changes in cells of the colon that are responsible for the transformation of "normal colon cells" into benign tumors and then into cancer. This will enable us to develop diets and drugs that inhibit these early changes in order to prevent colorectal cancer.
- *Exploiting the Rac Pathway to Inhibit Angiogenesis* - The goal of this project is to identify new protein targets to block the growth of blood vessels in cancer.
- *Identification of Genetic Markers Responsive to Gleevec in Gastrointestinal Stromal Tumors* - The purpose of this project is to enhance the understanding of genetic responses to Gleevec, a new therapeutic agent used in the treatment of Gastrointestinal Stromal Tumor (GIST).
- *BRAF Activation in Melanoma Development* - This project seeks to understand the role of the BRAF gene in the development of melanoma.

Immaculata University (\$6,378) - 1 Project

Grant Award Period: 01/01/03 - 12/31/03

Contact:

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Research Project:

- *Health Education to Reduce Osteoporosis Risk in Undergraduate University Women* - The purpose of this research is to complete an assessment of the health behaviors and educational preferences of Immaculata University undergraduate women, apply this information to the development of a peer-led osteoporosis prevention educational program for this population, and assess the impact of this education on health behavior.

Lankenau Institute for Medical Research (\$409,168) - 5 Projects

Grant Award Period: 01/01/03 - 12/31/03

Contact:

Vincent J. Cristofalo, Ph.D.
President and CEO
Lankenau Institute for Medical Research
100 Lancaster Avenue
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(610) 645-3475

Research Projects:

- *Mechanisms of Upregulation of Large Conductance Ca^{2+} Activated K^+ (BK_{Ca}) Channels in Hypertensive Arterial Smooth Muscle* - The purpose of this research project is to identify how the function of a protein in blood vessels is enhanced in subjects with

high blood pressure and to determine if this protein could be the target for the development of a novel class of medicines to treat this condition.

- *Tumorigenicity and Chemotherapeutic Sensitivity of Myc-transformed Cells Lacking Bin* Loss of the Bin1 gene has been implicated in but has yet to be directly tied to malignant progression. The goals of the proposed research are threefold: 1) directly confirm that Bin1 gene loss can enhance the tumorigenicity of oncogenically transformed cells in vivo, 2) determine whether suppression of tumorigenicity by Bin1 is specific for transformation mediated by the Myc proto-oncogene with which Bin1 can functionally interact, and 3) investigate whether Bin1 loss specifically sensitizes Myc-over expressing, transformed cells to the chemotherapeutic agent paclitaxel.
- *Carcinogen-Induced Stomach Cancer Alters Epithelial Tight Junctions* - The purpose of this project is 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.
- *ODC Genotype and Cancer Risk* - The purpose of this study is to find out if a variant form of the ornithine decarboxylase (ODC) gene modifies the effect of aspirin in preventing colon polyps and influences the risk of developing certain cancers of the digestive tract.
- *IDO Inhibitors for Cancer Therapy* - The purpose of this study is to test the hypothesis that chemical inhibitors of the immunomodulatory enzyme IDO (indoleamine 2,3-dioxygenase) stimulate the ability of the body's immune system to destroy tumors. This hypothesis will be tested in mice with bioactive chemical inhibitors of IDO. Proof-of-concept represents the first step in developing IDO inhibitors as innovative cancer therapeutics for the clinic.

Lehigh University (\$117,425) - 1 Project

Grant Award Period: 01/01/03 - 12/31/03

Contact:

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Research Project:

- *Functional Plasticity of the Vertebrate Nervous System* - The purpose of this research is to understand degenerative and regenerative biological processes. An understanding of disease-associated degeneration and repair will specifically increase available therapies and targets for intervention in biomedical arenas. Funding will support multiple projects that will generate novel approaches to restoration of function in the nervous system and support tissues.

Lincoln University (\$19,364) - 1 Project

Grant Award Period: 02/01/03 - 12/31/03

Contact:

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Research Project:

- *Study of Co-morbidity and Co-mortality of Sickle Cell Disease and Tuberculosis Among African Americans* - The purpose of this investigation is two-fold, to assess to what extent, if any, sickle cell disease (HbSS) directly influences one's risk of acquiring tuberculosis and how sickle cell disease affects the morbidity and mortality due to tuberculosis infection.

MPC Corporation (\$266,553) - 2 Projects

Grant Award Period: 01/01/03 - 12/31/04

Contact:

James V. Maher, Ph.D.
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Research Projects:

- *Brain Imaging Research Initiative* - This initiative will use powerful new brain imaging techniques to uncover and analyze critical information about the relationship between brain function and cognition. The research will be performed through the Brain Imaging Research Center (BIRC), a joint initiative between Carnegie Mellon University and the University of Pittsburgh.
- *NMR Research Initiative* - This research initiative will seek to advance the state-of-the-art in 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. The research will be conducted by scientists working in the Pittsburgh NMR Center for Biomedical Research (NMR Center).

Madlyn and Leonard Abramson Center for Jewish Life (\$41,864) - 1 Project

Grant Award Period: 01/01/03 - 01/31/04

Contact:

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Madlyn and Leonard Abramson Center for Jewish Life
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Research Project:

- *The Impact of Nurse Call Technology on Resident Functioning over Time in the Nursing Home* - The purpose of this research project is to determine whether new passive nurse call technology impacts on the quality of care and quality of life of nursing home residents with dementia over time. This project will extend a current pilot project in order to examine the impact of this technology on residents, staff, and operations in a nursing home environment at six-month follow-up.

Magee-Womens Health Corporation (\$681,269) - 1 Project

Grant Award Period: 01/01/03 - 12/31/04

Contact:

Robert G. France, M.H.A., M.B.A.

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Magee-Womens Health Corporation
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Research Project:

- *Transgenic Non-Human Primate Models of Breast Cancer Imaged Dynamically by microPET using Gene and Cell Infusion via Ductal Lavage* - This project has two main objectives, the development of a breast cancer model in the old-world monkey displaying similar characteristics to human tumors and the evaluation of the breast cancer screening tool ductal lavage. In addition, the use of non-invasive *in vivo* imaging during breast tumor development will further our understanding of this disease, which claims 40,000 Americans each year.

Medical Diagnostic Research Foundation (\$57,612) - 1 Project

Grant Award Period: 01/01/03 - 12/31/03

Contact:

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Research Project:

- *Early Detection of Breast Cancer in Underserved Populations* - The purpose of this project is to achieve a higher rate of patient consent and breast cancer examination.

Monell Chemical Senses Center (\$312,634) - 3 Projects

Grant Award Period: 01/01/03 - 12/31/03

Contact:

Gary K. Beauchamp, Ph.D.
Director and President
Monell Chemical Senses Center
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Research Projects:

- *Early Learning about the Sensory Properties of Tobacco* - The purpose of this project is to determine the impact of early sensory experiences with tobacco smoke in the home on young children's preferences for the odor of tobacco. This 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.
- *Aging, Sensory Change and Dehydration* - Our population is aging rapidly. Elderly individuals are at increased risk of dehydration in large part because they fail to feel thirsty. One way to prevent dehydration in older individuals is to provide them with beverages that they like to drink. In order to do this, we have to understand their sensory world. We already know that there are significant declines in two of the senses that contribute to sensation of flavor, taste and smell. However, nothing is known about aging and mouthfeel (texture, carbonation, spices). The purpose of this project is to gain a better understanding of beverage perception by the elderly

(especially mouthfeel) in order to design more palatable and nutritionally beneficial beverages that can promote better fluid balance.

- *Strain Survey of Mice Bone Density* - The purpose of this project is to conduct a survey of bone density in 40 mouse strains. This will help find genes involved in the control of calcium metabolism, osteoporosis and other bone diseases.

National Disease Research Interchange (\$80,999) - 1 Project

Grant Award Period: 01/01/03 - 12/31/03

Contact:

John Lonsdale, Ph.D.
Research Director
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Eight Penn Center, 8th Floor Philadelphia, PA 19103
(800) 345-4234 extension 271

Research Project:

- *Confirmation of Genetic Contribution and Stratification by Phenotype* - This study is designed to test the hypothesis that the age of onset and the severity of retinopathy, as a complication of diabetes, have a genetic basis. This study will focus on data collection from two cohorts: 1) a subset of 500 families from the Type I diabetes database where cell lines and DNA are already available and whose updates data and medical records were not obtained in phase I of this project and 2) a new collection of 100 multiplex families with blood collection expected to begin in program year 2003. With the addition of a larger family cohort for the genetic study of retinopathy, the statistical significance and validity of the studies conclusions will be increased.

Oncology Nursing Society (\$28,676) - 1 Project

Grant Award Period: 01/01/03 - 12/31/04

Contact:

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Research Project:

- *Impact of Nurse Staffing and Organizational Factors on Outcomes of Hospitalized Oncology Patients* - This study will determine the contribution of both nursing and organizational characteristics of hospitals associated with quality cancer care on outcomes for hospitalized adults with cancer.

Pennsylvania College of Optometry (\$47,559) - 1 Project

Grant Award Period: 01/01/03 - 04/30/04

Contact:

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Research Project:

- *Molecular Mechanisms Related to Cone and Rod Degeneration* - The purpose of this project is to understand how mutations that change activity of specific retinal enzymes can result in loss of vision and blindness by causing the death of light-sensitive retinal neurons.

Pennsylvania State University (\$9,286,165) - 25 Projects

Grant Award Period: 01/01/03 - 12/31/06

Contact:

Eva J. Pell, Ph.D.
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 The Pennsylvania State University
 110 Technology Center
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 (814) 863-9580

Research Projects:

- *Evaluation of a Transgenic Mouse Model of Cardiovascular Toxicity* - The overall aims of the project are: (a) to more fully characterize the cardiovascular effects associated with the overproduction of polyamines using a model in which transgenic mice were produced that had elevated levels of polyamines due to overexpression of ODC; and (b) to relate this model to human cardiovascular disease.
- *Research Center for Echocardiography in Small Animals* - The project was designed to establish a dedicated research echocardiographic laboratory devoted to study of cardiovascular function in small animals. Echocardiography is a technique that uses sound waves to non-invasively image the heart in animals that are either awake or slightly sedated. This was required to expand our research capabilities, enhance our infrastructure and develop cross-discipline programs involving cardiovascular research within the College of Medicine.
- *Muscle Interstitial ATP and Exercise in Congestive Heart Failure* - Blood pressure and heart rate are increased during exercise. These responses are termed the Exercise Pressor Reflex (EPR). In patients with congestive heart failure (CHF) the exaggerated cardiovascular responses to exercise are observed and the responses are partly mediated by an overactive EPR. However, neural mechanisms that mediate these cardiovascular responses are unclear. In this project we will measure ATP concentration in the muscle interstitium with the microdialysis method in rats with CHF. We will further examine the role played by ATP in the EPR in CHF rats.
- *GCRC Sleep Infrastructure* - The purpose of this project is to establish the clinical impact of sleep-disordered breathing in children and to establish a general sleep infrastructure within the General Clinical Research Center (GCRC).
- *MD Research Facilitation Awards (MDRFA)* - These awards are designed to encourage and enhance the productivity of outstanding physician faculty in clinical departments who have already demonstrated success in obtaining peer reviewed funding. This program is targeted towards faculty who commit to at least 40% of their time to the conduct of investigator-initiated, hypothesis driven, biomedical research.
- *Generation and Utilization of Genetic Animal Models for Biomedical Research Focused on Molecular Mechanisms of Altered Gene Expression Associated with Diabetes and Other Health Related Problems* – The purpose of this project is to generate and utilize research animal models in which one of the four genes involved in regulating a common signaling pathway that contributes to a number of disease states is disrupted, either individually or in various combinations.
- *Research Center for the Study of Type 2 Diabetes and Obesity* - The purpose of this grant is to engage new researchers and promote research on type 2 diabetes and obesity. To help promote the study of obesity, samples of tissues and cells are being

banked from obese patients before and after a weight loss intervention that causes very large weight losses and reverses type 2 diabetes in morbidly obese patients. These samples and special assays are being provided to scientists who may wish to begin to help cure this disease through research. We are also providing special genetically obese animals called Zucker rats to scientists.

- *Urinary Tract Infections and Cancers: Involvement of Meprin Metalloproteases* - The purpose of this project is to test the hypothesis that decreased urinary levels of meprins are associated with recurrent urinary tract infections (UTIs). In addition, the levels of meprins in kidney cancers will be determined, as meprins have been found to be elevated in some forms of cancer.
- *Role of the SV40 and JC Virus Oncogenes in Development and Immunomodulation of Human Cancer* - The purpose of the work is to define the mechanisms involved in induction and progression of human tumors associated with the viruses SV40 & JCV, how the viruses spread in the population, and to provide a basis of knowledge that can be brought to bear to develop strategies for immunomodulation of cancer progression.
- *Advance Care Planning for Cancer Patients via Interactive Computer* - The purpose of this project is to develop, refine, and evaluate among cancer patients a computer-based decision aid for advance care planning.
- *Molecular and Cellular Changes that Drive Liver Cancer* - The ultimate goal will be to define biomarkers for human liver disease that may also be biomarkers for early stages of liver cancer.
- *Tobacco-Genetic Interactions and Cancer Induction* – The purpose of this project is to better establish the significance of specific metabolizing enzyme pathways in tobacco-related cancer induction, to identify important targets for chemoprevention strategies, and to identify markers of cancer risk.
- *Population-Based Early Detection and Care of Cancer by the Penn State Cancer Institute (PSCI)* - The purpose is to initiate and conduct research that increases the utilization, availability, and quality of cancer screening and care in the geographic area of PSCI.
- *Manipulation of Signaling Pathways for the Treatment of Breast Cancer* - Breast cancer is the most common form of malignancy among women in the United States, and is now understood to be driven by abnormal processes that regulate cell growth and death. This project will integrate the efforts of several laboratories at Penn State, focusing on understanding these abnormal signaling pathways in breast cancer cells. This will allow the identification of new compounds that may be useful for the treatment of this disease.
- *Collection of Blood, Tissue and Phenotypic Data for Characterization of Molecular Pathways in Cancer* – The purpose of this project is to collect data, sera and tissues to establish a tumor bank. The mechanisms of disease, especially cancers, are being elucidated at the molecular and genetic levels, yet the detection of protein and genetic markers as diagnostic or treatment tools is in its infancy. Further advances require the availability of a library of specimens and information from actual patients that allows a characterization or "fingerprint" of the tumor and its genes to accurately predict prognosis and treatment response. With such a fingerprint, treatment can be targeted directly to specific markers or pathways for greater efficacy and fewer adverse effects.
- *A Multifaceted Approach to Mechanisms of Transcytosis in a Blood-Brain-Barrier Model* - The long-term goal of this line of research is to understand the dynamics of nutrient acquisition by the brain and apply this knowledge to the maladaptions that may contribute to neurological disease. During the period that we are working to achieve this goal, we will provide a database and model for development of

therapeutic strategies to utilize the endogenous nutrient transport system for intervention in CNS disease and injury. The question driving this project is: What is the set of acquisition signals that mediate brain nutrient uptake and where do they act?

- *Macrophage and Microglia Cell Dysfunction in Central Nervous System Diseases* - The project will examine M-phi/microglia cell dysfunction in the context of H/I and AIDS-associated dementia at the level of basic biochemical and cellular processes with the goal of applying these findings to the clinical setting.
- *Consortium on Nutritional Neuroscience* - The explicit aim of this consortium will be to enhance and expand our collaborative research efforts to become a leader in a newly developing area, Nutritional Neuroscience and to develop a graduate and postdoctoral training program unique in the United States.
- *Interleukin-1 Receptor 1 Deletion Confers Protection from Ischemic Brain Damage* - The purpose of this project is to examine the hypothesis that inactivating the inflammatory cytokine interleukin-1 (IL-1) would decrease the extent of damage caused by a hypoxic-ischemic insult.
- *Endo-Alpha-Galactosaminidases that Degrade the Malignancy-Associated Mucins* - The objective of this project is to identify and characterize endoglycosidase activities that can specifically release the Ser/Thr-linked oligosaccharides of from mucins and specifically mucin glycoproteins, which are associated with cancer.
- *A Mouse Model That Mirrors Human Melanoma Development* - We propose to examine tumors obtained from cancer patients in conjunction with our experimental melanoma tumor model to determine the biological significance of the genomic and proteomic changes occurring during melanoma tumor development.
- *Ricin Poisoning: Sensing, Blockade, and Immune Response* - The purpose of this project is to 1) identify cell surface saccharides to which ricin binds with high affinity and to apply that information to the development of binding antagonists; 2) characterize the humoral immune response induce by ricin toxoid in order to develop high affinity antibodies for biosensors; and 3) develop a stable, sensitive ricin magnetoelastic sensor for use in the laboratory, biocontainment facility, or in the field.
- *Biomaterials Center* - The purpose of the funding is to nucleate a Biomaterials Center focused on contemporary issues in the application of materials in human healthcare, servicing needs of next-generation medical devices by using modern approaches to materials development based on fundamental principles of biocompatibility.
- *Transgenic Mouse and Animal Research Infrastructure Facility Expansion* - This is a construction project that will provide additional space to conduct fundamental biomedical research involving animals, especially transgenic and knockout mice in order to provide the foundation for the development of molecular interventions for the prevention and treatment of human diseases.
- *General Clinical Research Center Infrastructure Expansion Project* - This construction project will provide the space needed for existing and new investigators to conduct expanded clinical research studies involving direct interaction with diverse patients and study participants.

Philadelphia College of Osteopathic Medicine (\$16,087) - 1 Project

Grant Award Period: 01/01/03 - 02/28/04

Contact:

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Philadelphia College of Osteopathic Medicine
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Research Project:

- *Multidisciplinary Treatment of Primary Care Patients with Chronic Illness Comorbid with Mental Health Disorders* - The purpose of this project is (1) to assess the efficacy of a multidisciplinary treatment program designed to assess, diagnose and treat urban primary care patients who have both chronic illness and mental health concerns; and (2) to promote collaboration among and enhance training programs for medical students in a Family Medicine clerkship and doctoral psychology interns, functioning under appropriate supervision, as part of the multidisciplinary treatment team for identified patients.

Philadelphia FIGHT (\$66,088) - 1 Project

Grant Award Period: 01/01/03 - 12/31/03

Contact:

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Research Project:

- *Structured Treatment Interruption Rollover Study* - The goal of this rollover study is to expand our data collection on the immunologic and virologic consequences as well as the safety of sequential treatment interruptions (STIs) in chronically infected HIV-1 infected persons.

Temple University (\$2,905,794) - 32 Projects

Grant Award Period: 01/01/03 - 12/31/06

Contact:

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Philadelphia, PA 19122
(215) 204-7467

Research Projects:

- *Extending and Evaluating a Multimedia System for Prostate Cancer* - The focus of project is the development and preliminary evaluation of a computer-based multimedia intelligent expert system, designed to inform patients diagnosed with early stage prostate cancer about the disease, their treatment options, and about potential treatment consequences.
- *Regulation of Tumor Angiogenesis by Kininostatin (D5)* - We have discovered a new molecule derived from a plasma protein kininogen called kininostatin (D5) that can inhibit the formation of new blood vessels, which are required for growth and spread of tumor cells. This research project consists of four parts: The first is clinical, which tests whether D5 can serve as a tumor marker that will correlate with the tumor burden and results of therapy. The second is basic science, to determine if a lipid derived from platelets (sphingosine phosphate), which can stimulate vessel wall cells, is inhibited by D5. The third, a basic project, tests which tissue factor

complexed with clotting factor VIIa and Xa can stimulate endothelial cells through a receptor, PAR-2. The fourth is a core facility that will develop a three-dimensional system to study vessel formation *in vivo* which can be used in the other three projects.

- *Aging, Vascular Disease, Cell Death, & Cognition* - The major aim of this project is to investigate the effects of vascular disease on learning and memory in aging organisms and to test interventions such as exercise to improve function. Parallel studies will be carried out in animal models of vascular disease and human patients to investigate mechanisms causing impaired learning and memory due to this disease.
- *Design, Synthesis, and Evaluation of Subtype-Specific Ligands for Retinoic Acid Receptors* - Retinoids are compounds related to Vitamin A that regulate important biological processes including the growth and differentiation of normal and cancerous cells. Retinoids exert these effects by binding to different classes of receptors. The ability of retinoids to regulate cell growth has resulted in their use as drugs for treating skin disorders and cancers. However, available drugs suffer from serious side-effects that may be due to their ability to bind and activate different subtypes of retinoid receptors. We hypothesize that by using molecular modeling we can develop ligands that discriminate between subtypes. The proposed compounds may serve as tools for studies into the precise role of the receptor subtypes and/or as safer drugs for the treatment of certain cancers.
- *Racial Differences in Familial Susceptibility to Cigarette Smoking* - Chronic obstructive pulmonary disease (COPD) is a disease that causes breathing restriction and is mostly related to smoking. The prevalence of COPD is known to be different between blacks and whites but reasons for this difference are not clear. The purpose of this study is to investigate the susceptibility of blacks to smoking and compare it to whites. This study will allow us to characterize the pattern of breathing abnormalities in family members of black and white patients already diagnosed with COPD.
- *Development of Non-Viral Gene Delivery Systems for the Treatment of Metastatic Breast Cancer* - The major reason that breast cancer causes death is metastases. Conventional therapeutic methods have limited effect on the advance of disease. Systemic cancer gene therapy may provide a novel approach to kill primary and metastatic tumors. In previous studies, we have developed a synthetic gene delivery system by complexing the DNA with natural proteins. Although the results showed significant increase in *in vitro* gene expression, the use of whole proteins can increase *in vivo* immune response against the system. Therefore, the purpose of this study is to test new approaches to improve the safety and efficacy of the developed system. We believe that these approaches will significantly enhance the therapeutic efficacy of cancer gene therapy by enhancing gene delivery efficiency.
- *Regulation of Myeloid Differentiation Primary Response (MyD) Genes During Terminal Myeloid Differentiation* - The purpose of the research is to increase understanding of the regulation of myeloid cell differentiation. The proposed studies on NF-Y, a transcription factor shown by this laboratory to play a role in myeloid differentiation, include: (1) to ascertain how NF-Y is modified during the course of myeloid cell differentiation, and (2) to ascertain if binding of NF-Y to the JunB promoter is developmentally regulated when examined *in vivo*.
- *The Prevalence of Osteopenia and Osteoporosis in HIV-infected Women* - Osteopenia and osteoporosis have been documented in HIV-infected individuals. Most studies have primarily evaluated HIV-infected men, but there has not been a study conducted to determine the prevalence of osteopenia or osteoporosis in HIV-infected women. We plan to conduct such a study to evaluate the prevalence of osteopenia and osteoporosis in HIV-infected women and to identify factors associated with this

abnormality. This will help establish the need for bone density screening in this population.

- *U.S. China Tobacco Pilot Study* - The purpose of this study is 1) to gather research data on tobacco use in two divergent populations in two big cities in China, one that is heavily dependent on tobacco industry, another that is exposed to heavy tobacco producers, and 2) to use the data to strengthen the development of tobacco prevention and cessation programs designed for Chinese and other Asian populations in the U.S.
- *Vestibulo-Ocular Reflex (VOR) Adaptation and Cerebellar Protein Modification* - One of the pre-eminent features of the brain is the ability to make adaptive changes to its neuronal circuitry i.e., to repair or re-wire itself (neuroplasticity). These adaptations are essential for the brain to operate properly and compensate for deficits associated with age-, injury-, or disease-related dysfunction. The overall objective of the proposed research is to understand the nature of the changes that are produced in the area (cerebellum) of the central nervous system (CNS) responsible for these changes during this "re-wiring" process. Production of new proteins and/or structural changes in existing proteins may be the basis for these neuroplastic adaptations. In order to investigate this we will (1) produce a discrete and highly quantifiable behavioral sensori-motor adaptive change that is controlled by a specific region of the brain, the cerebellum, (2) characterize the protein changes that occur this brain area, and (3) use exogenous and endogenous pharmacological active substances to inhibit or enhance these adaptive changes in order to determine if there is a correlative and associated change within the cerebellum.
- *Does Obesity Alone, Independent of Diet, Affect the Growth of Prostate Cancer?* - There is evidence associating a high fat diet to prostate cancer. However, there is controversy over the effects of obesity on the progression of these tumors. We hypothesize that sera from obese rodents could promote tumor biology more than sera from lean rodents, possibly due to increased growth factor activity and/or decreased immune system activity. If this is demonstrated, in future studies we plan to analyze sera from obese and lean individuals as well as examine the effects of weight reduction in the inhibition of tumor growth.
- *Effect of HIV-1 Tat on Neuronal Cell Proliferation and Differentiation* - Among many different factors related to HIV-associated dementia (HAD), the transactivating factor of HIV-1 (Tat) is known to modulate gene expression in a variety of cell types by interacting with different host proteins. The tropomyosin-related kinase (Trk) receptors, which are the mediators of neuronal signaling in the Central Nervous System (CNS) and in PC12 cell model, appear to function in a variety of cellular events like survival, differentiation and apoptosis, as well as in repair functions and oncogenesis. In this project, we will study the interference of Tat with the NGF network in respect to growth and differentiation of neuronal cells.
- *Gene Expression Monitoring in Hematological Malignancies* - This research effort is focused on the mechanisms operating in cancer, trying to pinpoint the differences between normal and cancer cells at the molecular level and using this knowledge to plan novel and more effective anti-tumor therapies. The microarray technology will be applied to screen for the differences in expression of thousands of genes in normal and cancer cells.
- *Creatine Ingestion and Neuromuscular Function in Chronic Fatigue Syndrome (CFS)* This study that will determine the effects of creatine ingestion on neuromuscular function and symptom severity in persons with CFS compared to persons without CFS.
- *Effect of Respiratory Muscle Training with or without the Addition of Creatine on Diaphragm Strength, Fatigability, and Thickness* - This protocol will exam the potential effect of inspiratory muscle training coupled with creatine on respiratory

muscle strength and endurance. These interventions may have implications in clinical practice of patients with respiratory failure.

- *UBASH3A- A Negative Regulator of c-Cbl-mediated Degradation of Protein Tyrosine Kinases* - The activity of protein tyrosine kinases is required for normal cell growth, but if unregulated, may result in cancerous transformation. Therefore, this activity is tightly regulated by a complex system of protein regulators. c-Cbl is one of these regulators. In spite of the importance of these mechanisms for basic biomedical research and possible clinical implications, little is known about the regulation of c-Cbl. We recently discovered a protein that may act as a c-Cbl regulator. The proposed project is focused on determining the role of this protein, called UBASH3A, in the regulation of the effects of c-Cbl on protein tyrosine kinases.
- *Bioinformatics Approach to Protein Disorder Characterization* - Protein disorder is a very common and important, but insufficiently explored property of proteins. The goal of this project is to develop several novel bioinformatics algorithms and apply them to large biological databases in order to better understand the role and importance of protein disorder.
- *Novel Ways to Improve Evaluation and Treatment of Patients in an Urban Setting* - 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 developing novel ways to improve the evaluation and treatment of patients, including those from urban minority populations.
- *Weight and Metabolic Effects of an Almond-enriched Hypocaloric, Low-Fat Diet in Overweight and Obese Persons* - For this trial, we will assess the palatability, safety and efficacy of an almond enriched diet in achieving and maintaining weight loss. Additionally, we will measure whether it will favorably affect both established and emerging lipid and non-lipid cardiovascular risk factors while being both palatable and safe.
- *The Involvement of Mark Signaling Pathways in Detrimental Vascular Changes Following Stroke* - The purpose of this study is to investigate whether manipulation of a cell signaling pathways activated during stroke can help to improve blood flow to injured areas of the brain and minimize damage. If this can be accomplished damage to the brain that occurs following stroke could be attenuated.
- *Analysis of Bex, a GTPase that has a Pivotal Role in Growth of Bacillus Subtilis* - GTPases function as biological switches; members of the Era group are critical for bacterial growth. Bex of Bacillus subtilis is the only member of the Era group that is not essential for viability. Because Bex is not essential, a series of studies of the action of these key regulators can be attempted. They will improve our understanding of spore formation, and may lead to new types of antibiotics.
- *Analysis of the Expression Pattern and Binding Properties of Retinoic Acid Receptor Isoform Specific Proteins* - Retinoic acid, the active form of vitamin A, is necessary for growth and differentiation. Pharmacological doses of retinoic acid and synthetic related compounds called retinoids have been used in the treatment of various type of cancer and dermatological conditions. The actions of retinoic acid and retinoids are mediated by retinoic acid receptors. A detailed understanding of the mechanism of action of these receptors will aid in the development of more effective retinoid drugs with fewer side effects for the treatment of cancer and dermatological conditions.
- *The Role of Connective Tissue Growth Factor (CTGF) in Mediating the Effects of TGF- β_1 and BMP-2 on Osteoblast Proliferation and Differentiation* - Based on data generated by our laboratory, we hypothesize that CTGF is an anabolic bone growth factor. CTGF mRNA and protein levels are regulated by TGF- β_1 and BMP-2, two well

known local bone growth factors. The purpose of this study is to determine whether CTGF acts downstream of TGF- β_1 and/or BMP-2 to mediate their biological effects on osteoblast development and bone formation.

- *Mechanism(s) of Dihydrodiol Dehydrogenase Mediated Cisplatin Resistance* - Increased expression of Dihydrodiol dehydrogenase 1 (DDH1) has been demonstrated to induce cisplatin / carboplatin resistance in human ovarian carcinoma cells. This study aims to decipher the mechanism(s) via which DDH1 mediates this phenotype in various human ovarian cancer cells.
- *Studies on the Isoforms of the Prostaglandin EP3 Receptor* - Prostaglandins are chemicals produced by many cells in the body, and are involved in a diverse set of physiological processes, such as blood pressure regulation and generation of fever. They act by binding to proteins on cells, called receptors, to invoke a number signaling events. There are several types of receptor called EP1, EP2, EP3 and EP4 that are responsible for different actions. In addition, the EP3 receptor occurs as eight subtypes, called isoforms. The isoforms are located in different organs in the body and may influence them in different ways. The purpose of the study is to discover the function of the isoforms of the prostaglandin EP3 receptor.
- *P53-independent Activities of the MDM2 Onco-protein in CDK4 Mutant-induced Tumors*
The purpose of this project is to investigate pathways that control normal cell proliferation and how alterations in these pathways contribute to the abnormal proliferation of the cancer cell.
- *Study of Chemotactic/Chemokine Receptor Function Regulation and Its Impact on HIV Infection* - The purpose of this project is to develop information regarding the regulation of the function of Chemotactic/Chemokine receptors. It is anticipated that this will help researchers better define the mechanisms of the immune system response and how it applies to HIV infection in particular.
- *The Effect of Intracellular Sodium on Contractile Function in Failing and Non-Failing Cardiac Myocytes* - The purpose of this project is to advance the understanding of congestive heart failure (CHF) and the study of relatively non-invasive, inexpensive tests to study CHF "phenotype", allowing for development of more efficient, patient-specific treatments.
- *The Electron Transfer Pathway in DNA Photolyase: A Stark Spectroscopic Study* - The purpose of this project is to examine the role of electron transfer in DNA photolyase, an enzyme that repairs UV-damaged DNA via a light-driven electron transfer reaction.
- *Effects in Humans of Withdrawal from Opioids on Immune Status and HIV Burden* - This project seeks to test the hypothesis that withdrawal from opioids in addicts will result in immunosuppression in humans or alterations in HIV load. This question is particularly significant given the strong association between intravenous drug abuse and HIV infection.
- *A 24-Week, Double-Blind, Randomized, Placebo-Controlled, Multicenter Study to Assess the Safety and Efficacy of MK-0677 for the Treatment of Sarcopenia in Patients Recovering From Hip Fracture* - The primary purpose of this project is to demonstrate an improvement in overall physical functional performance (as measured by the Continuous Scale Physical Functional Performance 10-item test), in patients who have recently experienced a hip fracture, following administration of MK-0677 25-mg once daily for 24 weeks relative to placebo.
- *A Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, Tolerability, and Pharmacokinetics of CP-533,536 in Subjects with Closed Fracture of the Tibial Shaft* - This project will assess the efficacy of a single dose of CP-533,536 (administered in a Poly-Lactide-Co-Glycolide (PLGH) matrix) in subjects

with a closed fracture of the tibial shaft using radiographic measurements, compared to PLGH matrix treatment and examine the hypothesis of a > 25% reduction in median healing time.

Thomas Jefferson University (\$6,229,638) - 10 Projects

Grant Award Period: 01/01/03 - 12/31/06

Contact:

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Research Projects:

- *Adenosine-Induced Cardioprotection is Mitigated by Selective Activation of Adenosine Receptor Subtypes* - Despite the potential clinical utility of adenosine infusion as a therapeutic modality for cardioprotection, the biology underlying adenosine-induced signaling within the heart remains undefined. Therefore, the objective of this project is to define the cellular biology of adenosine signaling within the heart. Data derived from these studies will enhance the clinical utility of adenosine infusion by elucidating the specific receptor subtypes and intracellular signal pathways that mitigate adenosine-induced cardioprotection.
- *Role of Akt Survival Pathway in the Mouse Heart* - The PI3K/Akt signaling pathway has been established as an important mediator of cardiac growth and survival. Thus, increasing the activity of this pathway may enhance heart protection from cardiotoxic conditions and agents. The purpose of this proposal is to generate mouse models with increasing or decreasing activities of the PI3K/Akt pathway. Such models will help to understand the role of this pathway during heart failure and will lead to new therapeutics in heart disease management.
- *Population-based Pharmacogenomics* - The purpose of this project is to develop an infrastructure for addressing genomics at a level of sophistication that would not be otherwise possible for any single laboratory and to create novel diagnostic and therapeutic opportunities by taking advantage of the full sequence of the human genome.
- *In Vivo Imaging of Autoreactive Cells in the Central Nervous System* - Experimental autoimmune encephalomyelitis (EAE) is an animal model of multiple sclerosis. The disease results from myelin damage in the Central Nervous System, i.e., brain and spinal cord, and is initiated by cells of the immune system (lymphocytes). These studies will apply high-resolution imaging techniques in an animal model of autoimmune CNS disease to provide non-invasive means of visualizing the normal and deleterious immune responses that occur during healthy and autoimmune states.
- *Ontogeny of Neuroadaptive Responses to Methylphenidate* - Children of all ages are increasingly exposed to psychostimulants, including therapeutic use of methylphenidate (Ritalin). This project is aimed at examining the molecular response of the immature brain to this drug, to help determine appropriate dosing, therapeutic targets, and possible long-term effects.
- *Animal Models of Headache and Neuroinflammatory Pain* - The purpose of this project is to study the chemical changes in the brain during a migraine attack. A neurochemical assay of the pain areas in the brain that respond to head pain will reveal the change in extracellular concentrations of neurotransmitters such as

glutamate, GABA, 5HT and NE and would assess the involvement of each in this pain disorder.

- *Role of WWOX Gene in Tumor Progression through a Proteomics Approach* - The purpose of the research is to establish a profile of protein expression and post-translational modifications modulated by WWOX suppression.
- *Application of DNA Microarray in Cancer Research* - The purpose of this research is to develop and apply high throughput microarray technologies to problems in cancer research. The project will be conducted at the Microarray Core Facility, Kimmel Cancer Center (KCC), a core facility supporting research projects in the Center and local community.
- *Enhancement of Pathology Core Facility* - The Pathology Core Facility of the Kimmel Cancer Center is a core facility supporting research projects in the Center and the local community. The purpose of this proposal is to expand the capabilities of the facility to support the histological needs of the research community.
- *Genetic Modifiers of Colorectal Tumorigenesis* - "Modifier" genes are genes that influence an individual's risk of developing cancer. Our experiments are designed to reveal the relationship between the effects of "modifier" genes and the development of colorectal tumors. These studies will define the role of "modifier" genes in human cancer, their predictive value in treatment outcome, and their potential use as preventive agents.

Treatment Research Institute (\$62,697) - 1 Project

Grant Award Period: 01/01/03 - 12/31/03

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Research Project:

- *Improving Access to Health Care and Social Services for Offenders through the Philadelphia Community Court* - This is a preliminary evaluation of the health care and social services provided to indigent offenders through the Philadelphia Community Court, an innovative problem-solving court designed to provide comprehensive treatment services to offenders in lieu of criminal prosecution or incarceration. This evaluation will assist the Community Court in increasing the availability, provision, and utilization of health care and social services among a population that may otherwise not receive such services. We will also develop an infrastructure for ongoing performance monitoring and establish a framework for conducting future randomized controlled trials.

University of Pennsylvania (\$10,924,900) - 26 Projects

Grant Award Period: 01/01/03 - 12/31/06

Contact:

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Research Projects:

- *Bio-behavioral Effects of Bupropion* - The goal of this behavioral pharmacology study is to increase our understanding of the bio-behavioral mechanisms by which bupropion, a non-nicotine medication, promotes smoking abstinence.
- *Use of Internet-Based Cancer Prevention and Treatment Information by Socioeconomically Disadvantaged Commonwealth Residents* - The purpose of this project is to assess the use of OncoLink by socioeconomically disadvantaged residents of the Commonwealth, with the goal of increasing access to accurate and timely cancer prevention and treatment information and, ultimately, decreasing cancer rates by emphasizing prevention and screening and helping residents enroll in the latest clinical trials.
- *Clinical Cell and Vaccine Production Facility: A Research Infrastructure Project* - The purpose of this project is 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.
- *Peptide/MHC Tetramers to Evaluate Anti-Cancer T Lymphocyte Responses* - The purpose of this project is to fund research that will build upon our technology platform of "tetramers" to enable state-of-the-art, real-time immunological evaluation of patients treated with novel anti-tumor immunotherapy. The ultimate goal is to establish a simple blood test suitable for rapid monitoring of patients' immune systems.
- *Molecular Epidemiology of Prostate Cancer* - The purpose of this project is to evaluate racial differences in candidate androgen metabolism genes, and to evaluate the relationship of these genes with prostate cancer incidence and outcome by race, with the ultimate goal of lessening health disparities related to prostate cancer.
- *Proteomics Research Initiative* - The purpose of this project is to advance biomedical and clinical cancer research at the University of Pennsylvania Cancer Center by establishing a central proteomics resource to enable scientists to identify and understand how proteins in a cell function together, during normal (healthy) conditions and during pathogenesis, when disease is developing.
- *Immune Responses in Patients with Cancer and Neurologic Disease* - The purpose of this project is to improve understanding of immune system response to cancer by studying immune reactions that occur in a group of cancer patients whose immune systems recognize and effectively fight developing cancers with the ultimate goal of informing the development of immunological cancer therapeutics.
- *Genomic Approach to Genetics of Common Disease* - The purpose of this project is to advance knowledge about genetic susceptibility to common diseases by bringing to bear the techniques and findings of genomics, including proteomics and functional genomics.
- *A Study of the Effect of Informed Consent Standardization and Automation on the Quality of Research Subject Informed Consent Construction* - The purpose of the study is to assess the effect of standardizing and automating the informed consent process on the quality of research subject informed consent.
- *Construction of Life Sciences Building (Phase I) Research Infrastructure* - 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.

- *Vivarium – Modular – Research Infrastructure* - 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.
- *Renovation of Space for University Laboratory Animal Resource: An Infrastructure Project* - The renovation is needed to provide improvements in the facilities for laboratory animal resources that are used to conduct Penn's extensive biomedical research program with laboratory animals. Space in the School of Veterinary Medicine will be renovated to become the new home to University Laboratory Animal Resources (ULAR), which operates Penn's animal research facility. Functions of this facility include but are not limited to: designing research studies that use laboratory animals; training researchers in the proper use of laboratory animals in all aspects of research; ensuring compliance with all federal and state regulations concerning the conduct of animal research; overseeing the conduct of all aspects of laboratory animal research; monitoring the health of the laboratory research animals; observing and recording experimental data.
- *Interaction of Toxoplasma gondii with Host Cell Signaling* - This is a multi-disciplinary project to understand how the parasite *Toxoplasma gondii*, a Category B agent of bio-terrorism, subverts host cell signaling, and to determine the consequences necessary for parasite survival. The primary focus of this study will be to examine the effects of *Toxoplasma* on the host defense system immune response through the analysis of a protein that regulates gene expression, termed NF- κ B.
- *Development of a Subunit Vaccine against Smallpox (Variola) Virus* - The purpose of this research is to develop a safer and more effective vaccine against smallpox. The current vaccine has an existing morbidity and mortality in human recipients that is unacceptable under standard conditions, although it might be appropriate under acute exposure and bio-terrorist threats.
- *Cell Biology and Antigenic Structure of West Nile Virus* - West Nile Virus (WNV) is a rapidly emerging viral disease with a very real potential to become a significant human and veterinary pathogen. Relatively little is known about the biology of WNV, few neutralizing antibodies have been described, and next to nothing is known about its immune structure. The purpose of the research will be two fold; first, to produce a preliminary vaccine used for the development of immunity; and second, to identify the cellular receptor that is essential for binding of WNV and infection of human cells.
- *Molecular Profiling of Immunogenic Ovarian Carcinoma* - The purpose of this project is to disclose the molecular make-up of ovarian carcinoma with evidence of anti-tumor immune response and good prognosis using state-of-the-art high throughput oligonucleotide and comparative genomic hybridization microarrays.
- *Pilot Study of Valproic Acid in Patients with Myelodysplastic Syndrome* - The purpose of this project is to determine whether Valproic Acid (VPA), a drug used to treat seizures, can be used to treat patients with Myelodysplasia (MDS), a bone marrow disorder which results in abnormal blood counts, by performing a clinical trial to investigate: (1) whether there is evidence of response to disease (2) the effects of VPA on the cells of patients with MDS and (3) whether there are studies that can be done on the cells of patients with MDS to help us learn more about the disease, its origins and its diagnosis.
- *Genetic and Biochemical Analysis of BRAF-AKT Interaction in Lung Cancer* - The purpose of this project is to increase understanding of BRAF gene mutations found in metastatic lung tumors and examine the biological effects of these BRAF mutations to determine whether the loss of BRAF regulation by the protein AKT likely contributes to the development of lung cancer, with an ultimate goal of contributing to the creation of targeted therapies for lung cancer.
- *Effects of Bupropion on Reinforcement of Nicotine* - The purpose of this project is to measure the metabolism and effects of bupropion on nicotine self-administration in

non-treatment seeking smokers using a transdisciplinary and translational research approach (behavioral pharmacology) with the ultimate goal of improving understanding of how bupropion helps people stop smoking and whether it might be useful in combination with nicotine nasal spray.

- *Development of mTOR Inhibitors for the Treatment of Acute Leukemia* – The purpose of this project is to conduct clinical trials to determine if rapamycins, a group of compounds that inhibit mTOR signaling proteins, are a safe and effective for the treatment of leukemia.
- *Role of EBV, HPV, and MHC Class 1 in Head and Neck Cancer* – The purpose of this project is to determine if two known tumor viruses can co-infect epithelial cells of the head and neck region and lead to the development of head and neck cancers. These two viruses were previously found in cancers of the head and neck. However, there are no studies investigating the co-operativity of these two viral agents in development of human cancers.
- *Nicotine, Oxidant Stress and Atherogenesis* - The purpose of this project is to determine the role of inflammation and oxidant stress in mediating the effects of nicotine on the vasculature.
- *Understanding Genes that Control Stem Cell Growth and Development* - This research project seeks to understand how adult (non-embryonic) stem cells grow and mature into different types of mature cells, including blood cells, liver cells, and muscle cells. In particular, we have recently identified a gene, called NF-Y, that appears to control stem cell expansion, and whose disappearance results in the production of mature blood cells. We propose to study how this gene is turned on and off by stem cells, and to explore which genes are regulated by NF-Y.
- *Tissue Bank to Support Cancer Research: A Research Infrastructure Project* - – The purpose of this project is to renovate space within the University of Pennsylvania Health System to house the Cancer Center’s tumor tissue bank that is required to support leading edge cancer research.
- *Pathways-Based Regression and Association Models for Integrative Analysis of Cancer Genomic Data* - New high-throughput technologies are generating various types of high-dimensional genetic, genomic and proteomic data in order to obtain a systems-level understanding of cancer. One great challenge is how to model such data in order to draw valid statistical and biological conclusions. The central goal of this project is to develop novel pathways-based regression and association models for integrative analysis of cancer genomics data, including methods for relating these high-dimensional genomic data to various clinical phenotypes and for constructing genetic association networks.
- *Assessment of the Feasibility of Implementing a Standardized Clinical Database Environment across a Variety of Clinical Research Projects* - This research project will assess the feasibility of defining institution-wide core data standards and applying those standards across a variety of research departments and project types through a standardized information technology infrastructure for clinical research databasing.

University of Pittsburgh (\$10,924,900) - 9 Projects

Grant Award Period: 01/01/03 - 12/31/06

Contact:

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Research Projects:

- *Bacteria/Environment Interactions in Lyme Disease - Borrelia burgdorferi*, the spirochete that causes Lyme disease, is maintained in an infectious cycle involving the transmission of the bacterium from an *Ixodes* tick to a mammalian host. The bacterium lives in the midgut of unfed ticks, and during transmission it encounters numerous alterations in environmental stimuli, including changes in pH and temperature. This study will examine protein turnover in *B. burgdorferi* for better understanding of how this bacterium can sense the environment and then alter transcription accessory proteins and gene regulation to compensate for the environmental changes.
- *Immunology and Human Disease* - The goals of this project are (1) to understand the basic biologic principles underlying immune defects that lead to important human diseases like autoimmunity, cancer, and AIDS, and (2) to design approaches for manipulating the immune system to prevent or treat these diseases. These same approaches are expected to contribute to better defenses against new emerging pathogens, like those used for bio-warfare.
- *The Zebrafish as a Model for Understanding Human Diseases* - The purposes of this project are (1) to study the genetic mutations that contribute to inheritable diseases of the kidney and gastrointestinal tract and (2) to develop and evaluate novel screening techniques to detect these mutations.
- *Interleukin-1 Receptor Signal Transduction* - This research project investigates the role of interleukin 1 (IL1) receptor signal transduction in protein-protein interactions. The IL1 receptor is critical in mediating inflammatory and immune responses and is therefore key in therapeutic design. The study will determine, through manipulations at the molecular level, the nature of IL1-dependent responses as well as the involvement of other compounds like the transcription factor NF- κ B.
- *Fundamental Aspects of Cancer Biology* - This basic research, to be conducted by the University of Pittsburgh Cancer Institute (UPCI), seeks to gain further understanding of the biological processes that underlie the initiation and development of cancer to provide knowledge that ultimately will facilitate the timely translation of the latest laboratory findings into clinical applications. These objectives will be accomplished through initiatives in immunology, molecular and cellular oncology, and molecular virology.
- *Translational Research on Cancer* - Translational research is critical to ensuring that laboratory findings about cancer biology are integrated into targeted therapeutic approaches for clinical application. This project includes a broad spectrum of investigations related to molecular therapeutics and drug discovery, angiogenesis, stem cell biology, and cancer imaging. These initiatives will significantly enhance the identification of new molecular targets, accelerate the development of targeted approaches to treating cancer and improving patient recovery after anticancer therapy, and advance the detection of cancer.
- *Cancer Control and Population Sciences* - This project will expand epidemiologic support for cancer programs, including those focused on melanoma, head and neck cancer, pancreatic cancer, and rare cancers. These initiatives emphasize biobehavioral, genetic, and environmental factors and their interactions in cancer development and progression. This work will seek to reduce Pennsylvania's cancer burden through research aimed at cancer prevention and control.
- *Integrative (Complementary and Alternative) Medicine* - The Integrative Medicine (Complementary and Alternative) Medicine project will improve the understanding of complementary and alternative medicine (CAM) applied to cancer patients by conducting preclinical and clinical studies of CAM to evaluate their effectiveness in

cancer care and by developing a comprehensive, credible resource for CAM-related information.

- *Research Infrastructure: Building Design and Construction Management of the Biomedical Science Tower #3 (BST#3)* - BST#3 is a new research building to be constructed at the University of Pittsburgh. The new structure will provide state-of-the-art research facilities to be used to explore the science that takes advantage of the discoveries of the human genome project. Key areas of study will be neuroscience, drug discovery, and aspects of wound healing and tissue engineering.

University of the Sciences in Philadelphia (\$9,779) - 1 Project

Grant Award Period: 01/01/03 - 12/31/04

Contact:

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Research Project:

- *Synthesis and Biophysical Characterization of RNA Segments from Brome Mosaic Virus Involved in Replication Complex Assembly* - The purpose of this study is to determine unique structural features of an important viral RNA replication element by analysis of several, partially overlapping RNA fragments of different sizes using biophysical and biochemical methods. From this, appropriate candidates will be selected for future high-resolution studies with nuclear magnetic resonance.

Weis Center for Research - Geisinger Clinic (\$183,198) - 1 Project

Grant Award Period: 01/01/03 - 12/31/04

Contact:

David J. Carey, Ph.D.
Director and Senior Scientist
Weis Center for Research - Geisinger Clinic
100 North Academy Avenue
Danville, PA 17822-2600
(570) 271-6659

Research Project:

- *Molecular Analysis of Cellular Growth* - The purpose of this study is to conduct basic biomedical research on the molecular mechanisms that regulate cell growth, using model systems that represent both normal and abnormal (malignant) growth. This information will provide new insights into these critical biological processes, and provide novel targets for therapeutic intervention.

Wills Eye Hospital (\$11,779) - 1 Project

Grant Award Period: 01/01/03 - 12/31/03

Contact:

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Research Project:

- *Detection of Retinoblastoma, the Most Common Malignant Eye Cancer in Children* - 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 (\$1,751,632) - 4 Projects**Grant Award Period:** 01/01/03 - 12/31/06**Contact:**

Russel E. Kaufman, M.D.
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Research Projects:

- *Molecular and Cellular Oncogenesis* - The goals of this project are guided by the basic tenet that proper spatio-temporal regulation of gene expression is fundamental to normal growth, development and cellular differentiation, and that defects in the basic mechanisms that regulate gene expression underlie all forms of cancer and govern both malignancy initiation and tumor progression. Thus, the goals of this project are to define at the molecular level these fundamental mechanisms of gene regulation that are targets for alteration during neoplastic cell growth. The ultimate outcome will be new and improved diagnostics and therapies for controlling and perhaps curing neoplastic disease.
- *Models of Neoplastic Disease* - The clinical application of basic biomedical research requires establishment of experimentally testable models of the disease process under investigation. This proposal is designed to establish both in vitro and in vivo (whole animal) models to evaluate the impact of new discoveries on tumor development and metastasis. These models will be used to study unregulated cell division, abnormal interactions of cells with their environment that lead to unregulated cell division and metastasis and ways to induce cell death (apoptosis) or senescence. Finally, funds are requested to bring in an additional investigator to establish new models of neoplastic disease in the mouse.
- *Systems Biology* - Prior to sequencing the human genome, most investigations were carried out in the context of single genes or proteins. However, this is much like listening to an orchestra one instrument at a time. The music can only be appreciated when all the parts are combined as one system. In much the same manner, the cell functions as a complex program of individual molecules whose final output must be appreciated in the context of the coordinated function of all the individual elements. The goal of Systems Biology is learn how the biological "symphony" is composed through an examination of the interaction of individual elements with the ultimate goal of understanding the modulations that lead to the disease process, thereby facilitating the design of more sophisticated diagnostic and therapeutic protocols.
- *Program for Vaccine Therapy* - This project has two major goals. One is to develop a new generation of vaccines that use non-replicating viral vectors to deliver immunogens of interest to the immune system to stimulate strong cellular and antibody-based immune responses against disease-causing agents, including small-pox and HIV. The second goal is to use this new technology to stimulate the

immune systems of cancer patients to arrest tumor growth and, perhaps, eliminate tumors.

2/26/2009