School of Medicine

Department of Pharmacology and Chemical Biology

Annual Report 2007-2008

General Description

During the 2007-2008 academic year, the Department of Pharmacology & Chemical Biology continued to grow its strengths in discovery and education related to the practice of pharmacology. Foremost, the department has evolved its name to include Chemical Biology. This evolution of our departmental name was intended to be more inclusive of modern pharmacology's use of basic chemical principles in developing an understanding of cell signaling events and the application of these insights in the creation of new therapeutic strategies.

This past year, we have successfully recruited prominent new departmental members, in the course of expanding the scope and strength of our research and educational missions in Pharmacology & Chemical Biology. We have made significant new advances in understanding fundamental mechanisms of cell and tissue communication, how these events impact on cell growth and function, and finally the creation of new drugs to control these processes. In recognition of our excellence in these pursuits, departmental members have been recognized with prestigious awards. Finally, in spite of challenging times, the concerted effort of both faculty and staff in making and communicating seminal research advancements has been rewarded by a 7% growth in extramural research support.

Of note, prestigious awards have been given to departmental faculty in recognition of their excellence in research and teaching. William deGroat, Ph.D. was the 2007 recipient of the Reeve-Irvine Research Medal, given annually by the Reeve-Irvine Research Center at the University of California to individuals who made recent critical contributions to promoting repair of the damaged spinal cord and recovery of function. Drs. John Lazo and Anthony Kanai were recipients of the 2008 American Society of Pharmacology and Experimental Therapeutics-Astellas Award in Translational Pharmacology. This award recognizes those individuals whose research has the potential to lead to the introduction of novel pharmacologic approaches or technologies that may offer significant advances in clinical medicine in the future. The Provost's Award for Excellence in Mentoring was presented to Donald DeFranco, Ph.D. Finally, Lori Birder, Ph.D. and Bruce Freeman, Ph.D. have been recognized with 10-year MERIT research grant awards from the NIH, in recognition of their past track records and future research objectives.

The teaching and research missions of the department both thrive and continue to evolve. Donald DeFranco, Ph.D., has been highly effective in his new position as Vice Chair for Education. We have continued to restructure and revise the Ph.D. Program in Molecular Pharmacology to be more responsive to student needs, rapidly-evolving training requirements and the challenge of spanning from chemistry to physiology in the practice of modern pharmacology. In this regard, the Molecular Pharmacology Graduate Program has refocused its areas of specialization to include signal transduction, and has placed more emphasis on cell and organ system pharmacology, cancer pharmacology and drug discovery. We are especially pleased with student reactions regarding the new integration of combined simulator- and animal-based "hands-on" training in organ physiology and pharmacology into our graduate curricula, with plans to further expand these endeavors in the upcoming year. Important contributions and leadership have also been lent in graduate education by Guillermo Romero, Ph.D., Associate Director of Graduate Education, and Daniel Altschuler, Ph.D., Co-Director of the Molecular Pharmacology course – in addition to our overall departmental faculty. The department has successfully deployed 7 students as Ph.D. graduates in the 07-08 year (Drs. Jenny Linnoila, David Werner, Dev Chandra, Robert Tomko, Alex Bank, Peter McDonald and John Caltagarone). Departmental faculty are particularly proud of the current quality of our outstanding Molecular Pharmacology Ph.D. and M.D./Ph.D. students who are contributing important new insight into fundamental cell signaling processes, drug action and drug discovery.

Jack Yalowich, Ph.D., one of the esteemed master educators and researchers in the Department of Pharmacology & Chemical Biology, has made important changes in our medical student educational missions as Director of Medical Education. In this capacity, Dr. Yalowich, with Dr. DeFranco, has dramatically improved the integration of pharmacology instruction into the organ-based, modular instructional approach currently given to Pitt medical students. With important advice and contributions from faculty colleagues, including Drs. Lazo and deGroat, we have devised a revised integrated Principles of Pharmacology core curriculum that provides our medical students with a stronger foundation of knowledge for their subsequent

organ-based modular medical education. Additionally, Dr. Yalowich has instituted and leads our faculty in the execution of multiple small group discussions focusing on clinically-relevant case studies in pharmacology. With constant attention to optimal teaching strategies and their evolution, we continue to strive to fulfill our mission to educate medical students and physicians in the conceptual basis for drug selection and administration.

Michael Palladino, Ph.D. again directed our highly-acclaimed American Society of Pharmacology and Experimental Therapeutics and NIH-funded summer undergraduate research program, which attracted some of the brightest young aspiring basic and physician-scientists from around the country. These students are exposed to challenging new laboratory skills, classroom experiences and an opportunity to interact with our internationally-renowned departmental investigators.

The stellar research environment that exists in the Department of Pharmacology & Chemical Biology is reflected by the high impact publications and abundant extramural support levels cited in this report. In order to grow and evolve this vibrant environment, new investments are being made in research tools utilized by departmental investigators. Dr. Ed Levitan has assumed leadership of the Department of Pharmacology & Chemical Biology's microscopy resources, and is integrating a unique upright confocal-multiphoton microscope into overall departmental and institutional microscopic imaging capabilities. This Olympus Fluoview 1000 features a spectral detector and can simultaneously scan with two lasers, a special asset for photobleaching and photoactivation experiments. The instrument is also equipped with a tunable titanium-sapphire multiphoton laser for imaging deep in tissue and exciting near-UV chromophores.

Dr. Thomas Conrads, who joined the department last year after directing the National Cancer Institute Proteomics Core Facility, has moved his laboratory to Magee-Women's Hospital to better house and expand departmental and institutional mass spectrometry resources. His well-equipped laboratory now houses two LTQ linear ion trap mass spectrometers equipped with electron transfer dissociation capabilities and an Orbitrap detector, three Quantum Ultra triple quadrupole mass spectrometers equipped with FAIMS (high Field Asymmetic waveform Ion Mobility gas phase ion separation capability), a Bruker Ultraflex MALDI-TOF/TOF, four nanoflow high-performance liquid chromatographs and a 20-node parallel virtual machine cluster. This, along with the 4 mass spectrometers in the Freeman laboratory, adds exciting new depth and potential to departmental and University of Pittsburgh basic and clinical investigation activities.

This year we are also enjoying the fruits of our ambitious faculty recruitment efforts, with new faculty members expanding the scope and excellence of departmental research and teaching capabilities. In this regard, we welcome:

Drs. Patrick Pagano and **Eugenia Cifuentes-Pagano** were previously at the Hypertension and Vascular Research Division of Henry Ford Hospital in Detroit. Patrick's research focuses on the modulatory role of the adventitia in vascular function and structure under both physiological and pathophysiological conditions. Eugenia works with Patrick and lends important depth into the cellular and molecular biological studies. Their labs are housed on the 7th floor of Biomedical Science Tower 3.

Sruti Shiva, Ph.D. was a L'Enfant Fellow at the Pulmonary and Vascular Medicine Branch of the National Heart, Lung and Blood Institute at NIH before joining our department. Prior to that she received superb graduate training from the Molecular and Cellular Pathology graduate program at the University of Alabama at Birmingham. Dr. Shiva's lab is also located in Biomedical Science Tower 3, where her work centers on the mechanisms by which nitric oxide regulate mitochondrial function. Dr. Shiva, Dr. Pagano and Dr. Cifuentes-Pagano are also members of the new Institute for Hemostasis and Vascular Biology, directed by another new Pitt/UPMC recruit, our new Chief of Pulmonary, Allergy and Critical Care Medicine, Mark Gladwin, M.D.

Bennett Van Houten, Ph.D. worked previously at the National Institute of Environmental Health Sciences at NIH where he was a Senior Investigator and the Branch Chief of the Division of Extramural Research and

Training. His current research focuses on molecular aspects of nucleotide and base excision repair in *E. coli*, yeast, *C elegans*, and mammalian cells. His laboratory is housed at the Hillman Cancer Center, where he is strategically positioned to assume leadership over UPCI research teams interested in DNA damage and repair, as our new Program Leader for the Molecular and Cellular Biology Program. In this capacity, Dr Van Houten will also be recruiting new faculty members to UPCI and, if positive synergy exists, also to our department.

Dr. Jean-Pierre Vilardaga was an Assistant Professor of Medicine at Harvard Medical School prior to his arrival in Pittsburgh. The Vilardaga laboratory, located in newly renovated space on the 13th floor of the Biomedical Science Tower, carries an interdisciplinary research program aimed at elucidating molecular mechanisms of signal transduction mediated by G-protein coupled receptors in renal, skeletal and other cell systems.

Drs. Rafael Radi and **Homero Rubbo** from the Universidad de la República in Montevideo, Uruguay, were given adjunct appointments in the department this past year. Dr. Radi, Professor and Chairman of the Department of Biochemistry, focuses his research on the biochemistry and metabolism of oxygen radicals and nitric oxide and the signal transducing and damaging actions produced by these species. Dr. Homero Rubbo, also a Professor in the Department of Biochemistry, directs a research group lending significant impact to understanding the biological properties of nitrated lipids and their roles in regulating inflammation.

Career development and strong mentorship for junior faculty are critical elements for nurturing a healthy future for the department. A new faculty mentoring process was instigated during the 07-08 year, whereby the Chair and senior faculty met with non-tenured and associate professor-level faculty to discuss and strategize how best to pursue career progression and key research objectives. Related to this, Alessandro Bisello, Yu Jiang and Lin Zhang were promoted to Associate Professor with tenure, in recognition of their excellence in key aspects of professional pursuit – teaching, service and research.

In summary, the practice of Pharmacology & Chemical Biology is unique among basic sciences, as it embraces a broad range of expertise to understand fundamental cell communication events, drug-target molecule reactions, and finally, the design, synthesis and therapeutic application of new drugs in patients. This latter effort requires strengths or critical collaborations in computational drug design, synthetic organic chemistry, biophysics, structural biology and organ physiology. Thus, Pharmacology & Chemical Biology maintains strong ties with a variety of basic science and clinical disciplines, while maintaining firm roots in fundamental elements of chemistry, cell and molecular biology, drug actions and drug metabolism. These precepts are exemplified by our premier educational and research missions that include the institution of new educational strategies, the creation of new centers of excellence, the recruitment of stellar new faculty and the scientific and teaching contributions of our dedicated faculty. We thus invite you to explore in more detail our 2007-2008 Annual Report and, if interested, to join us in fulfilling the departmental mission to excel in education, drug discovery and improved patient care.

Research and Other Scholarly Activities

Research Interests

Bruce A. Freeman Ph.D
Professor and Chair
Ph.D., University of California, Riverside

The basic investigation and clinical research activities of the Freeman Laboratory focus on the eukaryotic cell production, reactions and signal transduction properties of oxidizing and free radical inflammatory mediators (e.g., superoxide, hydrogen peroxide, nitric oxide (NO), peroxynitrite, nitrogen dioxide, oxidized/nitrated lipids). In particular, we are interested in the action of these reactive inflammatory byproduct as both cell signaling mediators under basal conditions and as pathogenic mediators of acute inflammation. Our observations regarding O_2 and NO-derived reactive species have revealed novel redox-dependent cell signaling events and new therapeutic strategies for treating acute/chronic inflammation, metabolic syndrome, type II diabetes, respiratory disorders and cardiovascular diseases.

We are presently investigating the pluripotent anti-inflammatory signaling actions of NO-derived, nitrated unsaturated fatty acids formed during enzymatic and autocatalytic lipid oxygenation. We now appreciate that nitrated fatty acid derivatives are abundant bioactive oxides of nitrogen in blood and tissues that rival levels of NO_2^-, nitrosothiols (RSNO) and nitrotyrosine derivatives. Nitrated fatty acids are robust PPAR ligands that exert potent receptor-dependent cell signaling and gene expression regulatory actions. Fatty acid nitro derivatives also serve as NO donors and react with nucleophilic targets in vivo, due to their electrophilic nature. Nitro fatty acid-protein adducts are clinically abundant, with this adduction reaction affecting protein structure, function and cellular distribution. In aggregate, nitrated fatty acids are a novel class of cell signaling mediators that represent a convergence of NO and oxygenated lipid redox signaling pathways.

In summary, our investigation of NO reactions with oxidant/free radical products of oxidases and peroxidases (e.g., xanthine oxidase, myeloperoxidase, cyclooxygenases, lipoxygenases) are revealing a) clinically-significant mechanisms of pathogenic NO scavenging that occurs during inflammation and b) novel byproducts that transduce NO-dependent signaling and modulate inflammatory injury in diverse disease processes.

Daniel Altschuler Ph.D
Associate Professor
Ph.D. (Biology), University of Buenos Aires, Argentina, 1989

Dr. Altschuler's laboratory studies mechanisms of signal transduction by the second messenger cAMP in cell proliferation. cAMP-dependent protein kinase (PKA) and Exchange protein activated by cAMP (Epac) represent the main effectors of cAMP action. Both pathways converge at the level of the small GTPase Rap1b, via its Epac-mediated activation and PKA-mediated phosphorylation. The role of Rap1 activation (Epac) and phosphorylation (PKA) coordinating the early rate-limiting events in cAMP-dependent cell proliferation are studied using a multidisciplinary approach including molecular and cellular biology techniques in vitro, as well as in vivo validation using transgenic/knock in technologies in endocrine tumor models.

Palaniappa Arjunan Ph.D.
Research Instructor
Ph.D., Indian Institute of Science, Bangalore, India

Dr. Arjunan determines the structure of macromolecules of biological interest, and then analyses structure-function relationships. He primarily uses X-ray crystallography to accomplish this. Dr. Arjunan's current research includes the high resolution three-dimensional structure determination of thiamin diphosphate(ThDP)-dependent enzymes, the yeast pyruvate decarboxylase (PDC) and pyruvate dehydrogenase multienzyme complex (PDHc) from Escherichia coli. The refined structure is then used to address long-standing issues regarding the structure and function of thiamin diphosphate-dependent enzymes. The structure determination

also includes the structure of PDHc E1 in complex with a covalently bound reaction intermediate analogue. Other interests are: a) the crystal structural analysis of native and mutant ThDP-dependent enzymes, either alone or in complexes with substrates, inhibitors, activators or with other related enzymes and b) development of techniques for the determination and analysis of macromolecular crystal structure.

Paul R. Baker, Ph.D.
Research Assistant Professor
Ph.D., Wake Forest University, NC, 2002

Dr. Baker's research interests are focused on understanding how cells communicate with one another during inflammation. Chemical messages called lipid signaling molecules act to initiate, propagate and resolve inflammatory responses. Dr. Baker is particularly interested in a new class of lipid signaling molecules called 'nitrated lipids'; these molecules mediate generally anti-inflammatory effects and may play an important role in the resolution of inflammation.

Dr. Baker's research has centered on a novel class of lipid mediators, nitrated fatty acids, which have distinct bioactivity from their non-nitrated counterparts. We have discovered that these signaling molecules are present clinically in a variety of vascular cells and plasma under basal conditions as well as clinical pathologies. The current hypothesis is that nitrated unsaturated fatty acids are formed by the "interplay" of nitric oxide and lipid oxidation/signaling reactions. In vitro, nitrated linoleic acid has been shown to regulate vessel relaxation by cGMP-dependent mechanisms and to modulate inflammatory responses including inhibiting neutrophil function and platelet activation via a mechanism involoving cAMP. His work has involved identifiying and quantifying nitrated lipid species in red blood cells and plasma and have found novel signaling actions that, in general, are anti-inflammatory. Specifically, he has found that nitrated linoleic and oleic acids (LNO_2 and $OA\text{-}NO_2$, respectively): a) up-regulate heme-oxygenase 1 protein expression; b) serve as a potent PPARα, δ and γ ligands that rival or exceed fibrates and thiazolidinediones in their ability to mediate PPAR activation; c) are strong electrophiles that covalently bind biological nucleophiles such as glutathione and protein histidine and cysteine residues, which has been shown to regulate protein functions including inihibition of cytokine release in LPS-stimulated inflammatory cells via adduction to the p65 unit of NF-κB; and d) prevent restenosis in animal models of vessel injury. These observations have broad implications in the clinical pathologies of atherosclerosis and diabetes. Furthermore, he has found that nitrated fatty acids can release nitric oxide during degradation, suggesting that allylic nitro derivatives may be a store of releasable nitric oxide.
Recent advances indicate that the diversity of endogenous nitrated lipids extends well beyond LNO2 and OA-NO2 to include nitrated fatty acids of varying chain length, multiple oxidized nitrated fatty acids (nitro-hydroxy and nitro-hydroperoxy adducts), complex lipids (e.g., nitrated cholesterol linoleate) and enzyme Co-A deriviatives. His primary interest is to elucidate the endogenous formation of these species to better understand the role(s) they play in inflammation and basal tissue homeostasis. Using mass spectrometry as a tool, He is currently engaged in structural identification of novel nitrated lipid species and studies to determine the mechanism(s) of their formation.

Dr. Alessandro Bisello
Assistant Professor
Laurea (Chemistry), University of Padova, Italy, 1992

G protein-coupled receptors (GPCRs) represent a major class of membrane-bound proteins that mediate a wide variety of biological functions, including sensitivity to light and odorants, endocrine and cardiovascular control, and neurotransmission. Because of their central role in many physiological processes, GPCRs represent one of the major targets for pharmacological intervention in a large number of pathologies.
The goal of our research program is the elucidation of the molecular mechanisms that determine activation, regulation and trafficking of GPCRs and their relevance to the (patho)physiology of peptide hormones.

These studies provide the opportunity to address key issues regarding the mode and specificity of actions of G protein-coupled receptors. Most importantly, these studies may provide the basis for the identification of novel therapeutic targets for the treatment of osteoporosis, diabetes and vasculopathies.
The general scientific theme in the laboratory is to define the role of accessory proteins (such as arrestins, caveolin, EBP50/NHERF1) in determining G protein-coupled receptor function. Our efforts focus on two specific areas:
1.) The signaling, trafficking and regulation of the parathyroid hormone type 1 and type 2 receptors (PTH1R and PTH2R) and their function in vascular smooth muscle cells, with particular emphasis on their role in mitogenesis. The cardiovascular tissue, and in particular vascular smooth muscle cells (VSMC), expresses and be exposed to the whole spectrum of parathyroid hormone ligand-receptor systems. VSMC express both the type 1 and type 2 parathyroid hormone receptors (PTH1R and PTH2R, respectively). Also, in addition to being exposed to circulating parathyroid hormone (PTH), they produce parathyroid hormone-related protein (PTHrP) and tuberoinfundibular peptide of 39 residues (TIP39). This complexity reflects the varied and distinct actions of these ligands and receptors in both pathophysiology and pharmacology of the cardiovascular system. The central hypothesis of this project is that signaling and regulation of the PTH receptors in VSMC, and consequently the tissue-specific responses, are determined by the expression and function of adaptor proteins.
2.) Cellular regulation of the glucagon-like peptide 1 (GLP-1R) receptor and its role in regulating beta cell function, proliferation and survival.One of the most promising therapeutic targets for the treatment of type 2 diabetes is the glucagon-like peptide 1 receptor (GLP-1R). The well documented ability of GLP-1R agonists, either GLP-1 itself or exendin-4, to stimulate glucose-dependent insulin secretion and increase beta cell proliferation and survival led to the approval of exendin-4 for the treatment of type 2 diabetes. Our studies show that the GLP-1R interacts with caveolin1 and this is necessary for the trafficking of the GLP-1R to the cell membrane and directs its localization to lipid rafts. The central hypothesis of this project is that the interaction between GLP-1R and caveolin1 and its localization in lipid rafts is a fundamental mechanism controlling both the insulinotropic and the proliferative actions of GLP-1 and exendin-4.

Alicia M. Celotto, Ph.D.
Research Instructor
Ph.D., University of Connecticut Health Center, CT (2002)

Dr. Celotto's interests are focused on studying the connection between energy production and neurological conditions, such as seizures, migraine and neurodegeneration. She has discovered mutations causing degeneration and reduced longevity that markedly reduce glycolysis or mitochondrial oxidative phosphorylation, neither of which results in a bioenergetic crisis. These results demonstrate that energy derived from different sources cannot fully compensate for such impairments suggesting certain essential processes are dependent upon specific sources of energy. It is believed that ATP produced through glycolysis is specifically generated at sites of high need in the neuromuscular system, for example the Na+/K+ pump, an important regulator of cellular ion homeostasis. Thus changes in the source of ATP production due to mutations affecting glycolysis or mitochondrial function may result in neurological disease by altering Na+/K+ activity. To study this, she uses Drosophila mutants affecting the glycolytic enzyme, triose phosphate isomerase (TPI), a component of the mitochondrial ATP synthase (ATP6) and the Na+/K+ pump (ATPalpha).

Thomas Conrads, Ph.D.
Visiting Associate Professor
Ph.D., Ohio State University

Armed with sequence information of the human and mouse genomes, a major aim of biological science is toward unraveling the underlying molecular events that lead to cellular function/dysfunction in disease with the goal of discovering better diagnostic markers and therapeutic targets. Proteomics aims to facilitate this process by applying newly developed methods and advanced analytical tools for the investigation of the protein complement and its repertoire of post-translational modifications en masse. Our efforts are, therefore, focused on development of new technologies that bridge the fields of chemistry and biology toward their application for

characterization of proteomic changes associated with pathophysiology, ascribing to the philosophy that effective biomedical investigation mandates creative multidisciplinary approaches. In practice, we utilize advanced mass spectrometry (MS) tools, molecular biology, and bioinformatics to conduct molecular investigations of human disease. In practiced our research has three major focus areas that include: 1) global profiling of protein and metabolite abundance changes, 2) global and targeted characterization of protein post-translational modifications, and 3) high-throughput assay development based on the use of selected reaction monitoring MS.

Donald DeFranco Ph.D
Professor & Vice Chair, Education
Ph.D., Yale University

The general goal of the neurodegeneration project is to understand the cellular changes that occur in nerve cells that are exposed to oxidative stress. In response to acute injury such as stroke or in many chronic neurodegenerative diseases such as Alzheimer's and Parkinson's disease, nerve cells are subjected to oxidative stress. Through a better understanding of the biochemical changes that occur in response to oxidative stress in nerve cells Dr. DeFranco hopes to identify molecules and pathways that could be targets for therapeutic intervention.

The DeFranco laboratory is also interested in prostate cancer and focuses on important components of the tumor microenvironment, (i.e. stromal cells) that provde the support necessary for cancer cells to survive and expand. The group has identified one molecular target in stromal cells that plays an important role in the communication between stromal cells and developing cancer cells in the prostate. The hope is to devise new strategies for limiting the contribution of the tumor microenvironment through detailed molecular studies of prostate stromal factors essential for cancer development and progression.

Finally, Dr. DeFranco examines the cell biology and clinical relevance of glucocorticoid signaling in various models. The basic mechanism of trafficking of the receptor for glucocorticoids (i.e. the glucocorticoid receptor) is examined using state-of-the-art fluorescence microscopy technology coupled with biochemical approaches. In addition, the impact of glucocorticoids on various tissues during development focusing on the brain in model studies in fetal mice and on white blood cells in critically ill children. Since glucocorticoids are a standard course of therapy for premature infants and critically ill children, we hope to provide insights into appropriate treatment strategies when glucocorticoids therapy is indicated.

W. Chet de Groat, Ph.D.
Professor
Ph.D., University of Pennsylvania Medical School

Dr. de Groat is interested in the autonomic nervous system and the neural regulation of pelvic visceral functions. Current studies focus on the reflex control of the urogenital tract and the mechanisms underlying transmission at central and peripheral autonomic synapses. These experiments are designed to examine (1) the neurotransmitters in the reflex pathways, (2) neuroplasticity during postnatal development or following neural injury, (3) the neural pathways responsible for the detection of visceral pain, and (4) the actions of drugs used to treat urogenital dysfunction. Experiments are conducted on a variety of preparations ranging from intact animals to isolated tissues, like spinal cord slices and dissociated neurons.

Julie Eiseman, Ph.D.
Research Associate Professor
Ph.D., Cornell University Medical College

Research in the Eiseman laboratory is directed at the preclinical evaluation of potential anti-cancer agents. Studies include the determination of the maximum tolerated dose, pharmacokinetics, pharmacodynamics and efficacy. The laboratory is also interested in non-invasively measuring compounds with absorbance spectra in the long visible range.
Specific studies include the pharmacokinetics and efficacy of the pyrimidine compounds, fluorodeoxycytidine (FdCyd) and gemcitabine (dFdCyd) in combination with a cytidine deaminase inhibitor, tetrahydrouridine in CD2F1 mice and SCID mice with human pancreatic cancer xenografts.
The pharmacokinetics and efficacy of tubulin interactive agents including docetaxel, paclitaxel and 6-epi-dictyostatin are also under investigation. Studies with docetaxel have examined the interaction with 9-nitrocamptothecin in an ovarian cancer xenograft (SK-OV3) and a physiological based pharmacokinetic model was developed to describe the disposition of docetaxel. This model will be evaluated for its usefulness in predicting patient docetaxel pharmacokinetics.
Dr. Eiseman is interested in understanding the mechanisms involved during photodynamic therapy with Pc 4 and other phototherapeutic agents and use elastic scattering spectrometry to measure changes in drug concentrations and hemoglobin saturation during and following photodynamic therapy. For these studies, we measure the concentrations of the drug and hemoglobin non-invasively as well as through destructive methods such as HPLC and LC/MS-MS.
Other agents investigated include a wide range of potential cancer chemotherapeutics including DB-67, CKD-602, 2,2-dimethylbutyrate, DA-3003-1, Zebularine, 17-allyl aminogeldanamycin and 17-dimethylamino-geldanamycin.

Melanie Flint, Ph.D.
Research Instructor
Ph.D., Imperial College, University of London, England

Dr. Flint researches hormonal influences on cell cycle regulation, targeted molecular therapies, drug metabolism, drug resistance and cancer. Her primary research project involves the direct interplay between stress hormones (cortisol, NE, and E), cancer and chemotherapy. This is accomplished through a mechanistic study of administration of stress hormones to cancerous cells, and observing these effects both in vitro and in rodent models. The goal is to identify predictive characteristics for molecular response, elucidating the mechanism of action of hormones in cancerous cells, and characterizing the genomic/proteomic profiles encoding cell cycle regulation.
Dr. Flint's primary research project involves the direct interplay between stress hormones (cortisol, NE, and E), cancer and chemotherapy. This is accomplished through a mechanistic study of administration of stress hormones to cancerous cells, and observing these effects both in vitro by proteomics and in rodent models. We are first investigating paclitaxel, a drug used to treat metastatic breast cancer which acts on the cell cycle.

Peter Friedman, Ph.D.
Professor
Ph.D., SUNY Upstate Medical Center

Studies in the Friedman laboratory focus on the regulation of parathyroid hormone receptor signaling and regulated trafficking. PTH controls extracellular calcium and phosphate homeostasis. Its effects on kidney and bone are mediated by its cognate receptor, the type I PTH receptor (PTH1R). Key advances have been made in understanding cell-specific PTH1R signaling and trafficking, and recent observations indicate that PTH1R

activation, desensitization and endocytosis are mediated through distinct structural states that derive from specific interactions between ligand and receptor.

Agonist- or antagonist-occupied receptor states induce discrete conformations with accessibility to intracellular receptor domains. The differential or inducible involvement of these domains in coupling to G proteins may represent a molecular basis for ligand-selective responses not only for the PTH1R, but also for other G protein-coupled receptors. Current work is directed at elucidating the molecular and structural mechanisms of how cytoplasmic scaffold proteins such as NHERF1 and Dishevelled legislate cell-, ligand-, and stage-specific receptor trafficking.

William Furey, Ph.D.
Professor
Ph.D., The State University of New Jersey

Dr. Furey's research involves the structure determination and analysis of large biological molecules and complexes by x-ray crystallography, and correlating the results with known functions. The work currently focuses on thiamin (vitamin B1) dependent enzymes and cell cycle regulating enzymes, as well as crystallographic methods development. Results of these studies could lead to development of therapeutic agents directed against pathogenic organisms, and anti-cancer drugs.

Ferruccio Galbiati, Ph.D.
Associate Professor
Ph.D., University of Milan

Most cells can not divide indefinitely due to a process termed cellular senescence. Because cancer cells need to escape cellular senescence in order to proliferate and eventually form tumors, it is well accepted that cellular senescence is a powerful tumor suppressive mechanism. In addition, since several molecular changes that are observed in senescent cells occur in somatic cells during the aging process, investigating the molecular mechanisms underlying cellular senescence will also allow us to better understand the more complicated aging process. Thus, molecules that regulate cellular senescence represent potential therapeutic targets for the prevention/treatment of cancer as well as the fight against aging.

Our work is directed at unraveling the role of caveolin-1 as a novel mediator of cellular senescence. Caveolin-1 is the structural protein component of caveolae, invaginations of the plasma membrane involved in signal transduction. Caveolin-1 acts as a scaffolding protein to concentrate, organize, and functionally modulate signaling molecules within caveolar membranes.

Senescent human diploid fibroblasts express higher levels of caveolin-1, as compared to non-senescent cells. We showed that mouse embryonic fibroblasts derived from caveolin-1 overexpressing transgenic mice are arrested in the G0/G1 phase of the cell cycle and display a premature senescent phenotype. In addition, we demonstrated that oxidative stress induces premature senescence by stimulating caveolin-1 gene transcription through p38 MAPK/Sp1-mediated activation of two GC-rich promoter elements in fibroblasts and epithelial cells. Interestingly, oxidative stress-induced premature senescence (SIPS) does not occur in fibroblasts where caveolin-1 expression is reduced using an antisense mRNA-based approach. Moreover, oxidative stress does not induce premature senescence in caveolin-1-negative MCF-7 breast cancer cells and reintroduction of caveolin-1 in these cells restores IPS.

Taken together, these data indicate that caveolin-1 plays a central role in the signaling events that lead to cellular senescence. We are currently investigating, at the molecular level, the signaling pathways that link caveolin-1 function to oxidative stress-induced premature senescence. These investigations will contribute to elucidate the molecular mechanisms underlying aging and cancerous cell transformation.

Pamela Hershberger, Ph.D.
Research Assistant Professor
Ph.D., Case Western Reserve University

Hormones such as estrogen and 1,25-dihydroxyvitamin D3 play an important role in controlling cell growth; estrogen tends to promote growth, whereas vitamin D tends to inhibit growth. The goal of Dr. Hershberger's research is to understand how such hormone responses are generated and controlled, and how they may be exploited to suppress the development or growth of lung cancer (a disease that claims the lives of more than 160,000 individuals in the United States annually). Molecules which are found to be important in regulating hormone responsiveness in our studies represent potential new targets for therapeutic intervention in lung cancer chemoprevention and treatment.
Dr. Hershberger's research uses molecular and cellular techniques to evaluate the role of nuclear steroid hormone receptors and their signaling pathways as therapeutic targets in solid tumors. Because the hormone vitamin D exerts anti-proliferative activity in a variety of tumor model systems, we initiated studies to explore its potential as a novel lung cancer therapy. She has found that although lung cancer cells express the vitamin D receptor, they were only moderately sensitive to vitamin D-mediated growth inhibition. In exploring the mechanistic basis for this response, we found that primary human lung tumors but not normal lung tissues express CYP24, the enzyme that catabolically inactivates vitamin D. As the only known function for CYP24 is the regulation of vitamin D metabolism, its frequent up-regulation in human lung tumors implies that tumor establishment and/or progression requires escape from the anti-proliferative action of vitamin D. Based on these findings, our lab is now exploring (1) the effect of CYP24 inhibitors on vitamin D pharmacokinetics and anti-tumor activity in lung tumor xenograft models (2) the potential use of CYP24 as a diagnostic or prognostic marker in lung cancer, and (3) the mechanisms contributing to CYP24 over-expression in lung cancer cells. Ultimately, she seeks to suppress CYP24 action in lung cancer cells to restore endogenous growth control by vitamin D.

Jing Hu, Ph.D.
Assistant Professor
Ph.D., Karolinska Institute, Sweden

Gene regulation is a key event that is essentially involved in all basic cellular processes and pathological process. A thorough understanding of the molecular mechanisms by which gene regulation is controlled is a necessary foundation for attempts to target deregulated gene expression events for cancer intervention. The main focus of Dr. Hu's laboratory is to investigate how posttranslational modifications (sumoylation, phosphorylation and ubiquitination) control gene expression at both transcriptional and translational level in the process of carcinogenesis.

Dr. Hu recently discovered that posttranslational modification of transcription factor NF-κB2/p100 by the small ubiquitin-like modifier (SUMO) is a determining factor for stimuli-induced p100 processing and subsequent activation of alternative NF-κB pathway. Her results indicate that a threshold of basal p100 sumoylation creates a privileged pool of p100 that are competent for stimuli-induced phosphorylation and subsequent recruitment of ubiquitin E3-ligase β-TrCP, polyubiquitination and ultimate NF-κB2/p52 generation and RelB nuclear translocation. Together, these findings not only provide mechanistic information regarding how SUMO modification participates in the regulation of signaling transduction, but also uncover a novel regulation mechanism of activation of alternative NF-κB pathway. In the future, Dr. Hu will continue explore how functional interplays among posttranslational modifications control the activity of transcription factors and translation initiators.
Dysregulation of protein synthesis is beginning to be recognized as a major step in malignant transformation and progression of tumors, therefore another research interest of Dr. Hu's laboratory is to screen and identify dietary or natural agents for targeting deregulated protein synthesis for cancer intervention. We found that dietary agent phenethylisothiocynate (PEITC), are major bioactive components of cruciferous vegetables,

inhibits cap-dependent translation by regulating level and phosphorylation of 4E-BP1. In the future, in addition to expand our understanding of PEITC-mediated translation inhibition by exploring the potential upstream signaling and downstream targets of translation inhibition, we will also search for natural compounds that target cap-dependent translation for cancer intervention through modulating SUMO pathway.

Edwin Jackson, Ph.D.
Professor
Ph.D., University of Texas at Dallas

Dr. Jackson's research focuses on cardiovascular and renal pharmacology with an emphasis on understanding the function and mechanisms of endogenous autocrine, paracrine and humoral systems that either augment or inhibit the development or progression of cardiovascular/renal diseases. This research is guided by the concept that a better understanding of the endogenous systems that modulate disease onset and progression will result in new approaches to prevent or treat cardiovascular and renal diseases by inhibiting or augmenting these endogenous factors.

Three endogenous systems are under intensive investigation: sex hormones; adenosine; and the renin-angiotensin system.

Sex Hormones: Based on epidemiological data, cardiovascular scientists once thought that estrogen replacement therapy would prevent cardiovascular/renal disease in postmenopausal women. Unfortunately, randomized clinical trials did not support this simple concept. Dr. Jackson has discovered that estradiol, the main endogenous estrogen, is converted to metabolites that exert cardiovascular/renal protection. Because clinical trials were conducted with horse estrogens (Premarin) that are not precursors of these metabolites, it is likely that use of the wrong estrogenic preparation contributed in part to the negative results from clinical trials. We are currently using the knowledge gained by our experimental studies to design improved hormone replacement therapy that would benefit both women and men.

Adenosine: Adenosine is a naturally occurring chemical in the body that serves to protect organ systems from injury. We have discovered that adenosine protects the heart from damage induced by a myocardial infarction (heart attack), the brain from damage induced by traumatic head injury and (unfortunately) tumors when attacked by the immune system. We are currently investigating how adenosine levels in organ systems are regulated, what adenosine does to cardiovascular/ renal/ brain/ immune cells and how we can better modulate the adenosine system with drugs for clinical benefit in diseases of the heart, kidneys, blood vessels and brain and in cancer.

Renin-Angiotensin System: Angiotensin II causes constriction of small blood vessels in the kidney, leading to kidney disease and high blood pressure. We have found that the renal affects of angiotensin II are intensified in animals with genetically-susceptible kidneys. This effect appears to be attenuated by a renal enzyme called dipeptidyl peptidase IV (DPP IV) which metabolizes (converts) a gut released peptide (PYY1-36) and a nerve-released peptide (NPY1-36) to less active forms that do not activate the so-called Y1R. A new class of antidiabetic drugs inhibits DPP IV. We are investigating whether this new class of antidiabetic drugs may adversely affect the kidneys by preventing the conversion of PYY1-36 and NPY1-36 to less active metabolites.

Yu Jiang, Ph.D.
Associate Professor
Ph.D., Yale University

Dr. Jiang's laboratory is interested how environmental conditions, such as nutrient and stresses, control cell growth and proliferation. The laboratory focuses on intercellular signal transduction pathways that sense and transmit the environmental cues to cellular machinery governing metabolism and biosynthesis. Understanding how these pathways work in normal and cancer cells would allow us to development drugs for cancer prevention.

Dr. Jiang's laboratory studies the mechanism underlying the action of rapamycin, a macrolide antibiotic that has been used clinically as immunosuppressant for transplantation and anti-neoplastic drug for cancer prevention. The intracellular target of rapamycin is a kinase called TOR (or mTOR in mammalian cells), which lies at the center of a signaling network that controls many growth-related cellular events in response to changes in nutrient, growth factor, oxygen and energy levels. His laboratory is currently trying to answer two key questions concerning the signaling mechanisms of TOR: 1) how is TOR regulated by many distinct upstream signals? 2) What are the mechanisms by which TOR control many diverse cellular events. Several projects centering on these two questions are ongoing.

The first project concerns the mechanism that controls mTOR. Jiang's laboratory has recently identified FKBP38, a member of the FK506 binding protein family, as an endogenous inhibitor of mTOR. They are trying to determine how nutrient, growth factor and oxygen levels regulate mTOR through FKBP38 in mammalian systems.

The second project aims to the role of FKBP38 in apoptosis. FKBP38 has been shown to interact with the anti-apoptotic proteins, Bcl-2 and Bcl-xL. Jiang's laboratory is investigating whether nutrient, growth factor and oxygen levels control the anti-apoptotic activity of Bcl-2 and Bcl-xL through FKBP38 in mammalian systems.

The third project focuses on the mechanism by which TOR elicits its pleiotropic roles in cell growth. Recent studies in Jiang's laboratory have established protein phosphatase 2A as a major downstream target of the Tor pathway. His laboratory is currently investigating how Tor mediates PP2A activity and how PP2A relays Tor signaling activity to many cellular processes using yeast Saccharomyces cerevisiae as a model system.

Paul Johnston, Ph.D.
Research Assistant Professor
Ph.D., University of East Anglia, England

Dr. Johnston's research interests range from macrophage activation, cytokine biology, and immunology to drug discovery and the development of assays for high throughput (HTS) and high content (HCS) screening. In addition to the development and implementation of biochemical assays for HTS, Dr Johnston has been a pioneer in the application of cell based screening, and is a leader in the field of HCS and the application of image-based assays to drug discovery.

High throughput screening (HTS) has become the dominant tool in the drug discovery process. Completion of the sequencing of the human genome has increased the number of potential drug targets. In parallel with these changes, developments in robotics and combinatorial chemical synthesis have driven the production of very large numbers of compounds with potential for pharmacological activity. The need to screen large libraries of chemical compounds against multiple targets has stimulated improvements in assay technology, instrumentation, and automation that evolved into the field of HTS and has revolutionized the field of drug

discovery. The purpose of HTS is the interrogation of large chemical collections in the context of a biological target to accurately identify active chemotypes. To achieve this purpose, assays must be configured to provide a robust, reproducible signal with adequate throughput to screen large compound libraries. Since the activity or inactivity of any given compound in an HTS will typically be determined in a single well at one concentration, the assay signal window (dynamic range) must be sufficiently rugged to provide adequate separation between the maximum and minimum responses, and should enable the response to active compounds to be discriminated from the background variability (noise) associated with the top and bottom of the signal window. The process of assay development encompasses studies designed to validate the kinetics and pharmacology of the assay, together with efforts to optimize the signal window and/or variability of the assay in the context of a number of variables dictated by the automated process; DMSO tolerance, reagent stability, and signal stability. Superimposed upon assay development parameters associated with biochemical HTS formats, the implementation of cell-based screens present additional challenges; generation and/or characterization of an appropriate cell model, production of sufficient cells for HTS, plating cells for the assay, effects of compound exposure, and capture of the assay signal.

In recent years there has been a growing trend in drug discovery towards the implementation of cell based assays where the target is screened in a more physiological context than in biochemical assays of isolated targets. As a drug discovery scientist Dr. Johnston has pioneered the application of cell based assays for lead generation and optimization. Dr. Johnston has led the development and implementation of 50 assays (22 primary & 28 secondary) for HTS and hit assessment campaigns representing 4 therapeutic areas and diverse target classes; kinases, transporters, GPCR's, ion channels and multidrug resistance. To date, these efforts have yielded quality hits for 22 targets that have evolved into 2 programs, 6 leads, ongoing hit-to-lead efforts, and 3 hit assessment efforts. Dr. Johnston also directed the development and implementation of four in vitro ADME/Tox surrogate assays to provide bioavailability information on hits and leads: kinetic turbidimetric solubility assay; Caco-2 absorption model; human liver microsome metabolism assay; and an L6 rat myoblast acute cytotoxicity assay.

Yung Kim, Ph.D.
Research Instructor
Ph.D., Pusan National University, Korea

The major focus of Dr. Kim's research is to evaluate and characterize the factors involved in the calcium ion transport and its hormonal regulation in the kidneys. Some techniques related to the electrophysiological and microperfusion studies are currently applied to examine the effect of parathyroid hormone and calcium sensing receptor on the calcium ion movement via the active transcellular and the passive paracellular pathways in the isolated thick ascending limbs.

Edwina Kinchington, Ph.D.
Research Instructor
Ph.D., University of Pittsburgh

Dr. Kinchington has had a long interest in cancer – how it develops and how researchers can develop more specific therapeutics targeted to the selective molecules that are involved. Her present research interests focus on targeting the molecular mechanisms of non-small cell adenocarcinoma of the lung (NSCLC) where no optimal therapy has been established. One type of molecule expressed on the cell that activates growth pathways in the lung is the gastrin releasing peptide receptor (GRPR). These receptors have a role in normal lung development, but also stimulate cells to grow enabling tumor formation.

Dr. Kinchington's research is focusing on the effects of GRPR antagonists alone or in combination with EGFR inhibitors to demonstrate that inhibiting both pathways is more effective in preventing tumor growth than either

one alone. Therefore, this combined mode of treatment may have therapeutic potential in non-smoking females with adenocarcinoma where high GRPR expression is observed.

Dr. Kinchington's present research interests focus on targeting the molecular mechanisms of non-small cell adenocarcinoma of the lung (NSCLC). Lung cancer, rare in women in the early 1900's, has reached epidemic proportions accounting for nearly 29% of all cancer deaths in females in the United States. Although lung tumors are classified into many different subtypes, the predominant risk factor for all tumor types is cigarette smoking. However, bronchioloaveolar carcinoma (BAC), a unique subtype of non-small cell lung cancer (NSCLC), is increasing in incidence, and it is most prevalent in females who have never smoked. Unfortunately, no optimal therapy has been established. Oral inhibitors targeting proteins on the cell surface, specifically the epidermal growth factor receptor (EGFR), have proven to be ineffective as the sole chemotherapy agent, resulting in regrowth of the tumor and death of the patient. Only those lung tumors that contain a specific mutation in the EGFR are sensitive to drugs, such as gefitinib or erlotinib. Emerging evidence indicates that the relative risk of BAC between men and women and the response to therapy may not be the same. One type of molecule expressed on the cell that activates growth pathways in the lung is the gastrin releasing peptide receptor (GRPR). These receptors have a role in normal lung development, but also stimulate cells to grow enabling tumor formation. The gene for GRPR is located on the X-chromosome, the chromosome that designates the female sex (XX chromosomes), allowing for women to have two actively transcribed copies of the gene, while men (XY chromosomes) have only one active copy.

Our laboratory has shown that GRPR expression is greater in nonsmoking females than nonsmoking males (55% vs 0%). More recent unpublished data shows that activation of the GRPR pathway causes the release of molecules that can activate EGFR causing this pathway to continue to produce growth signals despite the presence of a specific inhibitor. Dr. Kinchington's research is focusing on the effects of GRPR antagonists alone or in combination with EGFR inhibitors to demonstrate that inhibiting both pathways is more effective in preventing tumor growth than either one alone. In addition, we are designing high throughput screens to search for more selective molecules which may inhibit either the GRPR receptor or the ligand for the receptor namely gastrin-releasing peptide (GRP). Therefore, this combined mode of treatment may have therapeutic potential in non-smoking females with adenocarcinoma where high GRPR expression is observed.

Lynn Knowles, Ph.D.
Research Instructor
Ph.D., Pennsylvania State University

The lipogenic enzyme fatty acid synthase (FAS) is up-regulated in a broad range of cancers, including those of the head and neck. While normal cells obtain most fatty acids from circulating lipids, tumor cells have developed an increased reliance on endogenous fatty acid biosynthesis to satisfy their metabolic needs. The goal of Dr. Knowles' research is to exploit FAS as a target for the treatment of head and neck cancer. The focus of her studies are 1) to understand the role of the FAS in tumor cell function, 2) to delineate how a FAS blockade elicits tumor cell death, and 3) to explore mechanisms of sensitizing head and neck tumor cells to the apoptotic effects of FAS inhibition.

Joan M. Lakoski, Ph.D.
Professor
Ph.D., University of Iowa

Elucidating the cellular and molecular neuropharmacology of the aging brain is the focus of the Lakoski laboratory. Using multidisciplinary approaches to investigate biogenic amine receptor expression and function, both normal and pathological aging processes are being investigated in young, middle-aged and senescent small animal models. We are investigating the roles of the steroid hormones estrogen and corticosterone on serotonin receptors, their receptor-effector coupling to G-proteins and related signaling transduction cascades, including

the 5-HT1A and 5-HT2A receptor subtypes, and the serotonin neurotransporter (SERT) in discrete brain regions including cortical, hippocampal and midbrain regions; radioligand binding techniques, receptor autoradiography and functional neurochemical assays are among the technical approaches used to study the impact of the circulating hormone environment on the aging serotonergic neuronal system. Related ongoing studies are utilizing in vivo microPET image analysis techniques to elucidate SERT expression and function with respect to aging and hormone treatment. In addition, the impact of selective neurotoxic insults to the dopamine-containing neuronal system is being investigated using behavioral, neurochemical and molecular approaches to better understand how this neurotransmitter system responds and recovers from neuronal injury across the lifespan. Our goal is to contribute new information to understand the biology of central nervous system aging, including normal and neurodegenerative processes, in neurotransmitter systems established as key components in cognitive declines, mood disorders, and stress-related disorders common in the elderly. Ultimately, our aim is to improve the quality of life with advancing age by pharmacological interventions to delay the onset of neuronal decline and/or enhance endogenous repair mechanisms of the biogenic amine neurotransmitter systems.

John Lazo, Ph.D.
The Allegheny Foundation Professor
Ph.D., University of Michigan

My laboratory is primarily interested in the factors that regulate the levels and activity of critical protein tyrosine and dual specificity phosphatases. An example of a protein tyrosine phosphatase we are investigating is PRL-1, which appears to have a role in controlling cellular movement and intracellular structural motifs and is involved tumor cell migration and invasion. Using short hairpin RNAs for PRL-1, we have observed an altered phenotype, which includes increased adherence and cell spreading, decreased c-Src and p130 Cas expression and reduced Rac1 and Cdc42 activities. The results support a model in which PRL-1 has an important role in maintaining the malignant phenotype by exploiting Src activation processes. We believe PRL-1 could be a novel molecular target for new anticancer agents. Our laboratory group also has a major interest in the dual specificity phosphatases that control cell signaling and cell cycle. These include the Cdc25 family, Cdc25A, Cdc25B and Cdc25C, and the mitogen activated protein kinase phosphatases (MKP) of which there are eleven encoded in the human genome. Recently we discovered that acute hypoxia and NO can markedly decrease the levels of Cdc25A and we are studying the mechanisms responsible for these changes in protein levels. We are also probing the role of DNA-damage signaling pathways in the regulation of these phosphatases. We have identified new small molecule inhibitions of theses phosphatases and are studying their pharmacological activities.

Edwin Levitan, Ph.D.
Professor
Ph.D., Brandeis University

The Levitan lab studies long-term regulation of electrical activity and the control of neuropeptide release. The former studies are focused on electrical remodeling that contributes to the actions of antipsychotic drugs in the midbrain and promotes arrhythmias in the heart. The latter is aimed at understanding how electrical activity alters release of transmitters that are important for controlling mood, behavior and sensation. These topics are related because channels support the electrical activity that triggers neurosecretion, while motion and fusion of secretory vesicles support transmitter release and delivery of channels to the plasma membrane.
On the channel front, the lab is exploring how antipsychotic drugs increase Kv4.3 K+ channel expression in dopamine neurons known to be important in cognition and reward. In parallel, Kv4.3 downregulation in cardiac myocytes induced by angiotensin receptors is studied because this effect is thought to promote arrhythmias and sudden death. The lab is also collaborating on studies of other K+ channels. For example, Kv2.1 channel effects on apoptosis and exocytosis have been described with Drs. Aizenman (Neurobiology, University Pittsburgh) and Lotan (Physiology and Pharmacology, Tel Aviv University).

Another project uses in vivo fluorescent imaging of green fluorescent protein (GFP) constructs in transgenic Drosophila nerve terminals to determine how patterned electrical activity controls neuropeptide release. By optically detecting vesicle motion and signal transduction, new mechanisms have been discovered that acutely regulate secretion (e.g. vesicle mobilization) and maintain nerve terminal function (capture of transiting vesicles). Future studies will incorporate photoactivatable proteins and multiphoton microscopy to probe how neurons produce activity-dependent changes in secretory activity.

Elena Makhina, Ph.D.
Research Assistant Professor
Ph.D., Institute of Industrial Microbiology, Moscow

My research is focused on understanding the molecular mechanisms of potassium (K+) channel regulation. In one project we use functional expression of K+ channels in yeast to identify novel proteins involved in regulation of K+ channels. Using this approach we have identified several proteins that affect K+ channel function and are currently characterizing them using electrophysiology and molecular biology techniques. The second on-going project is aimed at the discovery of K+ channel drugs. Our yeast-based large scale drug screening procedure enabled us to identify novel K+ channel inhibitors and activators. We are currently examining the mechanisms of action and therapeutic potential of these drugs.

Mark Nichols, Ph.D.
Assistant Professor
Ph.D., Yale University

Research in Dr. Nichols' lab involves study of steroid hormone receptors, primarily the estrogen receptors alpha and beta (ERα, ERβ), and their role in normal, as well as in cancer tissue. Dr. Nichols has developed *in vitro* model systems that allow (a) the analysis of the effect of estrogen receptor (ER) mutations (that we found in breast cancers) on antihormone resistance and (b) screening of novel compounds for ER-subtype selective ligands. Better understanding of ligand activation of ERs may lead to improved endocrine therapies for treating and perhaps preventing breast and other estrogen responsive cancers.

Tamoxifen is one of the most effective drugs for treatment and prevention of breast cancer yet a substantial number of breast cancers (30%) fail to respond to tamoxifen or will become resistant, even if they have estrogen receptor (ER+). Dr. Nichols tests the hypothesis that the estrogen receptor, its co-regulator proteins, or their interaction is altered in breast lesions where tamoxifen is ineffective. Tamoxifen therapy (or other selective estrogen receptor modulators- SERMs) requires a functional ER, yet the clinical use of immunohistochemistry is unable to determine function. Coactivators amplify transcription via ER and are the target of antiestrogen inhibition. Dr. Nichols has found changes in ER affecting coactivator binding sites and tamoxifen-induced structure from tumor tissue. One recovered mutation makes tamoxifen a better agonist than estradiol.

Dr. Nichols has a collaboration with Endece Pharmaceuticals for mechanistic analysis of several anticancer drugs. He is testing a parent compound and several of its metabolites in experiments to assess their growth-inhibitory and estrogenic or anti-estrogenic character. They have high likelihood to interact with steroid receptors (most likely estrogen receptors) and with enzymes that metabolize steroids, e.g. aromatase.

Dr. Nichols also works with small molecule compounds, 1,1-dichloro-2,2,3-triarylcyclopropanes (DTACs), exhibiting antiestrogenic properties in several assays. He has demonstrated that a subset of these compounds have selectivity for ER alpha or ER beta. In collaboration with Dr. Bino John, we have begun work on an RNA fingerprint of breast cancer that involves computational and experimental work to look at microRNAs and breast cancer. He also develops methods of synthesis for small interfering RNA libraries to discover gene products related to alterable phenotypes.

Michael Palladino, Ph.D.
Assistant Professor
Ph.D., University of Connecticut

The Palladino lab uses *Drosophila*, the fruit fly, as a model system to elucidate the cellular and molecular mechanisms of neurodegenerative diseases and discover therapeutic interventions for these diseases.

Our lab has identified a large collection of novel neurodegenerative mutants using a powerful forward genetic approach. Characterization of these mutants will identify key proteins required for neural maintenance with age and a detailed understanding of the role of these gene products in human disease conditions. The Palladino research program is directed toward three main goals: 1) discovering and characterizing novel pathways that cause neurodegenerative diseases, 2) understanding the physiological, cellular and molecular dysfunction that causes neurodegeneration in vivo, and 3) using our animal system in pharmacological screens to identify neuroprotective compounds for the treatment of human neurodegenerative diseases. We are currently focusing on elucidating the mechanism by which mutations affecting Na/K ATPase, triose phosphate isomerase (TPI), and ATP6 function result in RDP (rapid-onset dystonia parkinsonism), glycolytic enzymopthy, and mitochondrial encephalaomyopathy, respectively.

Guillermo Romero, Ph.D.
Associate Professor
Ph.D., University of Virginia

G-protein coupled receptors (GPCR) are the largest family of cell surface receptors found in mammalian organisms. These receptors are a major target for drug development. Dr. Romero is interested in the dynamics and traffic of GPCR, with special emphasis on the parathyroid hormone receptor type 1 (PTH1R). His approach is based on the use and development of novel optical techniques to study membrane proteins and their interactions with other cellular components in live cells.

Dr. Romero's research focuses on two main areas: a) the role of the PDZ proteins sodium-hydrogen exchange regulatory factor (NHERF1) and Disheveled-2 in the regulation of the dynamics and traffic of GPCR; and b) the role of phospholipase D in the regulation of receptor traffic and function.

Dr. Romero's approach is based primarily on the analysis of the physical properties of molecules of interest in live cells, using advanced optical techniques such as confocal microscopy, fluorescence recovery after photobleaching (FRAP), total internal reflection microscopy (TIRFM), image correlation spectroscopy (ICS), quantum dots, and others.

Using these techniques, Dr. Romero has developed novel methods to examine protein-protein interactions in the temporal domain. For example, he has recently demonstrated that the PTH1R is tethered to the cytoskeleton and accumulates in the vicinity of subjacent actin stress fibers, forming bundles that are highly dynamic structures, moving along these bundles much more rapidly than between them. Figure 1 shows a high-magnification TIRF image of the distribution of the PTH1R on the plasma membrane of CHO cells.

James Roppolo, Ph.D.
Research Assistant Professor
Ph.D., University of Michigan

Dr. Roppolo's research is concerned with the autonomic nervous system's control of bladder activity in normal animals and those with central nervous system injuries. A variety of techniques are used to examine, at the level of the lumbosacral spinal cord and brainstem, the various neuronal processes that occur in maintaining normal excretory function. These methods include: (1) anatomical techniques (HRP tracing and immunohisto-chemical techniques) to determine the location of neurons and possible neuropeptides involved in these processes, (2) neurophysiological techniques (evoked potentials, intracellular and extracellular single neuron recordings) to determine the types of neuronal interactions that occur in this system, (3) neuropharmacological techniques (systemic and iontophoretic application of drugs), (4) behavioral techniques and microstimulation of the of the lumbosacral spinal cord.

Francisco Schopfer, Ph.D.
Research Assistant Professor
Ph.D., University of Buenos Aires, Argentina

Dr. Schopfer's research is focused on the understanding of the biological effects of electrophilic fatty acids. In particular, he studies the mechanism by which nitrated fatty acid activate and signal through peroxisome proliferator-activated receptor gamma (PPARγ). This receptor is the target of currently used antidiabetic drugs (thiazolidinediones). The activation of the receptor regulates fat and glucose metabolism, resulting in an overall decrease of glucose levels to normal values in patients with type II diabetes. The targeting of this receptor by nitrated fatty acids results in a decrease of the glucose levels to normal values like thiazolidinediones, but without the known secondary effects exerted by thiazolidinediones. In addition to the intrinsic therapeutic value of nitrated fatty acid, they will aid in the understanding of the biological mechanism involved in PPARγ activation, leading to improved designs of anti-diabetic drugs targeting the PPARγ receptor.

The role of the PPARγ receptor in diabetes has been well established. Nonetheless, the role of endogenous signaling molecules on the activation of PPARγ is still unclear and under debate. Nitrated fatty acids are endogenously formed and bind to PPARγ with high affinity rivaling Rosiglitazone (thiazolidinediones), resulting in receptor activation. In addition, nitrated fatty acids covalently modify a critical cysteine (cys285) in the ligand binding pocket of PPARγ, promoting a particular conformational change that results in partial receptor activation. This partial activation results in the expression of a particular subset of genes under PPARγ regulation and a biological outcome that differs from the one obtained when activating the receptor with Rosiglitazone. Dr. Schopfer's work focuses on understanding the mechanism of this selective activation and how it avoids the side effect presented upon full activation by agonist like Rosiglitazone.

Electrophilic fatty acids are constantly formed as fatty acid breakdown products during oxidative stress and as signaling messengers by enzymatic or non enzymatic pathways. Dr. Schopfer studies the formation of biologically relevant electrophiles, in particular nitrated fatty acids, and their signaling mechanisms. The study involves the detection and characterization of novel electrophiles formed during inflammation. Once the molecules are characterized, a chemical synthesis approach is used to generate enough quantities for biological experiments.

Electrophiles induce an important cellular response that includes the induction of phase II genes. This will in turn set up a more protective environment against damaging electrophilic molecules. A key player in the initiation of this biological response is the Keap 1/Nrf 2 couple. Keap 1 is usually bound to Nrf 2 in the cytoplasm. Upon formation of electrophiles, Keap 1, which contains several highly reactive cysteine, is targeted, dissociates from Nrf2 and is routed to degradation by the proteosome. These lead to Nrf2 nuclear translocation and activation of phase II genes. In particular, we study the mechanism by which different biologically relevant electrophiles target KEAP 1 and activate Nrf 2 responses. In addition, a more general proteomic approach is use to evaluate and characterize different electrophilic cellular protein targets. Once critical targets are identified using a mass spectrometry approach, a functional study of the modification is performed to determine the relevance and its cellular effects.

Adrian Sculptoreanu, Ph.D.
Research Assistant Professor
Ph.D., Université de Sherbrooke

We are using patch clamp techniques to study: a) the neurokinin-activated intracellular signaling mechanisms involved in the conversion of small DRG neurons from phasic to tonic firing; b) the neurokinin-activated intracellular mechanism involved in the TRPV1 desensitization in fast blue (FB) labeled bladder DRG neurons; and c) the neurokinin-activated intracellular mechanism involved in modulation of Ca^{2+} currents. In these studies we will measure TRPV1 currents activated by capsaicin before and after application of neurokinin agonists, inhibition of PKC, phosphatases or a combination of these treatments. To insure that the DRG neurons tested are UB neurons we will use identified FB labeled neurons from L1-S2 DRG. In these experiments we will test the hypothesis that activation of PKC is in part responsible for nociceptive sensitization mediated by neurokinins, which constitutes the central hypothesis of this grant. Preliminary experiments done by us in DRG neurons of normal cats and rats suggest that an NK_2 selective agonist prevents TRPV1 receptor desensitization and the action of this neurokinin agonist is mediated by PKC. The main goal of our present research is to establish which phosphatases and protein kinase C subtypes are involved in the modulation of TRPV1 currents, and K^+-, Na^+- and Ca^{2+}-currents and in what ways these mechanisms are contributing to changes in excitability and synaptic transmission in nociceptive sensitization. For this purpose we will use selective protein kinase activators, peptide inhibitors and phosphatase inhibitors as well as cell dialysis with active PKCe during recording of TRPV1 currents in whole cell configuration

Dinara Shakiryanova, Ph.D.
Research Instructor
Ph.D., Kazan State Medical University, Russia

Dr. Shakiryanova's research interests are focused on studying the mechanisms of neuropeptide release and signaling pathways involved in regulation of neuropeptide secretion. Neuropeptide vesicle dynamics and release can be measured in vivo at nerve terminals by imaging GFP-neuropeptide fluorescence in our Drosophila melanogaster model. Ca^{2+} signaling mechanisms induce long lasting presynaptic dense-core vesicle mobilization and synaptic plasticity. Specifically, voltage-gated Ca^{2+} channels, Ca^{2+}-induced Ca^{2+} release channels and Ca^{2+}/calmodulin-activated kinase II are studied because they are required for sustained mobilization of dense-core vesicles and post-tetanic potentiation of neuropeptide secretion.

Dr. Shakiryanova's study has revealed that DCVs are mobilized by Ca^{2+} in an F-actin independent manner. Persistence of vesicle mobilization for minutes following seconds of activity indicates a role for signaling in the control of vesicle mobility in synaptic boutons. We have demonstrated that ryanodine receptor mediated Ca^{2+} release from endoplasmic reticulum and activation of CamKII are necessary for initiating DCV mobilization and post-tetanic potentiation of neuropeptide release.
CamKII remains an active subject of our study. Currently she is exploring CamKII activation in animals expressing FRET-based CamKII indicator Camui. Electrical activity induces rapid activation of CamKII in synaptic boutons which persists after the return of Ca^{2+} back to baseline. Furthermore, activated presynaptic CamKII translocates from the cytoplasm to clusters, presumably active zones (Fig.2).

It has long been recognized that cyclic nucleotides regulate synaptictransmission. But determining the mechanisms responsible for activating cyclases that regulate synaptic transmission has been difficult because it has not been possible to directly measure cyclic nucleotides in living nerve terminals. Recently, a ratiometric FRET-based cAMP sensor called epac1-camps has been generated that reports activation of adenylyl cylase by forskolin and receptors. Our experiments revealed that activity rapidly induces a Ca2+-dependent epac1-camps response in Drosophila synaptic boutons. Surprisingly, this response cannot be attributed to activation of

rutabaga adenylyl cyclase and is unaffected by the dunce cAMP-specific phosphodiesterase. Instead, the activity-dependent presynaptic epac1-camps signal reflects elevation of cGMP in response to nitric oxide-activated guanylyl cyclase. Post-tetanic presynaptic cGMP is long-lived because of limited phosphodiesterase activity. Thus, nerve terminal biochemical signaling induced by brief bouts of activity temporally summates on a time scale orders of magnitude longer than fast transmission.

Elizabeth Sharlow, Ph.D.
Research Instructor
Ph.D., Pennsylvania State University

Dr. Sharlow's research focuses on the design and implementation of high throughput and high content screening assays that are used to interrogate large compound libraries for small molecule inhibitors of a molecule target (protein) of interest. Compounds identified in these primary screening assay activities are further characterized in secondary hit confirmation assays which assess the compound's activity and function to determine the specificity of the inhibitory response. Dr. Sharlow's primary goal is to identify small molecules that may have long term therapeutic efficacy as well as small molecules that can be used as chemical probes to help delineate the physiological roles of specific molecular targets (proteins).
The disease model systems with which Dr. Sharlow works include Salmonella, Bubonic plague, Malaria, Leishmaniasis and Cancer with the specific molecular targets being predominantly kinases and phosphatases. The majority of her HTS assays utilize recombinant proteins and, therefore, a significant effort is focused on expressing and purifying mammalian, bacterial and difficult to express Plasmodium falciparum proteins. She currently uses E.coli expression systems; however, she is also implementing wheat germ and insect cell expression systems to broader our protein expression and purification repertoire. Within the leishmaniasis disease model system, we also use whole organisms (i.e. parasites) for the basis of high throughput screening assays. One particular Leishmaniasis project focuses on examining the differences in drug sensitivity of Leishmania major life cycle forms (promastigotes, axenic amastigotes and cell-based amastigotes).

Jill Siegfried, Ph.D.
Professor
Ph.D., Yale University

Dr. Siegfried investigates the role of growth factors and hormones in the development and growth of human lung cancer. The laboratory focuses on the effects of these cytokines on activation of cell signaling pathways and control of tumor growth, as well as their role in risk for cancer. Growth factors and their receptors currently under investigation include estrogen and its receptors and hepatocyte growth factor and its receptor, c-Met. Growth factors and hormones are also being investigated as possible therapeutic targets and diagnostic or prognostic indicators for lung cancer. Hepatocyte growth factor has been found to be a strong negative prognostic indicator for non-small cell lung cancer, and expression of the the enzyme aromatase that mediates estrogen production has also been linked to poor outcome in women with lung cancer. Circulating growth factor levels may also correlate with active cancer. These studies are directed toward development of new methods to identify undetected lung cancer and new therapeutic strategies through increased knowledge of growth-regulatory processes in lung cancer cells.

Hepatocyte growth factor (HGF) and its receptor c-Met are a ligand-receptor pair that initiate signaling pathways promoting proliferation, survival, angiogenesis, and invasion. HGF is a mainly paracrine growth factor that is secreted by fibroblasts in the lung and acts upon the c-Met receptor expressed by airway epithelial and endothelial cells. In lung cancer, c-Met is often upregulated and the tumor cells induce elevated HGF production by neighboring stroma. Elevated HGF in lung cancer patients with early stage disease has identified a population of patients who are most likely to recur and die from their disease. As shown in the Kaplan-Meier

survival curves, HGF levels above the median of 22 units was associated with a higher proportion of deaths from all causes (A), lung-cancer specific deaths (B), and recurrence events (C). This observation among others has led us to focus on therapeutic targeting of HGF and its receptor c-Met for control of lung cancer.

To test therapeutic strategies, Dr. Siegfried has engineered a transgenic mouse that over-expresses the human HGF gene in the airways by placing the HGF gene under the control of the Clara cell secretory protein (CCSP) promoter. The lungs of these mice produce human HGF mRNA and protein and contain 2-3 times as many clara cells per micron of airway length as wild-type mice. While the mice show some abnormalities in airway branching, they have normal airway function and they do not develop lung tumors spontaneously at a rate above that of wild-type animals. However, the HGF transgenic mouse is more susceptible to the development of lung tumors initiated by the tobacco carcinogen NNK. Lung tumors produced by carcinogen treatment in the HGF transgenic animal are more invasive and contain higher numbers of blood vessels than wild-type tumors. These effects can be inhibited by a neutralizing antibody to HGF that is now in development for clinical use.

The Siegfried laboratory was one of the first to demonstrate the functional significance of estrogen receptors in lung tumors. This figure shows immunohistochemical staining of a non-small cell lung tumor for the estrogen receptor β, which we have found to be expressed to some degree in over 85% of lung tumors. Staining is observed both in the nucleus and cytoplasm, and we have evidence that both nuclear signaling through ERE elements in the promoter regions of estrogen-sensitive genes, as well as non-nuclear signaling through the EGFR and MAPK pathway occur in lung tumor cells.

Dr. Siegfried also has evidence that estrogen is locally produced by the enzyme aromatase within lung tumors, and this suggests an autocrine ligand-reecptor exists for estrogen and its receptor in many lung tumors. Clinical trials are currently on-going to test the clinical activity of estrogen antagonists for therapy of lung cancer.

Shivendra Singh, Ph.D.
Professor
Ph.D., Banaras Hindu University, India

Despite significant advances towards early detection and targeted therapies, prostate and breast cancers continue to claim thousands of lives each year. The Singh laboratory is interested in preclinical and clinical development of novel agents derived from dietary sources (e.g., garlic and broccoli) and traditional oriental and Indian medicinal plants potentially useful for prevention of prostate and breast cancer in humans.

The research interests of the Singh laboratory are thematically aligned with three main areas: (1) preclinical and clinical development of novel cancer chemopreventive agents, (2) rational design of combination chemoprevention regimens, and (3) elucidation of the mechanism of carcinogenesis by environmentally relevant chemicals. Cellular and transgenic animal models are used to screen potential cancer chemopreventive constituents from dietary sources and traditional oriental and Indian medicinal plants. Cutting edge molecular biological (gene manipulation) and imaging techniques (MRI and bioluminescence imaging in live animals) are used by Singh and colleagues to determine the mechanism of action of promising cancer chemopreventive agents and to monitor their effects on cancer progression.

Cancer chemoprevention is a relatively new but rapidly emerging sub-discipline in oncology and refers to the use of natural or synthetic agents to reverse or delay the process of carcinogenesis. Despite considerable advances towards early detection and targeted therapies, prostate and breast cancers continue to be the leading causes of cancer related deaths. The long latency of most epithelial cancers, including prostate and breast cancers, provides a large window of opportunity for intervention to prevent or slow disease progression. Accordingly, identification of agents that are relatively safe but can be used to prevent cancers could have a significant impact on disease-related cost, mortality, and morbidity for a large segment of population.

Epidemiological studies continue to support the premise that dietary intake of certain vegetables (e.g., garlic) may be protective against the risk of different types of cancers. Anticancer effect of garlic is attributed to volatile sulfur compounds (e.g., diallyl trisulfide), which are generated upon processing (e.g., cutting) of these vegetables. Recent work from the Singh laboratory has revealed that garlic constituent diallyl trisulfide (DATS) suppresses growth of prostate cancer cells irrespective of their androgen-responsiveness or p53 status by activating a novel checkpoint kinase 1-dependent prometaphase arrest (schematically illustrated in Figure 1) and complex signaling culminating into apoptotic cell death. The DATS-mediated apoptosis involves reactive oxygen species-dependent activation of c-Jun N-terminal kinase. Oral administration of DATS significantly retards growth of prostate cancer xenografts in athymic mice without causing weight loss or any other side effects. Studies are in progress to determine efficacy of DATS against prostate carcinogenesis and metastasis using transgenic animal models. Positive outcome of these preclinical studies would rationalize clinical investigations to determine prostate cancer prevention by DATS in humans. Similar preclinical efficacy and mechanistic studies are underway in the Singh laboratory on prostate and breast cancer chemoprevention by phytochemicals derived from cruciferous vegetables (e.g., isothiocyanates) and traditional oriental (honokiol) and Indian medicine (guggulsterone and withanolides). Another research interest of the Singh laboratory entails elucidation of the mechanism of chemical carcinogenesis by polycyclic aromatic hydrocarbon (PAH) family of environmental pollutants. Singh and his collaborators have discovered a novel mechanism involving cell cycle regulator Cdc25B in PAH-induced neoplastic transformation. These studies have shown that chronic exposure of mouse embryonic fibroblasts (MEFs) derived from the wild type mice, but not Cdc25B knockout mice, to a prototypical PAH (BPDE) results in neoplastic transformation characterized by colony formation and tumor production in nude mice. Investigations are planned to determine in vivo relevance of these cellular findings.

Robert Sobol, Ph.D.
Assistant Professor
Ph.D., Temple University

DNA repair proteins maintain genome stability and cell survival by efficiently removing cytotoxic and genotoxic DNA lesions generated by endogenous sources (cellular metabolites) and exogenous sources (environmental toxins and chemotherapeutic agents). The Sobol laboratory uses genomic and proteomic tools (i) to study regulation of the base excision repair (BER) pathway in normal and disease-derived cells (i.e., cancer stem cells, neurons), (ii) to study how this pathway repairs chemotherapeutic and environmental agent induced DNA damage, (iii) to identify novel DNA repair and DNA damage-response genes/proteins involved in chemotherapeutic response and (iv) to discover the mechanisms that govern the cellular response to DNA damage or failed DNA repair in normal and diseased cells (See Figure 1 on the Scientific Graphics Page - Model for Base excision repair).

Current projects include a study of the role of BER in the repair of DNA damage induced by alkylation, oxidation and radiation, an investigation of NAD+ and poly-ADP-ribose metabolism and catabolism proteins in DNA repair and DNA damage response, BER-mediated repair of oxidative DNA damage in the control of inflammation & neurodegeneration and epigenetic control of DNA repair gene expression in cancer. These studies involve the use of lentiviruses for gene expression and knockdown, human tumor and cancer stem cell culture, genetic and small molecule inhibitors to regulate DNA repair and DNA damage response, protein biochemistry and proteomic approaches, cell biological methods and molecular biological methods including cDNA cloning, recombinant protein expression & purification and single-gene and whole genome expression, SNP and methylation analyses (See Figure 1 - Model for Base excision repair).

BER protein complex formation and overall BER function is influenced by posttranslational modifications (PTMs) that arise from the cellular state or the DNA damage response. For example, Pol ß function is altered by methylation, acetylation and possibly SUMO-modification. How Pol ß and the BER pathway is controlled by PTMs is only beginning to be understood. The next goal is to assess the potential crosstalk between these PTMs, the ability to form productive repair complexes, and the stability and function of these BER proteins, as

a single PTM can positively or negatively influence both enzyme function and the signal for a second PTM. In this context, my lab is studying how Pol ß methylation or acetylation can regulate BER complex formation and therefore impact the stability and function of Pol ß by enhancing or inhibiting CHIP-mediated ubiquitylation and the potential for SUMO modification of Pol ß (See Figure 2 - Pol ß PTM Crosstalk).

In this project, the Sobol lab is studying the role of PARP1 and PARP2 in BER to define the cellular signal generated by aborted BER that leads to cell death. We have demonstrated that Pol ß-dependant sensitivity to alkylation damage in human cells requires repair initiation by Mpg and is contingent on a failure to repair the BER intermediate 5'dRP. Further, the group hypothesizes that PARP1/PARP2 acts as a sensor to incomplete BER, leading to rapid poly(ADP)ribosylation (PAR) and functional inhibition of target proteins that include the mitotic checkpoint kinase aurora B (AurB). Inhibition of AurB initiates a rapid loss of Histone H3 phosphorylation and a complete block to mitosis leading to a strong cell cycle block at the G2/M border. At later time points this translates to AIF-mediated translocation, the onset of cell death and activation of the ATM-mediated DNA damage response (See Figure 3 - PARP as a BER Checkpoint Protein).

A second modifier protein critical to the cellular response to DNA damage is the enzyme PARG, which removes the PAR moieties from PARP-modified proteins (See Figure 3). We hypothesize that the BER pathway, via activation of PARP1, triggers a specific signal that mediates a mitotic checkpoint and prevents tumor cells from dividing, leading to necrotic, autophagic and/or apoptotic cell death and this signal is regulated by PARG. Current studies will extend initial findings by using the clinical PARG inhibitor N-bis-(3-phenyl-propyl)9-oxo-fluorene-2,7-diamide as well as RNA interference (RNAi) to specifically down regulate PARG in glioma cells and evaluate the significance of PARG activity in the cellular response to DNA base damage. Finally, Dr. Sobol proposes to explore the significance of and identification of PARP modified proteins in the cellular response to base damage. The goal is to develop a complete human proteome map of PARP modified proteins and PAR binding proteins that respond to and control the cellular response to environmentally- and chemotherapeutically-induced base damage.

Gene expression variations in normal versus diseased cells impact both the control of genome stability and the cellular response to both environmental and chemotherapeutic exposures. However, gene expression is altered both by sequence variations [Single-nucleotide polymorphisms (SNPs) or disease-related gene mutations] and epigenetically, by cytosine methylation or post-translational modification of histones (methylation, acetylation or phosphorylation). In many cases, epigenetic changes can alter response to chemotherapy by deregulation of response genes. Dr. Sobol is interested in studying the role of cytosine methylation and histone modification in cancer, with an emphasis on epigenetic regulation of chemotherapeutic response. For example, in recent studies, hypermethylation of the promoter of the DNA repair gene MGMT has been found to be of progostic value in oropharyngeal cancer patient survival. Further, MGMT expression appears to correlate with outcome in childhood malignant glioma (see Figure 4 - MGMT Expression in childhood glioma). Finally, Dr. Sobol is using whole genome approaches to identify genetic alterations (SNPs) that may alter chemotherapeutic response to alkylator therapy.

Harish Srinivas, Ph.D.
Research Instructor
Ph.D., Indian Institute of Science, India

Every year nearly 170,000 people die of lung cancer in United States. Since no cure exists, there is an urgent need to develop novel strategies in this area. Dr. Srinivas is interested in studying the function of nuclear hormone receptors (NHRs) in normal and lung cancer cells, and to develop effective strategies for blocking these signaling pathways in an effort to prevent and treat cancer. One NHR Dr. Srinivas is currently interested in is estrogen receptor beta (ERβ), and its role in lung cancer progression.

Estrogens exert their biological effect through two estrogen receptor subtypes, ERα and ERβ. These transcription factors regulate gene expression by binding to estrogen response elements (EREs) in the promoter region of their target genes. Interestingly, recent reports have shown that estrogens can also activate signaling through "non-genomic" mechanisms by binding to membrane associated ERs, resulting in rapid cellular responses such as increased levels of Ca2+, nitric oxide (NO), and activation of kinases.

Dr. Srinivas has shown that estrogens promote the growth of non-small cell lung cancer (NSCLC) cells, whereas anti-estrogens inhibit them. Further, we observe that lung cancer cells express only ERβ but not ERα. Dr. Srinivas is currently investigating the non-genomic functions of ERβ in lung cancer cells. Dr. Srinivas believes that understanding these functions would lead to development of new strategies to block ERβ signaling to treat and prevent lung cancer.

Sanjay Srivastava, Ph.D.
Research Assistant Professor
Ph.D., Kampur University, India

Dr. Srivastava's laboratory is interested in understanding the molecular mechanism of chemopreventive agents of dietary origin against cancer. His studies have revealed that isothiocyanates present in cruciferous vegetables such as broccoli, and capsaicin present in chili pepper, functions as chemopreventive as well as chemotherapeutic agents against pancreatic and ovarian cancer in the cellular and animal model.

His group has demonstrated that benzyl isothiocyanate inhibits the growth of human pancreatic cancer cells by causing cell cycle arrest and induction of apoptosis, without affecting the viability of normal pancreatic cells. The studies suggested that apoptosis induced by benzyl isothiocyanate in cancer cells was associated with the inhibition of the NF-kB pathway, and activation of caspase-3 cascade.

In another project, Dr. Srivastava established that phenethyl isothiocyanate inhibits the proliferation of human ovarian cancer cells in culture and induces apoptosis. His studies further revealed that apoptosis induced by phenethyl isothiocyanate was linked with the inhibition of EGFR/Akt survival pathway. This pathway has been shown to be active in human ovarian carcinoma. Dr. Srivastava's laboratory is determining its anticancer effect in the animal model.

In the third project, Dr. Srivastava's laboratory has demonstrated that capsaicin (constituent of red chili pepper) is antiproliferative and induces apoptosis in pancreatic cancer cells by generating reactive oxygen species and activating the mitochondrial death pathway, without having any effect on normal pancreatic acinar cells. Detailed mechanistic studies are in progress.

Using genetic and pharmacological approaches, the Srivastava laboratory is trying to dissect out specific signaling pathways and their mechanism of action, targeted by these dietary agents.

Laura Stabile, Ph.D.
Research Assistant Professor
Ph.D., West Virginia University

Dr. Stabile is interested in the role of growth factors and hormones in the development of human lung cancer. The hepatocyte growth factor (HGF)/c-Met pathway and the estrogen pathway both play key roles in the development and progression of lung cancer and represent attractive targeted pathways for drug development. Lung cancer kills more Americans every year than any other type of cancer, and the 5-year survival rate is only

16% (Figure 1). Lung cancer patients are typically diagnosed at a late stage and have very few effective therapeutic options. Thus, new targeted strategies are essential to make an impact on this disease.

c-Met is a receptor tyrosine kinase whose activation by HGF can lead to transformation (conversion of a normal cell into a malignant cell) and tumorigenicity (growth of tumors) in a variety of human tissues. Since c-Met and HGF are frequently overexpressed in lung cancer and there is a strong correlation between overexpression and decreased patient survival, the HGF/c-Met signaling pathway is a potential target for tumor control. Primary projects in this area of interest include: 1) studying the development and inhibition of lung carcinogenesis in a novel transgenic mouse model that overexpresses HGF in the airways 2) preclinical development of therapeutic drugs that target this pathway using a variety of techniques such as neutralizing antibodies to HGF, c-Met small molecule inhibitors, c-Met guanidinium-peptide nucleic acid antisense technology and 3) understanding the mechanism of signaling interactions between c-Met and the epidermal growth factor receptor (EGFR) pathway.

Dr. Stabile has successfully developed a murine model that mimics the overproduction of HGF found in human lung tumors and have shown that a single human HGF neutralizing antibody, L2G7, has profound inhibitory effects on development of lung tumors in this transgenic mouse model. Furthermore, lung tumors with K-ras mutation are resistant to blockage of the HGF pathway using L2G7. In addition, we have recently demonstrated the importance of induction of the cyclooxygenase 2 (COX-2)/prostaglandin E2 (PGE2) pathway and subsequent activation of EGFR by HGF in lung cancer cells. Figure 2 describes the signaling pathway of HGF that we are studying and areas of therapeutic intervention.Another aspect of research involves the estrogen pathway in lung cancer.

Lung cancer is becoming increasingly common in women and in the U.S. accounts for more female deaths annually than breast cancer and all other gynecological cancers combined. Epidemiological studies show that male-female differences exist in the presentation of lung cancer. These observations suggest the role of estrogens in lung carcinogenesis. Primary projects in this area of interest include: 1) understanding both genomic and non-genomic effects of estrogen in the lung 2) elucidating cross-talk pathways between estrogen and the EGFR and VEGF pathways in the lung 3) understanding the differences in estrogen signaling in lung cancer patients who actively smoked versus those who never smoked and 4) preclinical development of therapeutic drugs that target this pathway such as estrogen antagonists and aromatase inhibitors.

Dr. Stabile has demonstrated that estrogen receptors are expressed in both normal lung as well as lung tumor cells and that estrogen promotes the growth of lung tumor cells. The growth stimulation is significantly inhibited in vitro and in vivo with the pure estrogen receptor antagonist, ICI 182,780 (Faslodex, fulvestrant). In addition, Dr. Stabile has demonstrated that the estrogen receptor pathway can cross-talk with the EGFR pathway and targeting both pathways simultaneously using clinically relevant agents show enhanced anti-tumor effects compared to targeting either pathway alone. This drug combination is currently being tested in clinical trials. Dr. Stabile is currently interested in elucidating the role of the newly discovered estrogen receptor, GPR30, which is thought to be responsible for some of the non-genomic actions of estrogen. Figure 3 describes the non-genomic estrogen signaling pathway in the lung that she is studying.

The overall goal for both areas of interest are to test different mechanisms by which these pathways control other growth-promoting proteins in the lung and test both available and novel drugs as single agent or combination therapies using novel animal models of lung cancer to determine how to inhibit these pathways most effectively. Optimal preclinical drugs will ultimately be translated to patient clinical trials.

Jean-Pierre Vilardaga, Ph.D.
Assistant Professor
Ph.D., Free University of Brussels, Belgium, 1996

The Vilardaga laboratory carries an interdisciplinary research program aimed at elucidating molecular mechanisms of signal transduction mediated by G-protein coupled receptors in renal, skeletal and other cell systems.

Fluorescence (e.g., FRET-, TIRF microscopy) techniques are used to study transmembrane signaling and intracellular trafficking mechanisms in the context of neurotransmitter, peptide hormone/G protein-coupled receptor systems.

Particular areas for development include: role of chemokines and receptors in cell polarization, molecular mechanisms by which the parathyroid hormone receptor regulate activity in bone, and regulatory mechanisms controlling the function of vasopressin receptor in kidney.

Dr. Vilardaga's objective is dissecting signaling mechanisms to discover novel principles in molecular medicine that will serve the medical community.

GPCRs are key initiators of biological signaling in virtually every type of cell. They recognize a wide variety of extracellular stimuli (hormones, neurotransmitters, ions, light, odors) and initiate transmembrane signaling to regulate cell behaviors. Their roles in many human pathological conditions underscore the importance of determining the molecular functioning of such receptors.

Adrenergic and peptide receptors, which transmit signals for respectively small neurotransmitters (such as noradrenaline and dopamine) and larger peptide hormones (vasopressin, parathyroid hormone, parathyroid hormone related peptide), are two well characterized distinct subtypes of GPCRs that serve as useful models for analyzing GPCR mechanisms. The objective is to elucidate the general principles of signal transduction from the extracellular ligand binding event to intracellular signaling cascades, which are involved in systems as diverse as neurotransmitter and hormonal signaling.

Using optical methods to monitor receptor activation, Dr. Vilardaga's research is aimed at gaining a better understanding of molecular mechanisms of receptor function. Since the publication of the original technology to record receptor activation in living cells in Nature Biotechnology (Vilardaga et al., July 2003) he has improved the approach to record and also image receptor activation – published in Nature Methods (Hoffman, March 2005). These technologies allow following many fundamental questions in receptor pharmacology: What is the nature of inverse agonism? How do ligands bind receptors? What is the signal transduction mechanism in receptor heterodimers? These questions were recently answered in Nature Chemical Biology (Vilardaga et al., June 2005, and Feb 2008), and in PNAS (Castro, Vilardaga, et al., Nov. 2005). Because this technology is likely to be a new standard for GPCR research, much more fundamental questions are and will be studied in receptor pharmacology, cell biology and physiology.

Andreas Vogt, Ph.D.
Research Assistant Professor
Ph.D., University of Hamburg, Germany

Dr. Vogt's major research interest is the discovery of new therapeutic agents for diseases related to cell proliferation and intracellular signaling. Specific targets of interest are the mitogen-activated protein kinase phosphatases (MKPs), cellular enzymes involved in cancer and inflammation that have thus far eluded discovery efforts. An important part of his research is the development of analysis tools to increase information content of biological assays and to enable small molecule drug discovery screening in whole organisms. It is his

hope that the combination of high information content assays with whole organism models of disease will result in higher quality candidate compounds for drug development.

Dr. Vogt's target-based discovery efforts center around mitogen-activated protein kinase phosphatases or MKPs. One MKP in particular, termed DUSP-1 or CL100, appears to be a mediator of the malignant phenotype. MKP-1 is overexpressed in many human tumors and can protect cells from apoptosis caused by DNA damaging agents or cellular stress, suggesting that inhibitors of MKP-1 might find applications as novel target-based antineoplastic therapies, either alone or in combination with clinically used antineoplastic agents. The search for small molecule inhibitors of MKP-1 has been challenging due to a lack of structural guidance for inhibitor design, ambiguities associated with in vitro assays for phosphatase activity, and the absence of definitive assays to probe MKP-1 inhibition in the context of the living cell. By developing an image-based, definitive cellular assay for MKPs, which he has termed "chemical complementation", Dr. Vogt has circumvented many of the challenges associated with MKP inhibitor discovery, screened several thousand small molecules for MKP inhibition in intact cells, and identified several cell-active inhibitors of MKP-1 and MKP-3. Future work will encompass discovery of multiple classes of MKP inhibitors, refinement of their structures and biological activities, evaluation of their mode of inhibition, and their credentialing as potential therapeutic agents. Recently, Dr. Vogt has extended the concept of chemical complementation to collaborations with members of the zebrafish community on the discovery of inhibitors of MKP-3.

Dr. Vogt's second focus is the continued development of novel drug discovery tools that enhance the information content of small molecule screens. Over the past five years, he has been involved in the establishment of the University of Pittsburgh Drug Discovery Institute (UPDDI) as one of only a handful of academic centers with high-content analysis (HCA) capabilities. HCA is an analysis tool to acquire, analyze, and manage multi-dimensional information about target activity and spatial distribution from individual cells. Our emphasis on HCA has substantially contributed to the UPDDI becoming one of nine national screening centers funded through the NIH roadmap initiative on Molecular Libraries and Imaging. Dr. Vogt's research has contributed to the center four R03 funded high-content screens (two for MKPs, one for microtubule stabilizing agents, and one for autophagy), which he is currently running on 200,000 small molecules from an NIH compound collection.

A natural extension of Dr Vogt's prior HCA work is the expansion of image-based analysis to whole organisms such as zebrafish. This work is based upon the observation that advances in high-throughput screening and laboratory automation have substantially improved the speed of target-based drug discovery but that these efforts have not resulted in increased research productivity. An increasingly popular sentiment is that better models are needed to improve the quality of new drug candidates, and it has been proposed that whole organisms could provide such models. Currently, however, there is no animal model that is compatible with the contemporary paradigm of drug discovery encompassing rapid screening of large compound collections. The zebrafish is an animal model that might fill this void. The NIH is currently supporting a collaboration with Neil Hukriede and Michael Tsang (Department of Molecular Genetics and Biochemistry) aimed at developing novel image-based methods to analyze fluorescent transgenic zebrafish embryos. Of particular interest is an intelligent image analysis method termed Cognition Network Technology (CNT). CNT is different from other image analysis methods in that it processes image information in an object oriented fashion, thereby emulating human cognitive processes.

Daniela Volonte, Ph.D.
Research Instructor
Ph.D., University of Milan, Italy

Tumor development is initiated by a multiplicity of genetic abnormalities. Tumor cells need to escape barriers that limit uncontrolled cell proliferation. One of these barriers is represented by cellular senescence. Cancer cells need to overcome this obstacle to produce a clinically relevant tumor mass. For these reasons, cellular

senescence represents a natural tumor suppressor mechanism. Thus, molecules that regulate cellular senescence are potential therapeutic targets for the treatment of cancer and the fight against aging.

Caveolae are invaginations of the plasma membrane enriched in cholesterol. Caveolin-1, the structural protein component of caveolar membranes, acts as a scaffolding protein to concentrate and functionally regulate signaling molecules.

In recent years, several independent lines of evidence have emerged suggesting that caveolin-1 may function as a "tumor suppressor protein" in mammalian cells. For example, caveolin-1 protein expression has been shown to be absent in several transformed cell lines derived from human mammary carcinomas, including MCF-7. In addition, caveolin-1 mRNA and protein expression are lost or reduced during cell transformation by activated oncogenes, such as v-Abl and H-ras (G12V); caveolae are absent from these cell lines. In addition, the human caveolin-1 gene is localized to a suspected tumor suppressor locus (D7S522; 7q31.1), a known fragile site (FRA7G) that is deleted in many types of cancer.

Oxidative stress is a known inducer of cellular senescence. We have shown that up-regulation of caveolin-1 is required for oxidative stress–induced cellular senescence in fibroblasts. To unravel the molecular mechanisms underlying oxidative stress-induced up-regulation of caveolin-1 in senescent cells, Dr. Volonte has shown that oxidants stimulate the activity of the caveolin-1 promoter reporter gene construct in fibroblasts. She has identified Sp1 binding to two GC-boxes as the core mechanism of oxidative stress–triggered caveolin-1 transactivation. In addition, through signaling studies she has shown p38 mitogen-activated protein kinase (MAPK) as the upstream regulator of Sp1-mediated activation of the caveolin-1 promoter following oxidative stress. For the first time Dr. Volonte has delineated the molecular mechanisms that modulate caveolin-1 gene transcription upon oxidative stress bringing new insights into the redox control of cellular senescence in both normal and cancer cells.

Thus, cellular senescence may represent one of the molecular mechanisms through which caveolin-1 acts as a tumor suppressor protein. Current efforts are aimed at identifying the signaling molecules which link caveolin-1's function to cellular senescence.

Q. Jane Wang, Ph.D.
Assistant Professor
Ph.D., Creighton University

Diacylglycerol (DAG) is a key second messenger in cells. It regulates a variety of fundamental cellular processes by binding to a large family of structurally and functionally divergent protein targets, "the DAG receptors". Deregulated DAG and its receptors actively contribute to the pathogenesis of many diseases including cancer and Type II diabetes.

The overall mission of the laboratory is to determine the function and regulation of these DAG receptors in normal cells and diseases. Current research primarily focuses on protein kinase D (PKD) - a novel family of high affinity DAG receptors, in addition to the best characterized protein kinase C (PKC) family. The PKD family that comprises PKD1, 2, 3 modulates vital cellular functions such as growth, survival, and protein transport. The activity of PKD is controlled by DAG through PKC-mediated phosphorylation. This places PKD downstream of PKC as a unique PKC-regulated DAG targets. However, it remains to be determined whether and how PKD involves in PKC-mediated cellular processes. PKD as a DAG target and a PKC effector has important therapeutic values for diseases with deregulated DAG signaling. Four areas of research are on-going in the laboratory:

The C1 domain is responsible for the binding to DAG and phorbol esters (PE), the pharmacological analogues of DAG. It is a 50 a.a. highly conserved structural motif shared among all DAG receptors. Focusing on the PKD and C1 domain interaction, we have characterized the structural requirements for the binding of PKD C1

domains to DAG and phorbol esters. Individual C1 domains of PKD isoforms selectively bind DAG, implying ligand-specific regulation of PKD isoforms. The relevance of this finding to the regulation of endogenous PKD by endogenously generated DAG is now under investigation.

DAG signaling is critically implicated in acquired insulin resistance. Levels of DAG and activities of certain PKC isoforms are up-regulated in insulin resistant states and Type II diabetes. Here, we are probing a potential role of PKD in the pathogenesis of insulin resistance. The effects of PKD in modulating glucose transport at basal state and in response to insulin stimulation are investigated in fat and muscle cells. Live cell imaging will be employed to evaluate the direct role of PKD in GLUT1 or GLUT4 transporter trafficking. Furthermore, crosstalk to insulin signaling pathways is also exploited as a potential mechanism through which PKD regulates insulin sensitivity and glucose metabolism.

DAG signaling has been implicated prostate cancer carcinogenesis and tumor progression. Isoforms of PKC are differentially involved in the process. The oncogenic PKCε contributes to metastatic transformation of prostate cancer, while PKCδ upon activation by phorbol esters induces apoptosis in androgen-sensitive prostate cancer cells. To gain more insights, we seek to investigate the involvement of PKD as a PKC effector in prostate cancer development. Our study has identified PKD3 as a potential downstream target of PKCε in modulating ERK and Akt activities in androgen-insensitive prostate cancer cells. PKD3 may contribute to prostate cancer progression through a constitutively active PKCε/PKD3 pathway. The study is now extended to other members of the PKD family including PKD1 and PKD2.

This study is conducted in collaboration with the University of Pittsburgh Drug Discovery Institute. We seek to identify highly potent and selective small molecule inhibitors of PKD for clinical application and for dissecting the biological functions of PKD.

Birgitte Wittschieben, Ph.D.
Research Instructor
Ph.D., University of Århus, Denmark

The DNA of living cells suffers constant damage, arising in the cell endogenously and as a result of environmental causes. The cellular response to DNA damage is complex and multi-faceted. My research is focused on a group of DNA polymerases known as translesion synthesis (TLS) polymerases, enzymes that play an essential role in tolerating damage by replication of damaged genomes. TLS polymerases act to bypass sites of DNA damage that the conventional replication machinery is unable to process. The result is restoration of DNA function, but rescue comes at a price, however, as the process of translesion synthesis (TLS) can introduce mutations. In addition, dysfunction of some of these TLS polymerases leads to genome instability. It is important to study TLS polymerases as they are central to the cellular defense of normal and tumor cells against agents that damage DNA, including chemotherapeutic agents. Hence these enzymes may be targets for new therapeutic and preventative strategies against cancer. However, very little is known regarding when and how these TLS polymerases function in the cell.

Dr. Wittschieben's current research is focused on 1) Dissection of functional protein domains in the essential human TLS polymerase POL zeta (REV1, REV3L and REV7). 2) Purification of DNA bypass polymerases from mammalian cells and identification of protein partners. 3) Analysis of how human cells partition and regulate the function(s) of these complexes, both in the absence and presence of genotoxic stress. She is primarily interested in DNA polymerases actively engaged in DNA damage bypass and has developed methods that include analysis of proteins tightly associated with chromatin.

John Wittschieben, Ph.D.
Research Instructor
Ph.D., Cornell University

Dr. Wittschieben's research interests focus on the mechanisms by which mammalian cells tolerate unrepaired DNA damage. DNA polymerase zeta is a key enzyme in an essential process known as translesion synthesis that functions to bypass sites of DNA damage. DNA polymerase zeta helps cells to tolerate diverse types of DNA damage, but at a cost of increased mutation frequency. Rev3L is the catalytic subunit of DNA polymerase zeta in mammalian cells. We have shown that targeted disruption of the mouse *Rev3L* gene causes lethality midway through embryonic gestation and that *Rev3L* null cells exhibit striking chromosomal instability.

The large increase in DNA translocation frequency in *Rev3L* null cells suggests that loss of Rev3L expression could contribute to neoplastic transformation and progression. To determine the importance of DNA polymerase zeta for genome maintenance in the adult mouse, we have developed a transgenic mouse model that generates *Rev3L* null cells in many tissues and organs. The mild to severe reduction in cell viability observed upon complete deletion of *Rev3L* in different adult tissues demonstrates cell-specific requirements for DNA polymerase zeta function. Absence of p53 promotes the ability of *Rev3L* null cells to continue dividing, most likely by removing normal safeguard responses to chromosome breaks. Aggressive cancers constituted by cells with complete *Rev3L* deletion can form in the mouse and indicate a role for DNA polymerase zeta in tumor suppression.

Richard Wood, Ph.D.
Professor
Ph.D., University of California, Berkeley

Many enzymes and regulatory proteins are devoted to the repair of DNA damage. This is necessary because genes are continually assaulted by agents inside cells and from the environment. Much of the work in our laboratory has concentrated on the biochemical mechanism of the DNA nucleotide excision repair pathway in human cells, and we have reconstituted this repair process in the test tube with 25 separate purified proteins. It is important to study DNA repair for two reasons. First, it is the front line defense against DNA damage. Unrepaired DNA damage can lead to mutations that can accumulate to cause cancer. Second, some of the compounds used in cancer chemotherapy and radiotherapy work by damaging DNA. The success of therapy with such agents is affected by repair in normal and tumor tissues. A deeper understanding of DNA repair should allow us to modulate the process in tumors in ways that could improve cancer therapy.

Ongoing projects include biochemical studies of how cells repair cross-links between DNA strands, investigation of newly discovered DNA polymerases that help tolerate DNA damage, genetic analysis of these enzymes in mouse models, and exploration of the role of DNA repair in the sensitivity of tumors to chemotherapeutic drugs.

Jack Yalowich, Ph.D.
Associate Professor
Ph.D., SUNY at Buffalo

Recent studies are focused on understanding the mechanisms by which the clinically effective anticancer agent etoposide (VP-16), a phenolic compound, and the environmental carcinogen, benzene, cause acute myelogenous leukemia (AML). The central testable hypothesis is that redox cycling of VP-16 and phenolic benzene metabolites initiated by myeloperoxidase (MPO) in bone marrow precursors amplifies the genotoxicity and carcinogenicity of these compounds via enhanced topo II inhibition. Nutritional antioxidants such as vitamin C and vitamin E homologs are under investigation as a mechanism-based chemo-prevention strategy to eliminate VP-16- and benzene-induced AML by reducing production of peroxidase-dependent free radical and electrophilic metabolites. The long-term goal of these studies is to increase the clinical efficacy of VP-16 in the treatment of cancer, and to prevent benzene leukemogenesis.

I. Etoposide (VP-16)-related secondary myeloid leukemias (t-AML) are most frequently associated with MLL gene translocations at 11q23. Our central hypothesis is that redox cycling of VP-16 initiated by myeloperoxidase (MPO) found prominently in myeloid precursors amplifies the genotoxicity and carcinogenicity of this otherwise clinically effective DNA topoisomerase II (topo II)-targeted anticancer agent. We propose that MPO converts VP-16 to free radical species and oxidized metabolites that induce oxidative DNA damage and initiate recombinogenic events in myeloid precursor stem cells leading to the chromosomal translocations responsible for t-AML. Specifically, it is proposed: 1) that oxidative DNA damage and abasic DNA sites formed as a consequence of peroxidative activation of VP-16 result in loci that increase topo II poisoning; and/or: 2) that electrophilic VP-16-ortho-quinone formed in MPO-rich progenitors will poison topo II by adduction to sulfhydryl groups on the enzyme. We further posit that nutritional antioxidants such as vitamin C and vitamin E homologs will prevent VP-16-induced AML by reducing or preventing production of peroxidase-dependent free radical and electrophilic metabolites. We propose to determine the mechanism(s) by which peroxidative activation of VP-16 to phenoxyl radical and ortho-quinone metabolites enhances its DNA damaging and recombinogenic activities in genomic regions of the MLL gene known to contain breakpoints associated with t-AML.

II. Benzene-induced acute myeloid leukemia (AML) is a result of exposure to this genotoxicant. Benzene leukemogenesis has been linked to P450-mediated metabolism of benzene to phenolic compounds. In myeloid progenitors, myeloperoxidase (MPO) converts these phenols to redox-reactive and arylating benzene metabolites such as 1,4-hydroquinone and 1,4-benzoquinone. These benzene metabolites are recently demonstrated DNA topoisomerase II (topo II) poisons like the anticancer agent etoposide (VP-16). Etoposide is a phenolic compound known to cause therapy-related AMLs associated with MLL gene translocations. Benzene-induced AML can also display MLL gene translocations. This knowledge serves as the foundation for our central hypothesis that MPO-catalyzed redox cycling of phenolic benzene metabolites in myeloid progenitors yields carcinogenic species linked to poisoning of topo II. Specifically, it is proposed: 1) that oxidative damage and abasic DNA sites formed as a consequence of peroxidative activation of benzene phenols result in loci known to poison topo II; and/or: 2) that benzoquinones formed in MPO-rich progenitors poison topo II by electrophilic adduction to critical sulfhydryl groups. We further posit that nutritional antioxidants such as vitamin C and vitamin E homologs will prevent benzene-induced AML by preventing production or scavenging of MPO-derived free radical and electrophilic metabolites.

Lin Zhang, Ph.D.
Associate Professor
Ph.D., University of Southern California

We are using a variety of approaches to study the genetic basis of differential sensitivity to anticancer drugs in human cancer cells. We are also trying to identify novel genes that can be used for predicting treatment outcomes, and the genetic alterations that cause resistance to anticancer drugs. Our long-term goal is to develop improved strategies and novel agents for chemotherapy and chemoprevention of human cancer.

Common epithelial malignancies, including cancers of breast, colon, prostate, and lung, are often resistant to standard treatments such as chemotherapy and irradiation. We are investigating how apoptosis regulators, including PUMA, Bax and SMAC/Diablo, mediate apoptosis induced by chemotherapeutic agents or irradiation, and whether deregulation of these genes contributes to acquired resistance to anticancer agents. We identified PUMA as a BH3-only Bcl-2 family protein an essential mediator of DNA damage-induced and p53-dependent apoptosis. We also found that the proapoptotic Bcl-2 family protein Bax and the mitochondrial apoptogenic protein SMAC/Diablo mediate apoptosis induced by anticancer agents. Efforts are currently undertaken to restore apoptosis regulation in human cancer cells by using small molecules that activate PUMA

through p53-independent mechanisms, and agents that mimic the functional domains of PUMA or SMAC/Diablo.

Prevention of human cancer through the use of chemical agents such as non-steroidal anti-inflammatory drugs (NSAIDs) has emerged as a promising strategy to reduce morbidity and mortality of cancer. However, the effects of NSAIDs are incomplete and resistance to NSAIDs often develops. The side effects associated with high doses of NSAIDs present a significant obstacle for general use of these agents for cancer prevention. Our studies demonstrated that apoptosis regulators Bax and SMAC/Diablo are both critical mediators of the anticancer effects of NSAIDs in colon cancer cells. We are studying the in vivo functional roles of these genes in chemoprevention using animal models. We are also testing whether manipulation of SMAC or other apoptosis regulators can be used to improve the chemopreventive effects of NSAIDs so that lower doses can be used for chemoprevention.

Lung cancer, the leading cause of cancer-related death in the US, is often detected at late stages and refractory to conventional anticancer therapies. In collaboration with the Lung Cancer Program at the Pittsburgh Cancer Institute, we identified a panel of novel genes that are frequently silenced by promoter hypermethylation in lung cancer. These genes are likely to be useful for early detection of lung cancer.

Study Sections, Advisory Committee Memberships and Editorial Service

Bruce Freeman, Ph.D.
Professor and Chair
Associate Editor:
- Environmental and Nutritional Interactions

Editorial Board:
- Journal of Biological Chemistry
- General Pharmacology: The Vascular System
- Nitric Oxide: Biology and Chemistry
- Critical Care Medicine

Grant Reviewer:
- NCI
- NIEHS

Daniel Altschuler, Ph.D.
Associate Professor
Ad Hoc Reviewer:
- Nature Cell Biology
- Journal of Biological Chemistry
- Proc. Natl. Acad. Sci. USA
- Molecular and Cellular Biology
- Endocrinology
- Molecular Endocrinology
- Molecular Pharmacology
- Journal of Cell Biology
- The Journal of Pharmacology and Experimental Therapeutics
- American Journal of Pathology
- Journal of Cell Science

Thomas Conrads, Ph.D.
Visiting Associate Professor
Ad Hoc Grant Reviewer:
- National Science Foundation
- National Cancer Institute
- Genome Canada
- Zurich Cancer Research Commission

Ad Hoc Reviewer:
- Nature Methods
- Proteomics
- Molecular and Cellular Proteomics
- Journal of Proteome Research
- Analytical Chemistry
- Neuroscience
- Journal of the American Society for Mass Spectrometry
- Electrophoresis
- Expert Reviews in Proteomics
- Molecular Diagnostics
- Biotechniques
- Libertas Academica
- Royal Society

Proteins
Biochimica Biophysica et Acta

Donald DeFranco, Ph.D.
Professor
Study Section:
Biomedical Research and Training (BRT-A) Study Section, NIGMS
Associate Editor:
Molecular Endocrinology
Steering Committee:
Endocrine Society Annual Meeting
Conference Organizer:
Great Lakes Nuclear Receptor Conference
Ad Hoc Grant Reviewer:
American Cancer Society
March of Dimes Birth Defects Foundation
National Science Foundation
NIH NIDDK U19 Program Project Review for "Nuclear Receptors and Coregulators in Health and Disease"
Ad Hoc Reviewer:
American Journal of Physiology
Biochemical Pharmacology
Biochemistry
Biotechniques
Cancer Research
Cell Biology and Toxicology
Cytogenetics and Genome Research
Endocrinology
European Journal of Biochemistry
Experimental Neurology
Immuno Modulation
Journal of American Physiology
Journal of Biological Chemistry
Journal of Cell Biology
Journal of Cell Science
Journal of Cerebral Blood Flow and Metabolism
Journal of Neurochemistry
Journal of Neuroscience
Journal of Steroid Biochemistry and Molecular Biology
Molecular Cell
Molecular Endocrinology
Molecular Biology of the Cell
Molecular and Cellular Biology
Molecular and Cellular Endocrinology
Molecular Pharmacology
Nature Biotechnology
Neurobiology of Disease
Neuroscience
Oncogene
Proceedings of the National Academy of Sciences USA
Trends in Cell Biology
Trends in Endocrinology and Metabolism

Science
Steroids
Urology

W. Chet de Groat, Ph.D.
Professor
Editorial Board:
Journal of Pharmacology and Experimental Therapeutics
Journal of the Autonomic Nervous System
Journal of Neurourology and Urodynamics
Life Sciences
Current Opinion in Central and Peripheral Nervous Systems
Editorial Consultant:
Brain Research
Journal of Neurophysiology
Science
Journal of Urology
Journal Comparative Neurology
European Journal of Pharmacology
Experimental Neurology.

Julie Eiseman, Ph.D.
Associate Professor
Grant Reviewer:
Veteran's Administration Merit Review (Central and local)
NCI, Program Project Grants, STIR/SBIR Developmental Therapeutics
ACS, IRG Grant University of Pittsburgh
Reviewer:
Antimicrobial Agents and Chemotherapy
Cancer Chemotherapy and Pharmacology
Oncology
Research Communications in Molecular Pathology and Pharmacology
Clinical Cancer Research
Journal of Pharmacology and Experimental Therapeutics
Molecular Pharmacology
Journal of AOAC International
Cancer Research
Journal of Photochemistry and photobiology

Peter Friedman, Ph.D.
Professor
Editorial Board:
American Journal of Physiology: Renal Physiology
Journal of Bone and Mineral Research
Reviewer:
National Science Foundation, Panel on Cellular and Molecular Biology
National Science Foundation, Panel on Regulatory Biology
Awards Committee:
American Physiological Society, Chair, 2005-2007

William Furey, Ph.D.
Professor
Ad Hoc Reviewer:
- J. Mol. Biol.
- Biochemistry
- Nature-Structure Biology
- Biochimica et Biophysica Acta
- Acta Crystallographica
- Proc. Natl. Acad. Sci.
- Proteins, J. Biol. Chem.
- Protein Science
- VA Merit Review Proposals

Study Section Member:
- NIH Macromolecular Structure and Function B Study Session

Ferruccio Galbiati, Ph.D.
Associate Professor
Ad Hoc Reviewer:
- Cancer Research
- Molecular Pharmacology
- Journal of Cell Science
- Journal of Applied Physiology
- Experimental Cell Research
- Journal of Molecular Medicine
- Human Genetics
- International Journal of Sports Medicine

Ad Hoc Grant Reviewer:
- Welcome Trust
- Muscular Dystrophy Association (MDA)
- Invited to serve as Ad-hoc reviewer by PTHE study section (NIH)

Pamela Hershberger
Research Assistant Professor
Ad Hoc Reviewer:
- Cancer Chemotherapy and Pharmacology
- Leukemia
- Oncology
- Gene Therapy
- Molecular Pharmacology
- Cancer Research

Jing Hu, Ph.D.
Assistant Professor
Ad Hoc Reviewer:
- Molecular Carcinogenesis and British Journal of Cancer
- Molecular Carcinogenesis
- Experimental Cell Research
- Biochemical Pharmacology
- Current Drug Metabolism

Edwin Jackson, Ph.D.
Professor
NIH Study Section, Permanent member:
Hypertension and Microcirculation)
Editorial Board Memberships:
Hypertension
Journal of Pharmacology & Experimental Therapeutics
Clinical and Experimental Hypertension
American Journal of Physiology - Renal Physiology
American Journal of Physiology - Regulatory, Integrative and Comparative Physiology
American Journal of Physiology – Heart and Circulatory Physiology
Journal Refereeing:
American Journal of Hypertension
American Journal of Physiology
Biochemical Pharmacology
Cardiovascular Research
Circulation
Circulation Research
Clinical and Experimental Hypertension
Clinical Pharmacology and Therapeutics
Hypertension
Journal of Cardiovascular Pharmacology
Journal of Clinical Investigation
Journal of Laboratory and Clinical Medicine
Journal of Pharmacology and Experimental Therapeutics
Kidney International
Life Sciences
Molecular Pharmacology
Nephrology Dialysis Transplantation

Yu Jiang, Ph.D.
Associate Professor
Ad Hoc Reviewer:
Cancer Research
EMBO J
FEM Yeast
Mol. Biol. Cell
Molecular carcinogenesis
Mol. Cell Biol.
Molecular Pharmacology
Yeast
Ad Hoc Grant Reviewer:
National Science Foundation

Paul Johnston, Ph.D.
Research Associate Professor
Ad Hoc Reviewer:
Journal of Leukocyte Biology
Biochemical Pharmacology
Arthritis and Rheumatism
International Journal of Immunopharmacology
Journal of Biomolecular Screening

Drug Discovery Today
Assays and Drug Development Technologies
Molecular Pharmacology

Grant Reviewer:

USDA - National Research Initiative Competitive Grants Program - Sustaining Animal Health & Well Being.
North Carolina Biotechnology Center "Collaborative Funding Assistance Program."
CHDI, Inc., MRSSI, Inc., and High Q Foundation for Huntington Disease (HD).
North Carolina Biotechnology Center "The Institutional Development Grant (IDG) Program"

Joan M. Lakoski, Ph.D.
Professor

Editorial Board:

Aging Cell

Study Section:

Neuroendocrinology, Neuroimmunology and Behavior

Committee Memberships:

Program Committee, National CTSA K12 Clinical Scholars Annual Meeting
Leadership Development Institute for National Postdoctoral Association
Society for Executive Leadership in Academic Medicine
The Committee on Teaching, IUPHAR

John Lazo, Ph.D.
Allegheny Foundation Professor

Reviewer:

Proceeding of the National Academy of Sciences USA
Cancer Research
Nature Reviews Cancer
Pharmacology and Therapeutics
Molecular Interventions
Journal of Molecular Biology
Cancer Chemotherapy and Pharmacology
European Journal of Cancer
Biochemical Pharmacology
Journal of Pharmacology and Experimental Therapeutics
British Journal of Cancer
Molecular Cancer Therapeutics

Grant Reviews:

NIH Special Emphasis Panel. RFA-RM-06-004: "Pilot-Scale Libraries for High-Throughput Screening"
NIH Special Emphasis Panel. RFA-RM-06-004: "Assay Development for High Throughput Molecular Screening"
Unité de Support à l'Agence nationale de la Recherche, Agence Nationale de la Recherche, France
Veterans Administration Competitive Pilot Fund Program

Committee Memberships:

University of New Mexico Cancer Research and Treatment Center – Scientific Advisory Board Member
Roswell Park Memorial Cancer Institute, Scientific Advisory Board Member
American Association for Cancer Research (AACR), Program Committee Member
American Society for Pharmacology and Experimental Therapeutics (ASPET), Board of Publications

Edwin Levitan, Ph.D.
Professor
Study Section Member:
Molecular Endocrinology

Adrian Sculptoreanu, Ph.D.
Research Assistant Professor
Ad Hoc Reviewer:
Canadian Journal of Physiology and Pharmacology.
Pflügers Archives.
American Journal of Physiology.
Molecular and cellular biochemistry.
Journal of Neurophysiology.

Jill Siegfried, Ph.D.
Professor
Committee Member:
Subcommittee A - Cancer Centers of the National Institute Initial Review Group Member
JCA-AACR Joint Special Conference on Lung Cancer Organizing Committee
14th Investigators' Workshop Planning Committee
Grants Reviewer:
NIH/DHHS/PHS, RFA CA-06-014 Tumor Microenvironment Network Review Committee
Associate Editor:
Cancer Research 2005-
Molecular Pharmacology, 2003-present
Editorial Board:
Clinical Lung Cancer 2000-present
Ad Hoc Reviewer:
Cancer Research
American Journal of Respiratory and Critical Care Medicine
American Journal of Respiratory Cell and Molecular Biology
Journal of the National Cancer Institute
Molecular Pharmacology
Experimental Lung Research
Lung Cancer
Radiation Research
Carcinogenesis
Molecular Carcinogenesis
American Journal of Physiology
British Journal of Cancer

Shivendra Singh, Ph.D.
Professor
Study Section Member:
Chemo/Dietary Prevention Study Section
Editorial Board:
Bulletin of Environmental Contamination and Toxicology
International Journal of Molecular Medicine
Molecular Pharmacology
Oncology
Ad Hoc Reviewer:
Archives of Biochemistry and Biophysics

Biochimica et Biophysica Acta
Biochemical Pharmacology
Cancer Research
Carcinogenesis, Molecular Carcinogenesis
Molecular Pharmacology
Molecular Cancer Therapeutics
Biochemistry

Robert Sobol, Ph.D.
Assistant Professor
Editorial Board:
DNA Repair

Sanjay Srivastava, Ph.D.
Research Assistant Professor
Ad Hoc Reviewer:
Nature
Cancer Research
Molecular Pharmacology
Carcinogenesis
International Journal of Cancer
Neoplasia
Grant reviewer:
Komen Breast Cancer Foundation, Risk and Prevention, Epidemiology Study Section
Irish Health Research Board, Ireland, 2006.

Laura Stabile, Ph.D.
Research Assistant Professor
Ad Hoc Reviewer:
American Journal of Physiology- Lung Cellular and Molecular Physiology
Steroids
Molecular Carcinogenesis
Grant reviewer:
Komen Breast Cancer Foundation Grants

Changfeng Tai, Ph.D.
Research Assistant Professor
Reviewer:
Journal of Spinal Cord Medicine
IEEE Transactions on Biomedical Engineering

Q. Jane Wang, Ph.D.
Assistant Professor
Reviewer:
BBA-Molecular and Cell Biology of Lipids
Molecular Pharmacology
Grant Reviewer:
US Army DoD Study Section, HBCU/MI Collaborative and Partnership Awards
US Army DoD Study Section, Breast Cancer Research Program-Concept Award

Birgitte Wittschieben, Ph.D.
Research Instructor
Ad Hoc Reviewer:
- Molecular cell
- DNA repair
- EMBO Journal
- Molecular and Cellular Biology
- Nucleic Acid Research

Grant Reviewer:
- Review of Cottrell Scholar award for the Research Corporation

John Wittschieben, Ph.D.
Research Instructor
Ad Hoc reviewer:
- European Molecular Biology Organization
- Molecular and Cellular Biology
- DNA Repair
- Nucleic Acids Research

Richard Wood, Ph.D.
Professor
Reviewer:
- EMBO Journal & EMBO Reports
- Nucleic Acids Research

Editorial Board
- DNA Repair

Associate Editor
- Molecular Carcinogenesis

Ad Hoc Reviewer:
- Science
- Cell
- Nature
- EMBO J.
- Molec. Cell Biol.
- J. Biol. Chem.

Jack Yalowich, Ph.D.
Associate Professor
Ad Hoc Reviewer:
- Cancer Research
- Clinical Cancer Research
- Biochemical Pharmacology
- Molecular Pharmacology
- Journal of Clinical Investigation
- Oncology Research
- Cancer Chemotherapy and Pharmacology
- Head and Neck
- Journal of the National Cancer Institute
- Molecular and Cellular Biology
- Biochimica Biophysica Acta
- Cancer Investigation
- Journal of Biological Chemistry

Journal of Pharmacology and Experimental Therapeutics
Biochemistry, Toxicology and Applied Pharmacology
Chemico-Biological Interactions
Proceedings of the National Academy of Science
Leukemia

Study Section Member:
NIH, BMCT (Biochemical Mechanisms of Cancer Therapy) Study Section

Lin Zhang, Ph.D.
Associate Professor
Ad Hoc Reviewer:
Science
Molecular Cell
Proc. Natl. Acad. Sci. USA
EMBO Journal
Cancer Research
Journal of Biological Chemistry
Clinical Cancer Research
Oncogene
Molecular Cancer Therapeutics
Trends in Biotechnology
Journal of Clinical Oncology
American Journal of Pathology
Journal of Cellular Physiology
Leukemia
DNA repair
International Journal of Cancer
Cancer Biology & Therapy
Gut
Gastroenterology
Biotechniques
Molecular Pharmacology
Expert Opinion on Therapeutic Targets
Brain Research
Cancer Letters
Oncology
BMC Genomics

Grant Ad Hoc Reviewer:
Medical Research Council (MRC), UK
Michael Smith Foundation for Health Research (MSFHR), Canada
National Natural Science Foundation (NSFC), P.R. China
Maryland Technology Development Corporation (TEDCO), MD
The Dutch Society for Cancer Research, Netherlands

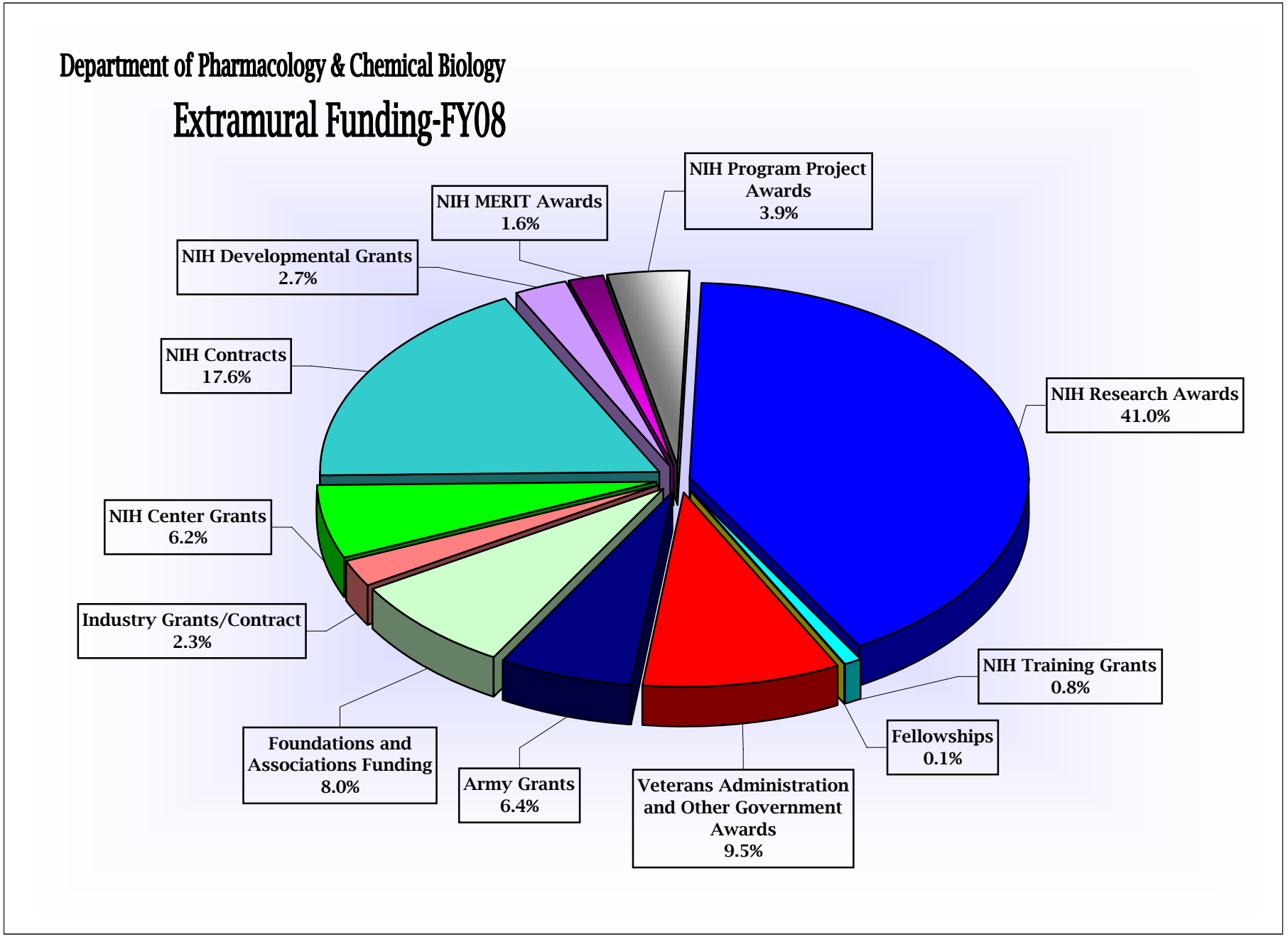
Research Grant & Contract Activity

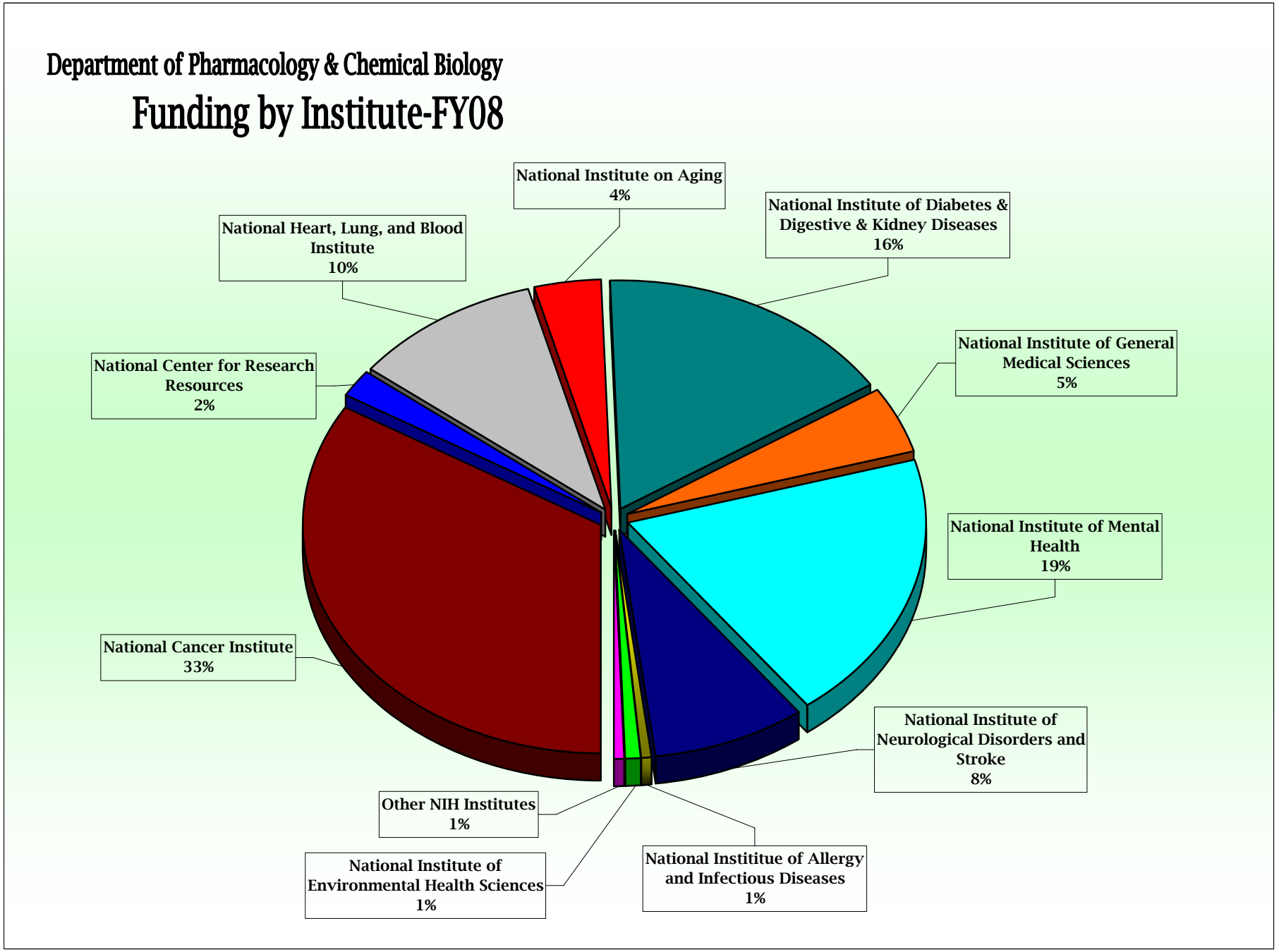
Trends in Research Support

Department of Pharmacology & Chemical Biology
FY08 Extramural Sponsored Project Funding

Army Grants	$1,309,296
Foundations and Associations Funding	$1,640,744
Industry Grants/Contract	$462,907
NIH Center Grants	$1,271,891
NIH Contracts	$3,613,059
NIH Developmental Grants	$549,074
NIH MERIT Awards	$335,591
NIH Program Project Awards	$794,290
NIH Research Awards	$8,402,663
NIH Training Grants	$163,451
Fellowships	$10,758
Veterans Administration and Other Government Awards	$1,953,005
Total Extramural Funding	**$20,506,729**

National Cancer Institute	$4,945,370
National Center for Research Resources	$293,651
National Heart, Lung, and Blood Institute	$1,497,935
National Institute on Aging	$545,164
National Institute of Diabetes & Digestive & Kidney Diseases	$2,413,718
National Institute of General Medical Sciences	$687,881
National Institute of Mental Health	$2,817,946
National Institute of Neurological Disorders and Stroke	$1,226,497
National Instititue of Allergy and Infectious Diseases	$102,104
National Institute of Environmental Health Sciences	$99,483
Other NIH Institutes	$98,178
Total National Institutes of Health Funding	**$14,727,927**


Department of Pharmacology & Chemical Biology
Extramural Funding-FY08
NIH Program Project Awards 3.9%
NIH MERIT Awards 1.6%
NIH Developmental Grants 2.7%
NIH Contracts 17.6%
NIH Research Awards 41.0%
NIH Center Grants 6.2%
Industry Grants/Contract 2.3%
NIH Training Grants 0.8%
Fellowships 0.1%
Foundations and Associations Funding 8.0%
Army Grants 6.4%
Veterans Administration and Other Government Awards 9.5%


Department of Pharmacology & Chemical Biology
Funding by Institute-FY08
National Institute on Aging
4%
National Institute of Diabetes & Digestive & Kidney Diseases
16%
National Heart, Lung, and Blood Institute
10%
National Institute of General Medical Sciences
5%
National Center for Research Resources
2%
National Institute of Mental Health
19%
National Cancer Institute
33%
National Institute of Neurological Disorders and Stroke
8%
Other NIH Institutes
1%
National Institute of Environmental Health Sciences
1%
National Instititue of Allergy and Infectious Diseases
1%

Last Name	Identifier	Agency Name	Title	Begin Date	End Date	Annual DC	Annual IDC	Annual TC
ALTSCHULER	R21 RR021708	National Institutes of Health	A Universal Mouse Line to Assess Tumor Clonality	08/03/05	07/31/08	$67,765	$32,866	$100,631
ALTSCHULER	R01 DK063069	National Institutes of Health	Rap 1B a Mitogenic Signal in Thyroid	07/01/03	05/31/08	$94,399	$36,757	$131,156
ALTSCHULER	R01 CA071649	National Institutes of Health	Transduction of Camp Signal by Rap 1	03/12/04	02/28/09	$173,928	$79,521	$253,449
ALTSCHULER	NIEHS P4508635	Courtesy Associates	IPA-Design Environmentally Sensitive Murine Thyroid Cancer Model Based on Expression of Mutated RAP	05/01/03	03/31/08	$69,783	$0	$69,783
BAKER	ADA	American Diabetes Association	Characterization of Nitrated Fatty Acids as Partial PPARgamma Agonists	07/01/06	06/30/09	$120,000	$18,000	$138,000
BISELLO	R01DK071158	National Institutes of Health	PTH Receptors in Vascular Smooth Muscle Cells	10/01/06	04/30/10	$162,120	$71,144	$233,264
BISELLO	R01DK051081	National Institutes of Health	Pathophysiology of PTH-related Protein (1-36) in Humans	04/01/07	03/31/08	$8,188	$3,971	$12,159
BISELLO	R01DK073039	National Institutes of Health	Modeling Bone Formation and 125 Vitamin D in Humoral Hypercalcemia of Malignancy	04/01/08	06/01/10	$2,829	$1,372	$4,201
CONRADS	R21 AI068784	National Institutes of Health	A Quantitative Proteomic Study of myD88 Pathway	03/01/07	02/28/09	$2,100	$1,018	$3,118
CONRADS	P50 CA090440	National Institutes of Health	SPORE in Lung Cancer - Project 3	05/01/08	04/30/11	$7,007	$3,399	$10,406
CONRADS	R43 CA132081	Expression Pathology	Quantitative Proteomics of Metastasis	05/01/08	04/30/09	$5,000	$0	$5,000
CONRADS	VUMC 31980-R	Vanderbilt University	Molecular Signatures of Lung Cancer	06/01/07	05/31/08	$13,748	$2,063	$15,811
CONRADS	2007 Hillman	Hillman Foundation	Hillman Y2 - Conrads	01/01/07	02/29/08	$52,184	$0	$52,184
CONRADS	081RA01	DSF Foundation	DSF Clinical Proteomics - Master	02/01/08	01/31/10	$165,359	$0	$165,359
CONRADS	081RA01	DSF Foundation	DSF Clinical Proteomics - Junior Pilot	02/01/08	01/31/10	$25,000	$0	$25,000
CONRADS	081RA01	DSF Foundation	DSF Clinical Proteomics - Senior Pilot	02/01/08	01/31/10	$12,500	$0	$12,500
CONRADS	3401 2919	Magee Womens Research Institute	Biomarker Discovery in Ovarian Cancer	04/01/08	03/31/09	$7,130	$0	$7,130
CONRADS	W81XWH-05-2-0005	US Army	Gynecologic Disease Program - Supplement	10/20/04	01/31/08	$95,183	$46,164	$141,347
CONRADS	W81XWH-05-2-0066	US Army	Proteomics and Bioinformatics Core Facilities	07/01/05	10/25/08	$430,808	$27,067	$457,875
DEFRANCO	F30 NS053013	National Institutes of Health	Signaling Mechnisms Behind nAChR Clustering at the NMJ	07/01/07	06/30/09	$10,758	$0	$10,758
DEFRANCO	R01 DK078394	National Institutes of Health	Intracellular mechanisms of glucocorticoid action	07/01/07	06/30/12	$184,500	$89,125	$273,625

Last Name	Identifier	Agency Name	Title	Begin Date	End Date	Annual DC	Annual IDC	Annual TC
DEFRANCO	R01 NS049560	National Institutes of Health	The Life History of Mitochondria in Neurons	09/01/04	06/30/08	$231,250	$110,686	$341,936
DEFRANCO	T32 GM008424	National Institutes of Health	Predoctoral Training in Pharmacological Sciences	07/01/05	06/30/10	$156,004	$7,447	$163,451
DEGROAT	R01 DK066138	National Institutes of Health	Proteomic Charaterization of IC Bladder	09/30/03	07/31/07	$1,291	$609	$1,899
DEGROAT	R01 DK068557	National Institutes of Health	Afferent Modulation in Bladder Dysfunction	01/01/04	12/31/07	$5,643	$2,737	$8,380
DEGROAT	R01 DK064280	National Institutes of Health	Study of Intrinsic Bladder Activity by Optical Imaging	01/15/04	11/30/07	$2,240	$1,086	$3,326
DEGROAT	R01 DK067226	National Institutes of Health	Neurophysiology and Biomechanics of Urethera and SUI	04/01/04	03/31/09	$16,311	$7,911	$24,222
DEGROAT	R01 HL57929	National Institutes of Health	Factors that initiate arrhythmias in the long QT syndrome	04/01/04	03/31/08	$7,784	$3,776	$11,560
DEGROAT	R01 DK071085	National Institutes of Health	Roles of Nitric Oxide and Superoxide in Cystitis	08/01/05	05/31/10	$10,839	$5,257	$16,096
DEGROAT	R01 DK057267	National Institutes of Health	Afferent Plasticity Underlying Urethral and Pelvic Pain	03/01/06	11/30/10	$7,624	$3,697	$11,321
DEGROAT	R01 DK077783	National Institutes of Health	Neuroplasticity of Urinary Tract Disorders after SCI	05/01/07	04/30/11	$140,410	$67,614	$208,024
DEGROAT	Procter & Gamble	Procter & Gamble, Inc.	Evaluation of the effects of beta-adrenergic receptor agonists on voiding function in normal and chronically ovariectomized rats	06/01/07	06/01/08	$63,036	$12,607	$75,643
DEGROAT	NAKFI SPO2	W.M. Keck Foundation	Neuromodulation of the External Urethral Sphincter to Promote Voiding after Spinal Cord Injury	05/01/07	04/30/08	$50,000	$12,500	$62,500
DEGROAT	R37 DK049430	National Institutes of Health	Afferent Mechanisms Underlying Bladder Pain- MERIT AWARD	05/15/05	02/28/10	$229,024	$106,567	$335,591
EISEMAN	P01 CA078039	National Institutes of Health	Combinatoral Approcahes for novel Anticancer Agents	12/14/09	12/14/09	$137,393	$6,305	$143,698
EISEMAN	R01 CA121105	National Institutes of Health	SMAC in Chemoprevention of Colon Cancer	12/14/09	12/14/09	$2,097	$1,017	$3,113
EISEMAN	U01 CA99168	National Institutes of Health	Phase I Clinical Trails of Novel Anticancer Agents	12/14/09	12/14/09	$3,664	$1,777	$5,441
EISEMAN	N01-CM-52202	National Institutes of Health	Preclinical Pharmacological Studies of Antitumor and Other Therapeutic Agents	12/15/04	12/14/09	$281,300	$91,872	$373,172
EISEMAN	GC 193460 NGC	Boston University	Optical Spectroscopy For Management Of Cancer Treatment	09/01/04	08/31/09	$29,962	$9,516	$39,478
EISEMAN	NDC E6S	Endece LLC	In vivo Plasma Pharmacokinetics of NDC E6S	12/14/09	12/14/09	$21,298	$5,324	$26,621
EISEMAN	CHP Acct #H0102	Children's Hospital of Pittsburgh	Evaluation of Molecular Inhibitors of the C MYC Oncoprotein	12/14/09	12/14/09	$1,684	$816	$2,500

Last Name	Identifier	Agency Name	Title	Begin Date	End Date	Annual DC	Annual IDC	Annual TC
FREEMAN	P30 DK046204	University of Pittsburgh Obesity and Nutrition Research Center	Nitro-Fatty Acid Modulation Type II Diabetes	08/01/07	03/31/08	$16,875	$8,184	$25,059
FREEMAN	R01 HL058115	National Institutes of Health	Nitric Oxide Regulation of Vascular Oxidant Injury	03/01/06	05/31/13	$309,633	$147,200	$456,832
FREEMAN	R01 HL064937	National Institutes of Health	Nitric Oxide-Dependent Oxidative Lung Injury	06/21/06	03/31/10	$262,719	$118,919	$381,638
FREEMAN	R03 TW007431	National Institutes of Health	Anti Inflammatory Properties of Cholesteryl Linoleate Derived Nitrated Lipids	03/17/06	02/28/09	$30,122	$5,953	$36,075
FRIEDMAN	R21 DK075014	National Institutes of Health	Novel Regulatory Mechnisms Controlling Bone Repair and Osteoporosis	07/01/07	06/30/09	$125,000	$60,625	$185,625
FRIEDMAN	R01 DK054171	National Institutes of Health	PTH Receptor: Function Meets Form	07/01/03	04/30/12	$224,848	$105,173	$330,020
FRIEDMAN	R01 DK054171	National Institutes of Health	Cellular Calcium Transport in Urinary Epithelia-Minority Supplement	12/01/04	04/30/08	$21,181	$10,273	$31,454
FRIEDMAN	R01 DK069998	National Institutes of Health	EBP50 Regulation of PTH Receptor Signaling and Trafficking	02/01/06	01/31/11	$199,055	$96,542	$295,597
FUREY	P01 CA078039	National Institutes of Health	Combinatorial Approaches for Novel Anticancer Agents	07/01/06	06/30/10	$7,739	$3,753	$11,492
FUREY	R01 GM061791	National Institutes of Health	Pyruvate Dehydrogenase E1: Structure-Function Studies	09/01/04	08/31/08	$142,000	$68,870	$210,870
GALBIATI	R01 AG022548	National Institutes of Health	Role of Caveolin-1 in Cellular Senescence & Aging	01/01/05	12/31/09	$170,751	$78,816	$249,567
HERSHBERGER	R21 CA125514	National Institutes of Health	A Nuclear Biosensor for Identification and Isolation of Nuclear Hormone Receptor Ligands	07/01/06	06/30/09	$3,894	$1,889	$5,783
HERSHBERGER	P50 CA090440	National Institutes of Health	SPORE in Lung Cancer - Project 1	06/01/06	04/30/11	$3,192	$1,548	$4,740
HERSHBERGER	P30 CA047904	National Institutes of Health	CCSG - Pilot Hershberger	06/01/07	07/31/09	$12,500	$6,063	$18,563
HERSHBERGER	Signaling Pathways	Endece LLC	Analysis of the Anti-Proliferative Activity and Signaling Pathways Induced by NDC 1022 in NSCLC Cells	06/01/07	05/31/11	$35,802	$8,951	$44,753
HERSHBERGER	Signaling Pathways	Endece LLC	Analysis of the Anti-Proliferative Activity and Signaling Pathways Induced by NDC 1022 in NSCLC Cells	01/01/08	04/30/09	$11,898	$2,975	$14,873
HERSHBERGER	2007 Hillman	Hillman Foundation	Improving Vitamin Das a Treatment for Lung Cancer	01/01/06	12/31/07	$14,679	$0	$14,679
HERSHBERGER	M2006-0039	Pittsburgh Foundation	CYP24 as a New Diagnostic Prognostic Marker and Therapeutic Target in Lung Cancer	08/01/06	07/31/08	$47,861	$0	$47,861
HU	K22 CA111394	National Institutes of Health	Regulation of NF kB2 by TSA Role of Acetylation	09/01/05	08/31/08	$143,825	$11,506	$155,331
HU	Hillman Y3	Hillman Foundation	Target Deregulation Transcription Factors and Co Factors	01/01/07	01/31/08	$28,124	$0	$28,124

Last Name	Identifier	Agency Name	Title	Begin Date	End Date	Annual DC	Annual IDC	Annual TC
HU	X Linked Gene Gastrin	The Joan Scarangello Foundation	Targeting the Gastrin releasing peptide receptor and peidermal growth factor receptor in female patitents with non-small cell lung cancer.	01/01/07	12/31/08	$50,000	$0	$50,000
HU	M2007-0054	Pittsburgh Foundation	Role of Translational Control in Anti Cancer Effects of PEITC	07/01/07	06/30/09	$72,556	$0	$72,556
JACKSON	R01 HL069846	National Institutes of Health	Potentiation of Ang II Induced Vasoconstriction	05/01/07	03/31/12	$251,960	$119,290	$371,250
JACKSON	R01 NS040125	National Institutes of Health	Mechanisms of Chronic Dysfunction after Brain Trauma	04/01/05	03/31/10	$17,222	$8,353	$25,575
JIANG	R21 NS058463	National Institutes of Health	Regulation of GTPase activity of LRRK2 and its implication in Parkinson's Disease	04/01/08	03/31/10	$2,200	$1,117	$3,317
JIANG	R01 GM068832	National Institutes of Health	The Role of PP2A in Yeast Cell Cycle Progression	02/01/05	01/31/10	$151,709	$73,579	$225,288
JIANG	R01 CA129821	National Institutes of Health	The Role of FKBP38 in tumorigenesis associated with Tsc deficiency	04/01/08	01/31/13	$42,884	$21,764	$64,647
KINCHINGTON	P50 CA090440	National Institutes of Health	Transgenic Mouse Model Overexpressing the Gastrin Releasing Peptide Receptor for Novel Therapeutic Evaluation.	01/01/08	12/31/08	$10,574	$5,128	$15,702
LAKOSKI	UPMC-CMRF	UPMC-Competitive Medical Research Fund	In Vivo Imaging of Serotonin Transporter Function in the Aging Brain	10/01/04	09/30/07	$1,563	$0	$1,563
LAZO	P01 CA078039	UPMC-Competitive Medical Research Fund	Combinatorial Approaches for Novel Anticancer Agents - Project 3	07/01/07	06/30/08	$152,591	$74,007	$226,598
LAZO	P01 CA078039	UPMC-Competitive Medical Research Fund	Combinatorial Approaches for Novel Anticancer Agents - Core A	07/01/07	06/30/08	$32,973	$15,992	$48,965
LAZO	P01 CA078039	UPMC-Competitive Medical Research Fund	Combinatorial Approaches for Novel Anticancer Agents - Core B	07/01/07	06/30/08	$139,139	$67,484	$206,623
LAZO	U19 AI068021	UPMC-Competitive Medical Research Fund	Mitochondrial Targeting Against Radiation Damage	09/01/07	08/31/08	$57,223	$28,040	$85,263
LAZO	U19 CA052995	University of Texas	Cancer Stress Relevant Protein Phosphatase	05/01/07	04/30/08	$83,834	$40,660	$124,494
LAZO	U54 MH074411	University of Texas	Pittsburgh Molecular Libraries Screening Center - Core 1	07/01/07	06/30/08	$422,351	$198,512	$620,863
LAZO	U54 MH074411	University of Texas	Pittsburgh Molecular Libraries Screening Center - core 5	07/01/07	06/30/08	$376,999	$182,845	$559,844
LAZO	U54 MH074411	University of Texas	Pittsburgh Molecular Libraries Screening Center - Outreach	07/01/07	06/30/08	$70,057	$33,978	$104,035
LAZO	U54 MH074411	University of Texas	Pittsburgh Molecular Libraries Screening Center - Core 2	07/01/07	06/30/08	$913,385	$442,992	$1,356,377
LAZO	U54 MH074411	University of Texas	Pittsburgh Molecular Libraries Screening Center - Raw Data Supplement	07/01/07	06/30/08	$125,000	$35,309	$160,309
LAZO	U54 RR022241	Cernegie Mellon University	Flourescent Probes & Imaging for Networks and Pathways	07/01/07	06/30/08	$129,980	$63,040	$193,020

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LAZO	SAP 4100027294	PA Department of Health	Detection, Diagnosis and Intervention in Dementia	06/01/07	05/31/08	$115,045	$55,798	$170,843
LAZO	SAP 4100026429	PA Department of Health	Small Molecule Protein Disruption Targeting Orphan Diseases	01/01/07	12/31/08	$1,782,162	$0	$1,782,162
LAZO	W81XWH-07-1-0396 612	Department of Defense	Antimalarial and Antileishmanial Drug Discovery	04/01/07	03/31/08	$452,188	$170,418	$622,606
LEVITAN	R01 NS032385	National Institutes of Health	Channels, Calcium and Peptide Secretion	06/01/04	05/31/12	$264,800	$91,497	$356,297
LEVITAN	R01 NS053050	National Institutes of Health	Regulation of Dopamine Neuron Excitability	04/01/05	03/31/09	$188,312	$83,246	$271,558
LEVITAN	R01 HL080632	National Institutes of Health	Long-Term Regulation of Potassiun Channels	12/20/05	11/30/09	$186,300	$90,355	$276,655
LEVITAN	R01 DK054824	National Institutes of Health	Nitric Oxide in Bladder Neural-Epithelial Signaling	04/01/07	03/31/12	$3,518	$1,706	$5,224
LEVITAN	U54 MH07441	National Institutes of Health	Pittsburgh Molecular Libraties Screnning Center- Core 1	07/14/06	06/30/08	$6,953	$3,372	$10,325
MAKHINA	R03 DA026212	National Institutes of Health	High Throughput Screening for Potassium Channel Modulators	06/01/08	05/31/09	$1,375	$708	$2,083
NICHOLS	Signaling Pathways	Endece LLC	Analysis of the Anti-Proliferative Activity and Signaling Pathways Induced by NDC 1022 in NSCLC Cells	01/01/08	04/30/09	$5,289	$1,323	$6,612
NICHOLS	NDC-1022	Endece LLC	Validation of Gene Targets Identified in Microarray Studies and Concomitant Development of an NDC-1022 Signal Trandsuction Pathway in NSCLC Cells	01/01/08	04/30/09	$1,841	$460	$2,301
NICHOLS	NDC-E65	Endece LLC	Mechanistic Analysis of Endece Anticancer Drugs	02/21/07	12/31/07	$38,257	$9,564	$47,821
PALLADINO	R25 GM073176	National Institutes of Health	PITT-SPURG Summer Program for Undergrad Research Growth	04/01/05	03/31/09	$81,733	$6,539	$88,272
PALLADINO	R01 AG025046	National Institutes of Health	Understanding Mechanisms of Neuropathogenesis	05/01/06	04/30/11	$199,055	$96,542	$295,597
PALLADINO	U54MH 074411	National Institutes of Health	Pittsburgh Molecular Libraries Screening Center-Core 2	07/14/06	06/30/08	$4,171	$2,022	$6,193
PALLADINO	M2005-0068	The Pittsburgh Foundation	PINK 1 in Neurodegeneration : A Multidisiciplinary Approach	08/15/05	08/14/07	$5,318	$0	$5,318
PALLADINO	M2005-0068	American Heart Association	Understanding Mechanisms of Mitochondrail Dysfunction & Progressive Encephalomypathies	01/01/06	12/31/09	$59,091	$5,909	$65,000
PALLADINO	ASPET	American Society for Pharmacology and Experimental	Summer Undergraduate Research Fellowships (SURF)	06/01/06	05/31/09	$9,000	$0	$9,000
PALLADINO	Jun-47	United Mitochondrial Disease Foundation	Devloping Therapies for Mitochondrail Disease	09/01/06	08/31/08	$44,062	$4,895	$48,957
ROMERO	6121002	Department of Defense	Antimalarial and antileishmanial drug discovery: in vitro and cell-based screening of novel chemical entities and combination therapies	04/01/07	03/31/08	$58,901	$28,567	$87,468

Last Name	Identifier	Agency Name	Title	Begin Date	End Date	Annual DC	Annual IDC	Annual TC
ROPPOLO	P50 DK064539	National Institutes of Health	Women's Health & Functional Visceral Disorders Center	09/01/07	08/31/08	$8,060	$3,974	$12,034
ROPPOLO	R01 NS045078	National Institutes of Health	Suprapontine Control of Micturition	12/15/02	11/30/07	$26,389	$12,327	$38,716
ROPPOLO	R01 DK064280	National Institutes of Health	Study of Intrinsic Bladder Activity by Optical Imaging	01/01/04	11/30/08	$9,723	$4,715	$14,438
ROPPOLO	R01 DK06429	National Institutes of Health	Role of Nitric Oxide in Interstitial Cystitis	08/01/05	06/30/09	$10,668	$5,174	$15,842
ROPPOLO	R01 EB007749	National Institutes of Health	Somatosensory feedback for controlling a neuroprosthesis	09/01/07	05/31/12	$3,602	$1,747	$5,348
ROPPOLO	R01 NS051671	National Institutes of Health	Locomotion Control by Lumbar Spinal Cord Injury	01/01/08	12/31/08	$13,779	$6,683	$20,462
ROPPOLO	R01 DK068566	National Institutes of Health	Bladder and Sphincter Control After Spinal Cord Injury	12/01/07	06/30/08	$8,170	$3,963	$12,133
ROPPOLO	Recordati	Recordati	The Role of Centeral Neurotransmitters in Overactive Bladders	01/01/07	12/31/08	$15,000	$2,250	$17,250
ROPPOLO	991764754	Ethicon, Inc.	Ethicon Corporate Research Agreement	12/15/07	12/31/11	$3,418	$854	$4,272
SCHOPFER	0665418U	American Heart Association	PPARgamma Regulation by Endogenous Nitro-Fatty Acids	07/01/06	06/30/08	$45,455	$4,545	$50,000
SHARLOW	R03 DA024898	American Heart Association	IMAP-Based Fluorescent Palarization Assay for High Throughput Screening	09/01/07	08/31/08	$0	$0	$0
SIEGFRIED	P50 CA097190	National Institutes of Health	Specialized Program of Research Excellence in Head and Neck Cancer- Head and Neck SPORE Project 4	07/01/04	06/30/09	$98,157	$46,124	$144,281
SIEGFRIED	P50 CA090440	National Institutes of Health	SPORE in Lung Cancer/Proj I Sub 2	09/13/06	04/30/11	$101,726	$45,867	$147,593
SIEGFRIED	P50 CA090440	National Institutes of Health	SPORE in Lung Cancer - UCLA Supplement	06/01/06	04/30/11	$50,364	$24,427	$74,791
SIEGFRIED	P50 CA090440	National Institutes of Health	SPORE in Lung Cancer - Minority Supplement	06/01/06	04/30/11	$79,187	$38,010	$117,197
SIEGFRIED	P50 CA090440	National Institutes of Health	SPORE in Lung Cancer - Project 1	06/01/06	04/30/11	$73,988	$35,514	$109,503
SIEGFRIED	P50 CA090440	National Institutes of Health	SPORE in Lung Cancer - Administrative Core	06/01/06	04/30/11	$245,495	$117,837	$363,332
SIEGFRIED	P50 CA090440	National Institutes of Health	SPORE in Lung Cancer - Developmental Funds	06/01/06	04/30/11	$77,000	$37,345	$114,345
SIEGFRIED	P50 CA090440	National Institutes of Health	SPORE in Lung Cancer - Career Development Funds	06/01/06	04/30/11	$77,000	$37,345	$114,345
SIEGFRIED	R01 CA079882	National Institutes of Health	Targeting the HGF/c-Met Pathway in Lung Cancer	09/30/04	06/30/08	$202,500	$98,213	$300,713
SIEGFRIED	R01 CA098372	National Institutes of Health	GRPR Signaling in SCCHN: Integration with EGFR	04/01/04	02/28/09	$26,692	$12,946	$39,638

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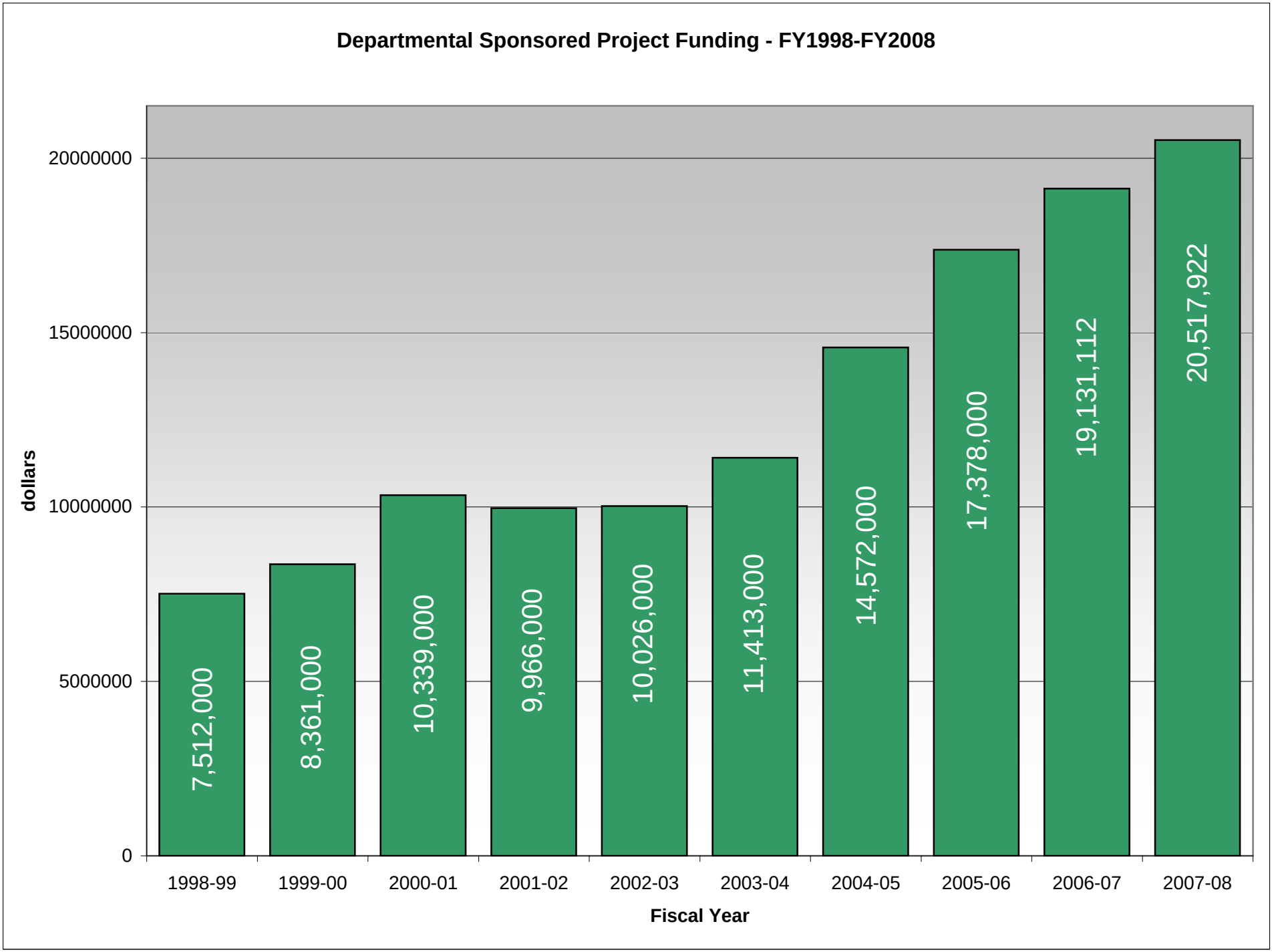
SIEGFRIED	N/A	Abbott Molecular, Inc.	Materials Agreement-Bilateral between University of Pittsburgh and Abbott Molecular	01/01/08	12/31/08	$3,226	$1,774	$5,000
SIEGFRIED	VUMC 31980-R	Vanderbilt University	Molecular Signatures of Lung Cancer	06/01/07	05/31/08	$14,005	$2,101	$16,106
SINGH	R01 CA129347	National Institutes of Health	Breast Cancer Prevention by Dietary Phytochemicals	09/07/07	07/31/12	$170,099	$82,962	$253,061
SINGH	R01 ES009140	National Institutes of Health	Toxicological Relevance of Human GST PL L Polymorphisms	09/23/02	07/31/07	$18,653	$9,047	$27,700
SINGH	R01 CA076348	National Institutes of Health	Novel GST and Detoxification of Diol Epoxides	02/19/03	01/31/08	$91,769	$44,508	$136,277
SINGH	R01 CA101753	National Institutes of Health	Anticarcinogenic Effect of ITCs Against Prostate Cancer	07/01/03	06/30/09	$147,558	$71,566	$219,124
SINGH	R01 CA113363	National Institutes of Health	Prostate Cancer Prevention by Diallyl Trisulfide	04/01/05	02/28/10	$92,045	$44,642	$136,687
SINGH	R01 CA115498	National Institutes of Health	Prevention of Prostate Cancer by Sulforaphane	07/01/05	04/30/10	$93,293	$45,247	$138,540
SINGH	R13 CA132241	National Institutes of Health	Bioactive Food Components Alternative Medicine and Cancer Chemoprevention Recent Advances	09/24/07	08/31/08	$12,000	$0	$12,000
SINGH	Hillman Y1	Hillman Foundation	Prostate Cancer Prevention by Guggulsterone a Constitutant	01/01/06	02/28/08	$9,231	$0	$9,231
SNEDDON	R21DK06806	National Institutes of Health	PTH1 Receptor Signaling by Cytoplasmic Binding Partners	08/01/04	07/31/07	$4,167	$2,021	$6,188
SOBOL	P20 CA132385	National Institutes of Health	Environmental Oncology Partnership Between Hampton University and UPCI	09/29/07	08/31/10	$106,754	$50,160	$156,914
SOBOL	R01 NS037704	National Institutes of Health	Molecular Markers as Predictors of Outcomes in Gliomas	02/28/08	02/28/10	$38,777	$40,237	$79,014
SOBOL	R01 NS037704	National Institutes of Health	Molecular Markers as Predictors of Outcomes in Gliomas	02/28/09	02/28/10	$55,963	$22,093	$78,055
SOBOL	R13 ES016721	National Institutes of Health	Annual Midwest DNA Repair Symposium	04/01/08	03/31/09	$2,000	$0	$2,000
SOBOL	119774 / 119772	University of Texas at SA	Base Excision Repair Genetic Integrity and Health Span	09/30/04	07/31/09	$63,064	$30,586	$93,650
SOBOL	P.O. # 10817	National Child Cancer Foundation	Correlating the DNA Repair Phenotype of Tumor Biopsies with the Response to Treatment with Temozolomide	03/01/04	02/28/06	$100,000	$50,000	$150,000
SOBOL	RSG-05-246-01-GMC	American Cancer Society	The Role of Base Excision Repair in the Anti Tumor Action of Temozolomide	07/01/05	06/30/09	$141,220	$27,794	$169,014
SOBOL	2007 Research Grant	Brain Tumor Society	PARG regulation of temozolomide Induced mitotic checkpoint activation	09/01/07	08/30/09	$83,333	$0	$83,333
SRINIVAS	Hillman Y2	Hillman Foundation	Hillman Y2 - Srinivas	01/01/07	11/30/08	$67,826	$0	$67,826

Last Name	Identifier	Agency Name	Title	Begin Date	End Date	Annual DC	Annual IDC	Annual TC
STABILE	FAMRI	Flight Attendent's Medical Research Initiative	Targeting the Estrogen Receptor and Epidermal Growth Factor Receptor for Lung Cancer Therapy	07/01/04	06/30/09	$100,000	$8,500	$108,500
STABILE	M2006-0039	Pittsburgh Foundation	CYP24 as a new diagnostic/prognostic marker and therapeutic target in lung cancer	08/01/07	07/31/08	$3,484	$0	$3,484
VOGT	R21 NSO57026	Pittsburgh Foundation	Throughput Content Screens for Dynein Inhibitors	09/15/06	0/8/31/07	$545	$264	$809
VOGT	R01 CA120792	Pittsburgh Foundation	Chemical Approaches for the Discovery of New Cancer Therapeutic Targets	06/01/07	04/30/08	$11,278	$5,470	$16,748
VOGT	R01 HDO53287	Pittsburgh Foundation	Utilizing Small Molecule Screens to Delineate Embryonic Signalling Mechanisms	08/03/07	05/31/08	$22,788	$11,051	$33,839
VOGT	R01 MH083154	Pittsburgh Foundation	High Content Cell-Based Screening for Modulators of Autophagy	10/01/07	09/30/08	$0	$0	$0
WANG	R01 DK066168	National Institutes of Health	Role of Protein Kinase D nu in Regulated GLUT4 Trafficking	03/01/04	02/28/09	$147,980	$68,860	$216,840
WANG	R03 DA024898	National Institutes of Health	IMAP-based fluorescent polarization assay for high throughput screening of protein kinase D inhibitors	09/01/07	08/31/08	$13,982	$6,852	$20,833
WITTSCHIEBEN	Hillman Y2	Hillman Foundation	Hillman Y2 - Wittschieben, J.	01/01/07	02/28/08	$41,536	$0	$41,536
WOOD	R01 CA101980	National Institutes of Health	The Role of Specialized DNA Polymerases in Processing Non B DNA Structures	07/01/03	06/30/08	$203,958	$98,920	$302,878
YALOWICH	R01 CA090787	National Institutes of Health	Mechanisms and Prevention of Etoposide-Induced Leukemia	07/26/07	05/31/12	$146,889	$71,242	$218,131
YALOWICH	U19 AI068021	National Institutes of Health	Mitochondrial Targeting Against Radiation Damage	09/30/05	08/31/10	$9,210	$4,513	$13,723
YALOWICH	RSG-05-246-01	American Cancer Society	The Role of Base Excision Repair in the Anti-Tumor Action of Temozolomide	07/01/05	06/30/09	$9,244	$1,849	$11,093
ZHANG	R01 CA106348	National Institutes of Health	Apoptotoc Response To DNA Damage Initiated By PUMA	04/01/04	03/31/09	$172,265	$83,763	$256,028
ZHANG	R01 CA121105	National Institute of Health	SMAC in Chemoprevention of Colon Cancer	09/01/07	07/31/08	$181,279	$87,920	$269,199
ZHANG	V Scholars	V Foundation	Defects in Apoptotic Machinery and Altered Response to Anticancer Agents in Human Cancer Cells	01/01/04	12/31/08	$2,083	$0	$2,083
ZHANG	RSG-07-156-01-CNE	American Cancer Society	Role of SMAC in NSAID mediated chemoprevention	07/01/07	06/30/11	$150,000	$30,000	$180,000
ZHANG	CI-49274-N	American Lung Association	PUMA as a Novel Sensitizer for the Treatment of Lung Cancer	07/01/07	06/30/08	$60,000	$0	$60,000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2006-07
2007-08
Fiscal Year

Percent of Faculty Support on Research Grants

Altschuler, Daniel	50%	Makhina, Elena	100%
Arjunan, Palaniappa	100%	Nichols, Mark	82%
Baker, Paul	90%	Palladino, Alicia	100%
Bisello, Alessandro	56%	Palladino, Michael	47%
Conrads, Thomas	85%	Ribeiro Neto, Fernando	100%
Defranco, Donald	50%	Romero, Guillermo	25%
Degroat, William	65%	Roppolo, James	100%
Eiseman, Julie	100%	Schopfer, Francisco	75%
Flint, Melanie	5%	Sculptoreanu, Adrian	100%
Freeman, Bruce	26%	Shakiryanova, Dinara	100%
Friedman, Peter	76%	Sharlow, Elizabeth	100%
Furey, William	0%	Siegfried, Jill	70%
Galbiati, Daniela	100%	Singh, Shivendra	83%
Galbiati, Ferruccio	27%	Sobol Jr., Robert	100%
Hershberger, Pamela	35%	Srinivas, Harish	83%
Hu, Jing	88%	Stabile, Laura	90%
Jackson, Edwin	90%	Vilardaga, Jean-Pierre	0%
Jiang, Yu	30%	Vogt, Andreas	100%
Johnston, Paul	100%	Wang, Qiming	30%
Kim, Yung	100%	Wittschieben, John	50%
Kinchington, Edwina	100%	Wood, Richard	53%
Knowles, Lynn	100%	Xiao, Dong	100%
Lakoski, Joan	13%	Yalowich, Jack	45%
Lazo, John	70%	Zhang, Lin	75%
Levitan, Edwin	86%	Pharmacology Average	**70%**

Training and Project Grants

Last Name	NIH Grant Number	Title	Begin Date	End Date	Annual DC	Annual IDC	Annual TC
CONRADS	P50 CA090440	SPORE in Lung Cancer – Project 3	05/01/08	04/30/11	$7,007	$3,399	$10,406
DEFRANCO	T32 GM008424	Predoctoral Training in Pharmacological Sciences	07/01/05	06/30/10	$156,004	$7,447	$163,451
EISEMAN	P01 CA078039	Combinatoral Approcahes for novel Anticancer Agents	12/14/09	12/14/09	$137,393	$6,305	$143,698
FREEMAN	P30 DK046204	Nitro-Fatty Acid Modulation Type II Diabetes	08/01/07	03/31/08	$16,875	$8,184	$25,059
FUREY	P01 CA078039	Combinatorial Approaches for Novel Anticancer Agents	07/01/06	06/30/10	$7,739	$3,753	$11,492
HERSHBERGER	P50 CA090440	SPORE in Lung Cancer – Project 1	06/01/06	04/30/11	$3,192	$1,548	$4,740
HERSHBERGER	P30 CA047904	CCSG - Pilot Hershberger	06/01/07	07/31/09	$12,500	$6,063	$18,563
KINCHINGTON	P50 CA090440	Transgenic Mouse Model Overexpressing the Gastrin Releasing Peptide Receptor for Novel Therapeutic Evaluation.	01/01/08	12/31/08	$10,574	$5,128	$15,702
LAZO	P01 CA078039	Combinatorial Approaches for Novel Anticancer Agents - Project 3	07/01/07	06/30/08	$152,591	$74,007	$226,598
LAZO	P01 CA078039	Combinatorial Approaches for Novel Anticancer Agents – Core A	07/01/07	06/30/08	$32,973	$15,992	$48,965
LAZO	P01 CA078039	Combinatorial Approaches for Novel Anticancer Agents – Core B	07/01/07	06/30/08	$139,139	$67,484	$206,623
ROPPOLO	P50 DK064539	Women's Health & Functional Visceral Disorders Center	09/01/07	08/31/08	$8,060	$3,974	$12,034
SIEGFRIED	P50 CA097190	Specialized Program of Research Excellence in Head and Neck Cancer- Head and Neck SPORE Project 4	07/01/04	06/30/09	$98,157	$46,124	$144,281
SIEGFRIED	P50 CA090440	SPORE in Lung Cancer- Proj I Sub 2	09/13/06	04/30/11	$101,726	$45,867	$147,593
SIEGFRIED	P50 CA090440	SPORE in Lung Cancer - UCLA Supplement	06/01/06	04/30/11	$50,364	$24,427	$74,791
SIEGFRIED	P50 CA090440	SPORE in Lung Cancer - Minority Supplement	06/01/06	04/30/11	$79,187	$38,010	$117,197
SIEGFRIED	P50 CA090440	SPORE in Lung Cancer – Project 1	06/01/06	04/30/11	$73,988	$35,514	$109,503
SIEGFRIED	P50 CA090440	SPORE in Lung Cancer - Administrative Core	06/01/06	04/30/11	$245,495	$117,837	$363,332
SIEGFRIED	P50 CA090440	SPORE in Lung Cancer - Developmental Funds	06/01/06	04/30/11	$77,000	$37,345	$114,345
SIEGFRIED	P50 CA090440	SPORE in Lung Cancer - Career Development Funds	06/01/06	04/30/11	$77,000	$37,345	$114,345
SOBOL	P20 CA132385	Environmental Oncology Partnership Between Hampton University and UPCI	09/29/07	08/31/10	$106,754	$50,160	$156,914

Participants in research

Graduate Students

Name	Mentor
Aleksandr Bank	Zhang
Pallavi Bansal	Lazo
Nicholas Bateman	Conrads
Janine Bartholomew	Galbiati
Neil Bhola	Grandis
John Caltagarone	Defranco
Serah Choi	Bakkenist
Austin Dulak	Siegfried
Amy Furda	Yalowich
Gregory Gan	Wood
Melanie Grubisha	Defranco
Eva Goellner	Sobol
Alison Groeger	Freeman
Michael Hezel	Galbiati
Sangeetha Iyer	Homanics
Carolyn Kitchens	Lazo
Nicole Kotchey	Palladino
Jenny Linnoila	Halfter
Peter McDonald	Lazo
Courtney MacNeil	Wang
Shoghag Panjarian	Smithgall
Teodora Pene Dumitrescu	Smithgall
Pierre Queiroz-Oliveira	Lazo
Maranda Sarachine	Day
Joshua Snyder	Stripp
Robert Tomko	Lazo
Yan Wang	Lazo
Man Wong	Levitan
Xixi Wong	Singh
Yi Zhou	Levitan

Undergraduate Students

Name	Lab
Ndang Azang-Njaah	Lazo
Muhammad Ali	Freeman
Jennifer Adams	Defranco
Blake Armstrong	Cavanaugh
Name	**Lab**
Luiz Araujo	Palladino
Kimberly Autore	Yalowich
Faith Bazley	Degroat
Ryan Barlow	Baker
Brandy Benoit	Yalowich
Elise Bertoti	Siegfried
Alvin Chan	Xu

Stephanie Choing	Bisello
Megan Coldren	Lazo
Vanessa Cole	Palladino
Charmaine Dogans	Palladino
Katherine Durgin	Palladino
Laura Epperly	Lazo
Cassandra Edwards	Degroat
Patrick Fawcett	Wang
Janet Gonzalez	Grandis
Alexandra Gordon	Department
Lorin Grieve	Palladino Media
Jenna Gwyn	Freeman
Christine Hall	Surp
Christopher Henry	Surp
Brian Holt	Yalowich
Zachary Horne	Surp
Jenna Hendershot	Palladino Media
Anna Hall	Lazo
Michael Ickes	Degroat
Nicholas Ierovante	Palladino Media
Robert Jack, Ii	Siegfried
Michia Johnson	Siegfried
Heini Kansanen	Freeman
Hansol Kim	Siegfried
Grace Kim	Singh
Mark Langhans	Palladino
Samantha Lee	Palladino
Henry Liu	Palladino Media
Tatiana Lavrinenko	Yalowich
Leigh Medaris	Freeman
Hilary Mccarren	Bisello
Amy Mccarty	Defranco
Bradley Morneweck	Galbiati
Paul Musille	Galbiati
Uche Motanya	Freeman
Name	Lab
Christan Martone	Palladino Media
Zane Mclain	Palladino Media
Nicole O'Neill	Friedman
Victoria Oravec	Defranco
Elizabeth Paladin	Surp
Neil Patel	Johnson
Eva Procopio	Grandis
Radhika Patnam	Surp
Saned Raouf	Palladino
Jonathan Raso	Palladino
Alicia Rosenbloom	Palladino
Mitchell Silverman	Defranco
Allison Smith	Singh
Rachel Stewart	Surp
Mansi Shah	Degroat
Quentin Smith	Palladino

Jacquelyn Seigle	Palladino
Shannon Stauffer	Palladino Media
Alexa Swailes	Palladino
Jason Tchao	Jiang
Briana Vecchio	Defranco
Christopher Wickens	Degroat
Sean Wo	Siegfried
Shawn Zuratovic	Palladino

Staff Employees

Name	Lab
Stacey Barrick	Bisello
Andrew Bodnar	Yalowich
Chen-Shan Chen	Baker
Kristofer Fertig	Department
Autumn Gaitherdavis	Siegfried
Guangzu Gao	Bisello
Holly Gergely	Administration
Angela Giorgianni	Yalowich
Karthik Giridhar	Wang
Franca Golin Bisello	Freeman
Christopher Gubish	Siegfried
Marjet Heitzer	Defranco
James Kaczynski	Administration
Yumei Lai	Jiang
Name	Lab
Marcia Lewis	Defranco
Melanie McClain	Administration
Jeanette McDew	Administration
Lisa McGreal	Administration
Charlotte McKinnon	Administration
Rosalie Miller	Palladino
Virginia Reiner	Administration
Mary Rothstein	Siegfried
Roxanne Scarano	Defranco
Richard Serventi	Administration
Lynda Sorch	Administration
Richard Smith	Administration
Patricia Smith	Administration
Emily Trostel	Administration
Timothy Ungerer	Degroat
Chandra Vignere	Levitan
Georgeanna Williams	Administration
Yanmei Yang	Friedman

Researchers

Name	Lab
Susan Abbatiello	Conrads
Hiroyuki Achiwa	Lazo

Name	Lab
Veronica Alonso	Friedman
Juan Ardura	Friedman
Debra Artim	Degroat
Lesley Ashmore	Palladino
Lihua Bai	Eiseman
Xiaochun Bai	Jiang
Laura Baker	Freeman
Pallavi Bansal	Lazo
Guillermo Barila	Altschuler
Ajaykumar Bommareddy	Singh
Gustavo Bonacci	Freeman
Krishnamoorth Chandrasekhar	Furey
Jun Chen	Wang
Peng Cheng	Nichols
Marsha Cole	Freeman
Crissy Dudgeon	Zhang
Drew Dudgeon	Lazo
Martin Edreira	Altschuler
Timothy Feinstein	Vilardaga
Jose Garrido	Romero
Jianxia Guo	Zhang
Shuguang Guo	Jiang
Eun-Ryeong Hahm	Singh
Daniel Hochbaum	Altschuler
Kyoungja Hong	Altschuler
Stacey Hrizo	Palladino
Leonel Joannas	Altschuler
Shunqian Jin	Yalowich
Florenta Kullmann	Degroat
Heini Kansanen	Freeman
Nicholas Khoo	Freeman
Piotr Kos	Palladino
Fumito Koizumi	Lazo
Luis Leiva-Vega	Romero
Hua Li	Zhang
Dongzhu Ma	Jiang
Masanao Nakashima	Lazo
Lakshminarasi Pasupulati	Furey
Anna Powolny	Singh
Ilva Putzier	Levitan
Brian Reese	Lazo
Tanja Rudolph	Freeman
Volker Rudolph	Freeman
Ely Sebastian	Friedman
Mineaki Seki	Wood
Bing Shen	Roppolo
Kunwar Singh	Singh
Maria Soares	Lazo
Gyun Jee Song	Bisello
Silvia Stan	Singh
Keiichi Takata	Wood

Ram Trivedi	Sobol
Jaya Vatsyayan	Singh
Peng Wang	Zhang
Tao Wang	UPCI
Renaud Warin	Singh
Irene Wolf	Defranco
Steven Woodcock	Freeman
Xiang Xu	Zhang
Name	Lab
Gonghong Yan	Jiang
Hanqing Ye	Altschuler
Yongbei Yu	Degroat
Fang Zhang	Lazo
Chao-Ming Zhou	Levitan
Fangdong Zou	Zhang
Huafei Zou	Jiang

New Research Recruits

Name	Lab
Veronica Alonso	Friedman
Juan Ardura	Friedman
Debra Artim	Degroat
Lesley Ashmore	Palladino
Crissy Dudgeon	Zhang
Drew Dudgeon	Lazo
Timothy Feinstein	Vilardaga
Guangzu Gao	Bisello
Marjet Heitzer	Defranco
Stacey Hrizo	Palladino
Shunqian Jin	Yalowich
Leonel Joannas	Altschuler
Heini Kansanen	Freeman
Hua Li	Zhang
Masanao Nakashima	Lazo
Tanja Rudolph	Freeman
Volker Rudolph	Freeman
Tao Wang	UPCI
Irene Wolf	Defranco
Gonghong Yan	Jiang
Fang Zhang	Lazo
Huafei Zou	Jiang

Major Collaborations

Bruce Freeman, Ph.D.
Professor and Chair

Fadi Lakkis and Timothy Billiar (University of Pittsburgh): Organ Preservation for Transplantation
Mitchell Fink and Derek Angus (University of Pittsburgh): Anti-inflammatory strategies for treating sepsis/ARDS

Robert Squires and David Hackam (University of Pittsburgh):Anti-inflammatory strategies for treating GI surgical patients
Kaikobad Irani (University of Pittsburgh): Prevention of cardiac ischemic injury

Thomas Conrads, Ph.D.
Visiting Associate Professor

Dr. Nigel G. J. Richards (Department of Chemistry, University of Florida, Gainesville, FL) - Development of a quantitative assay for asparagine synthetase for patients with recurrent acute lymphoblastic leukemia.
Dr. George R. Beck (Division of Endocrinology, Metabolism and Lipids, Emory University School of Medicine, Atlanta, GA) – Proteomic and metabolomic investigations toward understanding the mechanism of osteoblast development.
Dr. Gary Siuzdak (Department of Molecular Biology and the Center for Mass Spectrometry, The Scripps Research Institute, La Jolla, CA) – Proteomic and metabolomic investigations of viral infection.
Dr. Aly Karsan (Pathology and Laboratory Medicine, University of British Columbia, Vancouver, British Columbia) – Biomarker investigations in mouse models of Lewis lung carcinoma.

W. Chet de Groat, Ph.D.
Professor

Dainippon Sumitomo Pharma Ltd., Osaka Japan: Evaluation of Na^+ channel blockers on the electrical properties of sensory nerves
Hydra Biosciences, Inc.: Evaluation of the effects of TRPA1 antagonists on bladder activity
Johnson & Johnson Pharmaceuticals: Investigation of the effect of TRPV1 antagonist JNJ-17203212 on voiding in rats
Procter & Gamble Pharmaceuticals: An Investigation of the Effect of Hormone Levels on Bladder Hyperactivity in the Female Rat as a Model for Predicting Potential Drug Efficacy in Postmenopausal Women with Detrusor Overactivity ($82,520 grant provided)

Jing Hu, Ph.D.
Assistant Professor

Dr. Nahum Sonenberg. Dr. Sonenberg is a distinguished investigator of the CIHR, Howard Hughes International Scholar

John Lazo, Ph.D.
Allegheny Foundation Professor

Scott Diamond. Department of Chemical and Biomolecular Engineering. Penn Center for Molecular Discovery. New compound screening platforms.

Ray Dingledine. Department of Pharmacology, Emory University. New compound screening platforms.
Alan Waggoner, Carnegie Mellon University. Probe development
Garth Powis, University of Arizona. New cancer chemotherapy agents targeting cell stress.
Marc W. Halterman, Department of Neurology, University of Rochester School of Medicine and Dentistry. Regulation of c/EBP and CHOP-10 Influence the Pathologic Switch in a Model of Hypoxia-Induced Neuronal Death.
Vojo Deretic, Dept. of Molecular Genetics and Microbiology, University of New Mexico. HCS for small molecule inducers of autophagy.
James Morris, Dept. of Genetics and Biochemistry, Clemson University. Inhibitors of T. burcei hexokinase 1.

Lin Zhang, Ph.D.
Assistant Professor

Collaboration with Dr. We Zhou at Emory University, which resulted in joined publication:
Yue, W., Dacic, S., Sun, Q.H., Landreneau, R., Guo, M.Z., Zhou, W., Siegfried, J.M., Yu, J. and Zhang, L. (2007) Frequent inactivation of RAMP2, EFEMP1 and Dutt1 in lung cancer by promoter hypermethylation. Clinical Cancer Research (In Press).

Collaboration with Dr. Gerry P. Zambetti at St Jude Children's Research Hospital, which resulted in joined publication:
Wu, B., Qiu, W., Wang, P., Yu, H., Cheng, T., Zambetti G.P., Zhang, L. and Yu, J. (2007) p53-independent induction of PUMA mediates intestinal apoptosis induced by ischemia reperfusion. Gut 56:645-654.

Entrepreneurial Activities

Edwin Jackson, Ph.D.
Professor

Anti-No-Reflow Guide Wire For Vascular Interventional Procedures. (Provisional Patent Filed by Inventors). Currently forming LLC around this technology.

Lin Zhang, Ph.D.
Associate Professor

Collaboration with TetraLogic Pharmaceuticals for study of SMAC mimetics

Awards and Honors

William C. de Groat
Professor

Recipient, Reeve-Irvine Research Medal, 2007

Don DeFranco, Ph.D.
Professor

Finalist, Provost's Award for Excellence in Mentoring, 2007
Recipient, Provost's Award for Excellence in Mentoring, 2008

Edwin Jackson, Ph.D.
Professor
"Master Lecturer" at the Michael E. DeBakey Institute, Texas A&M University, College Station, TX, June 21, 2007

John Lazo, Ph.D.
Professor
The Dean's Teaching Excellence Award, The Warren Alpert Medical School of Brown University, 2007
Pitt Innovator of the Year Award, 2007
ASPET – Astellas Award in Translational Pharmacology, 2008

Shivendra Singh, Ph.D.
Professor
Outstanding Achievement Award, Society of American Asian Scientists in Cancer Research (SAASCR) (2007).

Invited Talks

Bruce Freeman, Ph.D.
Professor and Chair

Department of Neurobiology, University of Pittsburgh, Pittsburgh, PA; January 9, 2007
"Convergence of fatty acid and nitric oxide cell signaling reactions"

Pulmonary, Allergy & Critical Care Medicine Joint Collaborative Conference, University of Pittsburgh School of Medicine, Pittsburgh, PA; February 20, 2007, "Convergence of NO and fatty acid signaling pathways"

University of Utah, Department of Medicine, Salt Lake City, UT; May 7, 2007, "Nitric Oxide Regulation of Lipid Signaling"

Frontiers in Biomedical Research, Nobel Foundation, Stockholm, Sweden; June 1, 2007
"Nitric Oxide, Nitrite and Redox Signaling"

American Society of Nephrology, Annual Meeting; San Francisco, CA; October 31 - November 2, 2007,
"Transgenic Approaches to Lipid and Protein Nitration Reactions in Inflammatory Processes"

University of South Alabama Department of Pharmacology, Mobile, AL; February 14th, 2008
"Nitro-Fatty Acids - Transducers of Nitric Oxide and Redox Signaling"

University of Georgia Department of Biochemistry & Molecular Biology, Athens, GA; March 7th, 2008,
"Convergence of Nitric Oxide and Eicosanoid Signaling"

University of Massachusetts Medical School, Worcester, MA; April 16th, 2008
"Convergence of Nitric Oxide and Lipid Signaling - Nitro Fatty Acid Derivatives"

Wake Forest Nitrogen Oxide Meeting, Farmington, PA; May 23rd, 2008
"Fishing for NO-derived Electrophiles and Catching Moby Dick"

NIEHS Council Meeting, Research Triangle Park, NC; May 29th, 2008, "Xenobiotic and inflammatory-induced fatty acid nitration products – potent anti-inflammatory mediators"

Paul Baker, Ph.D.
Research Assistant Professor

"Identification and Pharmacologic Properties of Nitrated Fatty Acids," for the Department of Pharmacology at the University of Pittsburgh School of Medicine (Pittsburgh, PA) Feb. 2, 2007

"Analysis of Nitrated Lipids by Mass Spectrometry," for the Fifth International Conference of Peroxynitrite and reactive oxygen species (Montevideo, Uruguay) Set. 4, 2007

Alessandro Bisello
Assistant Professor
"Accessory for GPCRs". Senior Vice Chancellor Research Conference, University of Pittsburgh School of Medicine, February 2007.

Thomas Conrads, Ph.D.
Visiting Associate Professor

"Emergent Technology for Proteomics Discovery Using Formalin-fixed Paraffin Embedded Tissue" Gordon Research Conference: New Frontiers in Cancer Detection and Diagnosis, Ventura, CA, January 21-26, 2007.

"Applications of High Resolution Mass Spectrometry for Biomarker Discovery from Tissue Interstitial Fluid" University of Lisbon, Lisbon, Portugal, January 16, 2008.

"Biomarker Discovery in Renal Cell Carcinoma by High Resolution Mass Spectrometry from Tissue Interstitial Fluid" Center for Cellular and Molecular Biology, Hyderabad, India, February 17, 2008.

"Applications of Mass Spectrometry and Proteomics for Cancer Biomarker Discovery" 2008 Annual Meeting on Women's Cancer, Society of Gynecologic Oncologists, March 9, 2008.

"Tissue Proteomics: Application of High-Resolution Mass Spectrometry and Label-Free Differential Analysis for Cancer Biomarker Investigations" United States Human Proteome Organization, Bethesda, MD, March 18, 2008.

Donald DeFranco, Ph.D.
Professor

"Nuclear Steroid Receptors and the Brain", Department of Physiology, University of Illinois, April 2007

Innovative Minds in Prostate Cancer Today (IMPaCT), Sept 2007

FASEB Conference,"Nuclear Steroid Receptors and the Brain", April 2008

W. Chet de Groat, Ph.D.
Professor

Mechanisms Underlying Sensitization of Visceral Nociceptors. IN: Science 2006, University of Pittsburgh Annual Science Conference. Pittsburgh, PA, October 6, 2006.

Inflammation and Visceral Afferent Activity. IN: NIH 2006 International Symposium: Frontiers in Painful Bladder Syndrome and Interstitial Cystitis. Bethesda, MD, October 26-27, 2006.
Alpha-Bungarotoxin in Urinary Voiding Dysfunction. IN: International Conference on Neurotoxins (ICON). Hollywood, FL, November 29-December 2, 2006.

Peter Friedman, Ph.D.
Professor

University of Connecticut, Endocrine Scholar, February, 2007.

St Jude Children's Research Hospital, February, 2008.

William Furey, Ph.D.
Professor

High Throughput Protein Crystallography, University of North Carolina, Chapel Hill, January, 2007.

Ferruccio Galbiati, Ph.D.
Assistant Professor

Department of Medicine, Division of Endocrinology and Metabolism, University of Pittsburgh School of Medicine, 2007

Pamela Hershberger, Ph.D.
Research Assistant Professor

1st annual meeting Organization for the Study of Sex Differences Washington, D.C. 5/2007

Edwin Jackson, Ph.D.
Professor

Enhanced interaction between the Gi-coupled receptors and angiotensin II in the SHR renal vasculature: Implications for PP-fold peptides and renal dipeptidyl peptidase IV. Presented to the Renal Division, University of Pittsburgh, Pittsburgh, PA, May 23, 2007.

Adenosine: The Little Molecue that Could. Presented as a "Master Lecturer" on behalf of the Michael E. DeBakey Institute, Texas A&M University, College Station, TX, June 21, 2007.

Enhanced interaction between Gi-coupled receptors ande angiotensin II in the SHR renal vasculature. Presented to the FASEB Summer Research Conference on Renal Hemodynamics: Biomolecular Control Mechanisms Integrating Vascular and Tubular Function. Vermont Adademy, Saxtons River, Vermont, July 8, 2007.

2-Methoxyestradiol: A safe and effective cardiorenal protective hormone therapy for women and men. Presented to the American Physiological Society Conference on Sex Steroids in Cardiovascular-Renal Physiology and Pathophysiology. Austin, Texas, August 11, 2007.

Adenosine-releasing polymers for preventing complications during vascular interventions. Presented to the Cook Group Incorporated, Bloomington, IN, October 3, 2007.

Paul Johnston, Ph.D.
Research Associate Professor

"HCS Applications at the Pittsburgh Molecular Library Screening Center" (17-OCT-2007) Combined Presentation on the NIH Molecular Libraries Session at the IBC Assays & Cellular Targets Conference, San Diego.

Joan M. Lakoski, Ph.D.
Professor

AAMC Group on Faculty Affairs Professional Development Conference Collaborative Conversations on Faculty Vitality, San Diego, CA, January 26-29, 2007

Chair of Program Committee, 2007 National Clinical and Translational Science Award K12 Scholars Annual Meeting, "Transforming Career Development in Clinical and Translational Research," Omni Shoreham Hotel, Washington, DC. March 27, 2007.

Invited Speaker with Dr. Robert Milner, NPA 2007 Workshop "NIH Pathway to Independence (K99/R00) Award Workshop: Know your Kangaroo", National Postdoc Association Meeting, Berkeley CA, March 31, 2007.

Organizer and Moderator, "Career Transitions and Preparation: A Workshop for Senior Graduate Students and Postdoctoral Fellows", Postdoc Preparation Institute: "Leadership in the Lab-Increasing the Research Productivity of your Team". Experimental Biology 2007, Washington, DC, April 28, 2007.

Invited Speaker: Endocrine Fellows & Students Day Program Developing Clinical Management Skills: "Choosing a Mentor", Endocrine Society Annual Meetings, Toronto, Ontario, Canada, June 1, 2007.

Invited Speaker: Endocrine Fellows & Students Day Program Developing Clinical Management Skills: "Choosing a Mentor", Endocrine Society Annual Meetings, Toronto, Ontario, Canada, June 1, 2007.

Invited Faculty, International Program in Aging Research, "Neurophysiology of Aging" Jonkoping, Sweden, June 13, 2007.

Michael Palladino, Ph.D.
Assistant Professor

(2007). Cellular energetics and progressive neuromuscular disease. Wadsworth Center. New York Department of Health, Division of Molecular Medicine. Faculty Host: Carmen Mannella.

(2007). Roundtable presentation entitled *Use of Drosophila for high-resolution 3D-TEM and cryoTEM studies.* Wadsworth Center. New York Department of Health, Division of Molecular Medicine. Host: HHMI Tomography Imaging Group.

(2007). Mitochondrial Encephalomyopathy in *Drosophila*: Pathogenic Mechanisms and Therapeutic Approaches. 48th Annual Drosophila Research Conference.

(2008). Neuromuscular Degenerative Diseases Modeled in Drosophila

University of Connecticut, School of Medicine. Host: Dr. Asis Das.

(2008). Common fruit fly, uncommon possibilities: Modeling neuromuscular diseases. U.Pitt. SOM Winter Academy.

Francisco Schopfer, Ph.D.
Research Assistant Professor

Plenary session speaker at Free radical Gordon Conference, Ventura, California, March 2007
Invited speaker, 2007 Gordon Research Conference, Oxidative Stress and Disease, Ventura, CA.

Invited speaker, V Meeting of Society for Free Radical Research in Biology and Medicine (SFRBM) South American group and V International Meeting on Peroxynitrite and Reactive Nitrogen Species, 2007.

Dinara Shakiryanova, Ph.D.
Research Instructor

Shakiryanova D, Klose M, Zhou Y, Hewes RS, Gu T, Deitcher DL, Levitan ES. Presynaptic Ryanodine Receptor-activated Calmodulin Kinase II Increases Vesicle Mobility and Potentiates Neuropeptide Release. 6th Junior Academics meeting "Molecular mechanisms of exocytosis and endocytosis", 1-3 April 2007, Edinburgh, United Kingdom

Shivendra Singh, Ph.D.
Professor

11-9-07, Invited Speaker, The Nanjing International Symposium of New Frontiers in Cancer Research, Nanjing Medical University, China. Title: Novel Responses to Phenethyl Isothiocyanate in Human Prostate Cancer Cells.

12-3-07, Invited Speaker, 9th International Conference on Mechanisms of Antimutagenesis and Anticarcinogenesis (ICMAA-2007), Cheju International University, Jeju Island, Korea. Title: Cellular Responses to Garlic Organosulfides: Implications for Cancer Prevention.

12-7-07, Invited Speaker, International Symposium on Genetic, Pharmacologic and Nutritional Modulation of Carcinogenesis. Seoul National University, Seoul, Korea. Title: Novel Responses to Phenethyl Isothiocyanate.

12-10-07, Invited Speaker, 2nd International Symposium on Translational Research on Natural Products & Cancer. Fariyas Resort, Lonavala, India. Title: Molecular Characterization of Autophagic Response to Cancer Chemopreventive Agent Sulforaphane.

Robert Sobol, Ph.D.
Research Assistant Professor

'PARP-1 is a base excision repair checkpoint protein', CRED seminar, U.T. M. D. Anderson Cancer Center, Science Park - Research Division, Department of Carcinogenesis. Smithville, Texas. January 16, 2008

'Base Excision Repair and Chemotherapy Response', Rhode Island INBRE Seminar Series, October 30, 2007

'Genome Stability Calls for Balanced Base Excision Repair Protein Expression', Symposium on Base Excision Repair as a Tumor Suppressor Mechanism; 2007 Annual Environmental Mutagen Society Meeting, October 21-24, 2007

'Human Base Excision Repair and Resistance to Chemotherapeutic Alkylating Agents', USC College of Pharmacy, Columbia, South Carolina, September 11, 2007

'Human Base Excision Repair and Resistance to Chemotherapeutic Alkylating Agents', Department of Molecular Biology, University of Bergen, Bergen, Norway, June 18, 2007
'Human Base Excision Repair and Resistance to Chemotherapeutic Alkylating Agents', 2nd International Conference on MGMT and Alkylating Drug Resistance; June 13-16, 2007

'Does Base excision repair (BER) regulate DNA damage induced histone modification or does histone modification regulate BER - or both?'; Pittsburgh Chromatin Club, May 4, 2007

'Human DNA Base Excision Repair Proteins Mediate Resistance to Chemotherapeutic Alkylating Agents', Gittlen Cancer Research Foundation, The Pennsylvania State University College of Medicine, Milton S. Hershey Medical Center, April 5, 2007

Richard Wood, Ph.D.
Professor

US-Japan DNA Repair meeting (Sendai, Japan), Invited Speaker, May 2007
Department of Pharmaceutical Sciences (University Pittsburgh), Invited Seminar Speaker, January 2007

Lin Zhang, Ph.D.
Assistant Professor

Invited Seminar, Department of Genetics, Case Western Reserve University, Feb. 27th, 2008.

Invited Speaker, "Cancer Immunology, Immunotherapy, Immunoprevention (CI3) Symposia", University of Pittsburgh (2007).

Invited Seminar, Novartis Institute For Biomedical Research, Shanghai, P.R. China (2007)

Invited Speaker, "Bioactive Food Components, Alternative Medicine and
Cancer Chemoprevention: Recent Advances"/12th World Congress on Advances in Oncology and 10th International Symposium on Molecular Medicine, Crete, Greece (2007)

Invited Seminar, National Institute of Biological Sciences (NIBS), Beijing, P.R. China (2007)

Teaching Activities

Teaching Programs and Courses

Medical Student Instructional Activities

FAC LAST NAME	FAC FIRST NAME	ACTIVITY TYPE	ACTIVITY TITLE	COURSE / CLERKSHIP TITLE	DATE	START TIME	END TIME	MEDICAL STUDENT LEVEL
Bisello	Alessandro	Workshop	Physiology Workshop 1 - Diffusion and Membrand Potential	Cell Tissue and Physiology	10/25/06	13:00	14:30	MS-1
Bisello	Alessandro	Workshop	Physiology Workshop 2 - Receptors	Cell Tissue and Physiology	10/27/06	10:30	12:00	MS-1
Bisello	Alessandro	Workshop	Physiology Workshop 3 - Second Messengers	Cell Tissue and Physiology	10/30/06	10:15	11:45	MS-1
Bisello	Alessandro	Workshop	Neuropharmacology Workshop	Neuroscience	4/3/07	13:00	15:00	MS-1
DeFranco	Donald	Lecture	Phamacology 5: Anti-inflammatory Agents	BFH Pulmonary	11/2/06	13:00	13:50	MS-2
DeFranco	Donald	Lecture	Transition to Tissues, Cells and Molecules: Course Introduction	Cell and Tissue Physiology	10/17/06	9:25	9:50	MS-1
DeFranco	Donald	Lecture	Proteins I: General Structure and Functional Properties	Cell and Tissue Physiology	10/17/06	10:00	10:50	MS-1
DeFranco	Donald	Lecture	Proteins II: Synthesis, Folding, Degredation	Cell and Tissue Physiology	10/17/06	11:00	11:50	MS-1
DeFranco	Donald	Lecture	Proteins III: Enzymes	Cell and Tissue Physiology	10/17/06	13:00	13:50	MS-1
DeFranco	Donald	Lecture	Techniques	Cell and Tissue Physiology	10/17/06	14:00	14:50	MS-1
DeFranco	Donald	Lecture	Protein Trafficking II: Nucleous	Cell and Tissue Physiology	10/23/06	11:00	11:50	MS-1
DeFranco	Donald	Workshop	Question Session 1	Cell and Tissue Physiology	10/24/06	9:00	9:50	MS-1
DeFranco	Donald	Lecture	Steroid Hormone/Nuclear Receptors	Cell and Tissue Physiology	10/24/06	13:00	13:50	MS-1
DeFranco	Donald	Lecture	Apoptosis	Cell and Tissue Physiology	10/24/06	14:00	14:50	MS-1
DeFranco	Donald	Workshop	Question Session 2	Cell and Tissue Physiology	10/31/06	13:00	14:00	MS-1
DeFranco	Donald	Exam	Interim Exam	Cell and Tissue Physiology	11/1/06	13:00	14:00	MS-1

FAC LAST NAME	FAC FIRST NAME	ACTIVITY TYPE	ACTIVITY TITLE	COURSE / CLERKSHIP TITLE	DATE	START TIME	END TIME	MEDICAL STUDENT LEVEL
DeFranco	Donald	Small Group	Investigators and Evaluators	Methods and Logic in Medicine	1/17/07	8:30	9:45	MS-1
DeFranco	Donald	Small Group	Investigators and Evaluators	Methods and Logic in Medicine	1/24/07	8:30	9:45	MS-1
DeFranco	Donald	Small Group	Investigators and Evaluators	Methods and Logic in Medicine	1/31/07	8:30	9:45	MS-1
DeFranco	Donald	Small Group	Investigators and Evaluators	Methods and Logic in Medicine	2/14/07	8:30	9:45	MS-1
DeFranco	Donald	Small Group	Investigators and Evaluators	Methods and Logic in Medicine	2/28/07	8:30	9:45	MS-1
DeFranco	Donald	Small Group	Cases/Presentations	Methods and Logic in Medicine	3/28/07	8:30	9:45	MS-1
DeFranco	Donald	Small Group	Cases/Presentations	Methods and Logic in Medicine	4/4/07	8:30	9:45	MS-1
DeFranco	Donald	Small Group	Cases/Presentations	Methods and Logic in Medicine	4/25/07	8:30	9:45	MS-1
DeFranco	Donald	Small Group	Cases/Presentations	Methods and Logic in Medicine	5/2/07	8:30	9:45	MS-1
Defranco	Donald	Workshop	Neuropharmacology Workshop	Neuroscience	4/3/07	13:00	15:00	MS-1
DeFranco	Donald	Lecture	Pharmacology (Anti-androgens, Anti-estrogens, etc.)	Reproductive and Developmental Biology	2/7/07	15:45	16:45	MS-2
DeFranco	Donald	Lecture	Pharmacology (Estrogens and SERMS)	Reproductive and Developmental Biology	2/21/07	15:45	16:30	MS-2
DeGroat	William	Workshop	Neuropharmacology Workshop	Neuroscience	4/3/07	13:00	15:00	MS-1
Eiseman	Julie	Lecture	Prelcinical Studies in Cancer	ILS Neoplasia and Neoplastic Diseases	2/28/07	9:00	10:00	MS-4
Freeman	Bruce	Workshop	Neuropharmacology Workshop	Neuroscience	4/3/07	13:00	15:00	MS-1
Friedman	Peter	Workshop	Physiology Workshop 2 - Receptors	Cell Tissue and Physiology	10/27/06	10:30	12:00	MS-1
Friedman	Peter	Workshop	Physiology Workshop 3 - Second Messengers	Cell Tissue and Physiology	10/30/06	10:15	11:45	MS-1

FAC LAST NAME	FAC FIRST NAME	ACTIVITY TYPE	ACTIVITY TITLE	COURSE / CLERKSHIP TITLE	DATE	START TIME	END TIME	MEDICAL STUDENT LEVEL
Galbiati	Ferruccio	Lecture	Pharmocology 5: Thereapy of Pulmonary Vascular Disease	BFH Pulmonary	11/8/06	15:00	15:50	MS-2
Galbiati	Ferruccio	Lecture	Pharm - Drugs: Diarrhea, Constipation & IBD Part 1	Digestion and Nutrition	11/30/06	15:00	15:50	MS-2
Galbiati	Ferruccio	Lecture	Pharm - Drugs: Diarrhea, Constipation & IBD Part 2	Digestion and Nutrition	11/30/06	16:00	16:50	MS-2
Galbiati	Ferruccio	Workshop	Neuropharmacology Workshop	Neuroscience	4/3/07	13:00	15:00	MS-1
Galbiati	Ferruccio	Lecture	Pharmacology (Drugs affecting sexual function)	Reproductive and Developmental Biology	2/8/07	10:45	11:45	MS-3
Hershberger	Pamela	Lecture	Pharmacology (Effect of pregnancy on drugs; Drugs affecting labor)	Reproductive and Developmental Biology	2/14/07	16:00	17:00	MS-2
Jackson	Edwin	Lecture	Pharmacology Kinetics/Dynamics	Board Review	3/20/07	12:00	12:45	MS-2
Jackson	Edwin	Lecture	Pharmacology of Diuretics	Body Fluid Homeostasis Renal	10/9/06	8:30	10:30	MS-2
Jackson	Edwin	Lecture	Pharmacology of Drugs for the Treatment of Nephropathies and Chronic Kidney Disease	Body Fluid Homeostasis Renal	10/13/06	10:45	11:45	MS-2
Jackson	Edwin	Lecture	Diuretics- How do they work? Diuretics- What do they do?	Clinical Pharmacology	4/11/07	9:00	9:55	MS-2
Jackson	Edwin	Lecture	Diuretics- When do I use them? Diuretics- How do I use them?; Case Presentation and Instruction	Clinical Pharmacology	4/11/07	10:05	11:05	MS-3
Jackson	Edwin	Small Group	Neurological Disorders	Clinical Pharmacology	4/11/07	13:00	14:30	MS-3
Jackson	Edwin	Lecture	Introduction to Lecture Series	Neuroscience	3/29/07	8:00	8:15	MS-1
Jackson	Edwin	Lecture	Brief Overview of Mechanisms of Drug Action	Neuroscience	3/29/07	8:15	8:45	MS-1
Jackson	Edwin	Lecture	Drug Absorption	Neuroscience	3/29/07	8:45	9:15	MS-1
Jackson	Edwin	Lecture	Drug Distribution	Neuroscience	3/29/07	9:30	10:00	MS-1
Jackson	Edwin	Lecture	Relationship Between Drug Dose and Effect	Neuroscience	3/29/07	10:00	11:00	MS-1

FAC LAST NAME	FAC FIRST NAME	ACTIVITY TYPE	ACTIVITY TITLE	COURSE / CLERKSHIP TITLE	DATE	START TIME	END TIME	MEDICAL STUDENT LEVEL
Jackson	Edwin	Lecture	Drug Metabolism	Neuroscience	3/29/07	11:15	12:00	MS-1
Jackson	Edwin	Lecture	Pharmacokinetics: Designing & Adjusting a Drug Regimen	Neuroscience	3/30/07	8:00	9:00	MS-1
Jackson	Edwin	Lecture	Pharmacokinetics: Designing & Adjusting aDrug Regimen	Neuroscience	3/30/07	9:15	10:15	MS-1
Jackson	Edwin	Lecture	Pharmacokinetics: Practice Problems	Neuroscience	3/30/07	10:30	11:30	MS-1
Jackson	Edwin	Lecture	Question and Answer Session	Neuroscience	3/30/07	11:30	12:00	MS-1
Jackson	Edwin	Lecture	Introduction to MS2 Pharmacology	Pharmacology	8/28/06	8:00	8:15	MS-2
Jackson	Edwin	Lecture	Brief Overview of Mechanisms of Drug Action	Pharmacology	8/28/06	8:15	8:45	MS-2
Jackson	Edwin	Lecture	Drug Absorption	Pharmacology	8/28/06	8:45	9:15	MS-2
Jackson	Edwin	Lecture	Drug Distrubition	Pharmacology	8/28/06	9:30	10:00	MS-2
Jackson	Edwin	Lecture	Relationship Between Drug Dose & Effect	Pharmacology	8/28/06	10:00	11:00	MS-2
Jackson	Edwin	Lecture	Drug Metabolism	Pharmacology	8/28/06	11:15	12:00	MS-2
Jackson	Edwin	Lecture	Pharmacokinetics: Designing & Adjusting a Drug Regimen	Pharmacology	8/29/06	8:00	9:00	MS-2
Jackson	Edwin	Lecture	Pharmacokinetics: Designing & Adjusting a Drug Regimen	Pharmacology	8/29/06	9:15	10:00	MS-2
Jackson	Edwin	Lecture	Pharmacokinetics: Practice Problems	Pharmacology	8/29/06	10:30	11:30	MS-2
Jackson	Edwin	Lecture	Questions and Answers	Pharmacology	8/29/06	11:30	12:00	MS-2
Jiang	Yu	Lecture	Immunosupressive Agents for Transplantation & Autoimmunity	Immunology in Health and Disease 2007	1/26/07	9:00	10:00	MS-1
Jiang	Yu	Workshop	Neuropharmacology Workshop	Neuroscience	4/3/07	13:00	15:00	MS-1

FAC LAST NAME	FAC FIRST NAME	ACTIVITY TYPE	ACTIVITY TITLE	COURSE / CLERKSHIP TITLE	DATE	START TIME	END TIME	MEDICAL STUDENT LEVEL
Lakoski	Joan	Lecture	Pharrmacy Automomics	Board Review	3/13/07	18:15	20:00	MS-2
Lakoski	Joan	Lecture	Introduction to Autonomic Pharmacology	Pharmacology	8/30/06	8:00	10:00	MS-2
Lazo	John	Lecture	Pharmacology 4: Bronchodialators	BFH Pulmonary	11/2/06	10:30	11:20	MS-2
Lazo	John	Lecture	Antineoplastics then Pulmonary	Board Review	3/20/07	12:45	13:30	MS-2
Lazo	John	Lecture	Chemotherapy I	Hematology	1/10/07	13:00	14:00	MS-2
Lazo	John	Lecture	Chemotherapy II	Hematology	1/10/07	14:00	15:00	MS-2
Lazo	John	Lecture	Lecture 26: Cancer Treatment Approaches	Human Genetics	12/8/06	8:30	9:30	MS-1
Lazo	John	Lecture	Lecture 27: Cancer Chemical Genetics and Chemo	Human Genetics	12/8/06	9:45	10:45	MS-1
Lazo	John	Workshop	Neuropharmacology Workshop	Neuroscience	4/3/07	13:00	15:00	MS-1
Levitan	Edwin	Lecture	Receptor Regulation	Cell and Tissue Physiology	10/27/06	9:30	10:20	MS-1
Levitan	Edwin	Workshop	Question Session 2	Cell and Tissue Physiology	10/31/06	13:00	14:00	MS-1
Levitan	Edwin	Workshop	Physiology Workshop 1 - Diffusion and Membrand Potential	Cell Tissue and Physiology	10/25/06	13:00	14:30	MS-1
Levitan	Edwin	Workshop	Physiology Workshop 2 - Receptors	Cell Tissue and Physiology	10/27/06	10:30	12:00	MS-1
Levitan	Edwin	Workshop	Physiology Workshop 3 - Second Messengers	Cell Tissue and Physiology	10/30/06	10:15	11:45	MS-1
Levitan	Edwin	Lecture	Anticholinesterase Agents	Neuroscience	4/2/07	9:00	10:00	MS-1
Levitan	Edwin	Workshop	Neuropharmacology Workshop	Neuroscience	4/3/07	13:00	15:00	MS-1
Levitan	Edwin	Lecture	Pharmacology of Local Anesthetics in PNS	Neuroscience	4/11/07	13:00	14:00	MS-1

FAC LAST NAME	FAC FIRST NAME	ACTIVITY TYPE	ACTIVITY TITLE	COURSE / CLERKSHIP TITLE	DATE	START TIME	END TIME	MEDICAL STUDENT LEVEL
Palladino	Michael	Workshop	Neuropharmacology Workshop	Neuroscience	4/3/07	13:00	15:00	MS-1
Romero	Guillermo	Lecture	Receptors I	Cell and Tissue Physiology	10/24/06	10:00	10:50	MS-1
Romero	Guillermo	Lecture	Receptors II	Cell and Tissue Physiology	10/24/06	11:00	11:50	MS-1
Romero	Guillermo	Lecture	G-Proteins I	Cell and Tissue Physiology	10/25/06	14:40	15:30	MS-1
Romero	Guillermo	Lecture	G-Proteins II	Cell and Tissue Physiology	10/25/06	15:40	16:30	MS-1
Romero	Guillermo	Lecture	Second Messengers I	Cell and Tissue Physiology	10/26/06	9:00	9:50	MS-1
Romero	Guillermo	Lecture	Second Messengers II	Cell and Tissue Physiology	10/26/06	10:00	10:50	MS-1
Romero	Guillermo	Workshop	Question Session 2	Cell and Tissue Physiology	10/31/06	13:00	14:00	MS-1
Romero	Guillermo	Workshop	Neuropharmacology Workshop	Neuroscience	4/3/07	13:00	15:00	MS-1
Siegfried	Jill	Lecture	Pharmacology 2: Nicotine	BFH Pulmonary	11/1/06	15:00	15:50	MS-2
Siegfried	Jill	Lecture	Pharmacology 3: Smoking Cessation	BFH Pulmonary	11/1/06	16:00	16:50	MS-2
Siegfried	Jill	Lecture	Lung Cancer: Basic Aspects	ILS Neoplasia and Neoplastic Diseases	3/6/07	10:00	11:00	MS-4
Siegfried	Jill	Workshop	Neuropharmacology Workshop	Neuroscience	4/3/07	13:00	15:00	MS-1
Yalowich	Jack	Lecture	Board Review - Anti-bacterials and Anti-fungals	Board Review	3/13/07	15:00	16:00	MS-2
Yalowich	Jack	PBL	PBL 1: Initial Session	Human Genetics	11/17/06	10:30	12:00	MS-1
Yalowich	Jack	Small Group	Case 4	Integrated Case Studies	3/7/07	9:00	11:00	MS-2
Yalowich	Jack	Small Group	Case 4	Integrated Case Studies	3/8/07	9:00	11:00	MS-2

FAC LAST NAME	FAC FIRST NAME	ACTIVITY TYPE	ACTIVITY TITLE	COURSE / CLERKSHIP TITLE	DATE	START TIME	END TIME	MEDICAL STUDENT LEVEL
Yalowich	Jack	Small Group	Case 5	Integrated Case Studies	3/12/07	9:00	11:00	MS-2
Yalowich	Jack	Small Group	Case 5	Integrated Case Studies	3/13/07	9:00	11:00	MS-2
Yalowich	Jack	Small Group	Case 5	Integrated Case Studies	3/14/07	9:00	11:00	MS-2
Yalowich	Jack	Small Group	Case 6	Integrated Case Studies	3/15/07	9:00	11:00	MS-2
Yalowich	Jack	Small Group	Case 6	Integrated Case Studies	3/16/07	9:00	11:00	MS-2
Yalowich	Jack	Small Group	Summer Reading Assignments	Introduction to Being a Physician	8/21/06	14:00	16:00	MS-1
Yalowich	Jack	Small Group	Interview - Patient/family - Cystic Fibrosis	Introduction to Being a Physician	8/22/06	10:00	11:00	MS-1
Yalowich	Jack	Small Group	Interview Older Adults - Geriatrics	Introduction to Being a Physician	8/22/06	14:15	15:15	MS-1
Yalowich	Jack	Small Group	Breast Cancer	Introduction to Being a Physician	8/23/06	9:45	10:45	MS-1
Yalowich	Jack	Small Group	Public Health	Introduction to Being a Physician	8/23/06	14:15	16:30	MS-1
Yalowich	Jack	Small Group	Public Health	Introduction to Being a Physician	8/24/06	14:00	16:00	MS-1
Yalowich	Jack	Small Group	HIV AIDS	Introduction to Being a Physician	8/25/06	10:45	12:00	MS-1
Yalowich	Jack	Lecture	Antibacterials I	Medical Microbiology	2/12/07	9:15	10:15	MS-1
Yalowich	Jack	PBL	Intro to PBL #1	Medical Microbiology	2/12/07	10:30	12:00	MS-1
Yalowich	Jack	Lecture	Antibacterials II	Medical Microbiology	2/13/07	9:00	9:45	MS-1
Yalowich	Jack	Lecture	Antibacterials III	Medical Microbiology	2/13/07	10:00	10:45	MS-1
Yalowich	Jack	PBL	Resolution of PBL #1	Medical Microbiology	2/15/07	10:15	12:00	MS-1

FAC LAST NAME	FAC FIRST NAME	ACTIVITY TYPE	ACTIVITY TITLE	COURSE / CLERKSHIP TITLE	DATE	START TIME	END TIME	MEDICAL STUDENT LEVEL
Yalowich	Jack	Lecture	Quiz #1 and Review of Week #1 material	Medical Microbiology	2/16/07	11:15	12:00	MS-1
Yalowich	Jack	PBL	Intro to PBL #2	Medical Microbiology	2/19/07	10:30	12:00	MS-1
Yalowich	Jack	PBL	Resolution of PBL #2	Medical Microbiology	2/22/07	10:00	12:00	MS-1
Yalowich	Jack	PBL	Intro to PBL #3	Medical Microbiology	2/26/07	10:30	12:00	MS-1
Yalowich	Jack	PBL	Resolution of PBL #3	Medical Microbiology	3/1/07	10:10	12:00	MS-1
Yalowich	Jack	PBL	Intro to PBL #4	Medical Microbiology	3/5/07	10:30	12:00	MS-1
Yalowich	Jack	PBL	Resolution of PBL #4	Medical Microbiology	3/6/07	13:00	15:00	MS-1
Yalowich	Jack	Conference	Infectious Disease Conference	Medical Microbiology	3/7/07	13:00	15:00	MS-1
Yalowich	Jack	Workshop	Neuropharmacology Workshop	Neuroscience	4/3/07	13:00	15:00	MS-1
Yalowich	Jack	Lecture	Introduction to MS2 Pharmacology	Pharmacology	8/28/06	8:00	8:15	MS-2
Zhang	Lin	Lecture	Pharm - Drugs: Anticancer, COX2 Inhibitors Part 1	Digestion and Nutrition	11/30/06	13:00	13:50	MS-2
Zhang	Lin	Lecture	Pharm - Drugs: Anticancer, COX2 Inhibitors Part 2	Digestion and Nutrition	11/30/06	14:00	14:50	MS-2

Graduate Student Instructional Activities

FAC LAST NAME	FAC FIRST NAME	ACTIVITY TYPE	ACTIVITY TITLE	COURSE/PROGRAM TITLE	DATE	START TIME	END TIME	STUDENT LEVEL
Altschuler	Daniel	Lecture	G proteins II	MSMPHL 2360: Biology of Signal Transduction	01/23/07	9:00	10:30	GS
Palladino	Michael	Exam	MidTerm exam	MSMPHL 3375: Neuropharmacology	02/05/07	15:00	16:30	GS
Altschuler	Daniel	Lecture	GTP Binding Proteins I	INTBP 2000: Foundations of Biomedical Science	09/19/06	9:00	9:55	GS
Altschuler	Daniel	Lecture	GTP Binding Proteins II	INTBP 2000: Foundations of Biomedical Science	09/19/06	10:00	11:00	GS
Altschuler	Daniel	Lecture	Second Messengers I	INTBP 2000: Foundations of Biomedical Science	09/21/06	9:00	9:55	GS
Altschuler	Daniel	Lecture	Second Messengers II	INTBP 2000: Foundations of Biomedical Science	09/21/06	10:00	11:00	GS
Altschuler	Daniel	Lecture	Methods based lectures	INTBP 2000: Foundations of Biomedical Science	09/22/06	9:00	9:55	GS
Altschuler	Daniel	Exam	Exam 2	INTBP 2000: Foundations of Biomedical Science	10/05/06	9:00	12:00	GS
Altschuler	Daniel	Exam	Exam 4	INTBP 2000: Foundations of Biomedical Science	11/28/06	9:00	12:00	GS
Altschuler	Daniel	Lecture	Adenylate Cyclase	MSMPHL 2360: Biology of Signal Transduction	01/16/07	9:00	10:30	GS
Altschuler	Daniel	Lecture	G proteins I	MSMPHL 2360: Biology of Signal Transduction	01/18/07	9:00	10:30	GS
Altschuler	Daniel	Lecture	G proteins III	MSMPHL 2360: Biology of Signal Transduction	01/25/07	9:00	10:30	GS
Bisello	Alessandro	Lecture	Signal termination: Receptor desensitization and downregulation I	INTBP 2000: Foundations of Biomedical Science	09/29/06	9:00	9:55	GS

FAC LAST NAME	FAC FIRST NAME	ACTIVITY TYPE	ACTIVITY TITLE	COURSE/PROGRAM TITLE	DATE	START TIME	END TIME	STUDENT LEVEL
Bisello	Alessandro	Lecture	2. Signal termination: Receptor desens. and downregulation II	INTBP 2000: Foundations of Biomedical Science	09/29/06	10:00	11:00	GS
Bisello	Alessandro	Lecture	Drug - Receptor Interactions I	MSMPHL 2310: Principles of Pharm.	01/17/07	16:00	17:25	GS
Bisello	Alessandro	Lecture	Drug - Receptor Interactions II	MSMPHL 2310: Principles of Pharm.	01/24/07	16:00	17:25	GS
DeFranco	Donald	Lecture	Nuclear receptors	MSMPHL 3360: MOLECULAR PHARMACOLOGY	09/26/06	10:00	11:30	GS
DeFranco	Donald	Lecture	Anti-inflamatory action of glucocorticoids	MSMPHL 3360: MOLECULAR PHARMACOLOGY	09/28/06	10:00	11:30	GS
DeFranco	Donald	Lecture	Nuclear/Cytoplasmic Trafficking I	INTBP 2000: Foundations of Biomedical Science	11/09/06	9:00	9:55	GS
DeFranco	Donald	Lecture	Nuclear/Cytoplasmic Trafficking II	INTBP 2000: Foundations of Biomedical Science	11/09/06	10:00	11:00	GS
DeFranco	Donald	Small Group	Robb Tomko	MSMPHL 3320: Journal Club	11/09/06	12:00	13:00	GS
DeFranco	Donald	Small Group	Robb Tomko	MSMPHL 2350: Research Seminar	11/10/06	12:00	13:00	GS
DeFranco	Donald	Lecture	Steroid Receptors	MSBMG 3510 Advanced Topics in Gene Expression	11/28/06	10:00	11:30	GS
DeFranco	Donald	Lecture	Steroid Receptors	MSBMG 3510 Advanced Topics in Gene Expression	11/30/06	10:00	11:30	GS
DeFranco	Donald	Lecture	Introduction to Neurobiology	MSMPHL 3375: Neuropharmacology	01/04/07	15:00	16:30	GS
DeFranco	Donald	Lecture	Drugs and Neurodegeneration - Other Diseases	MSMPHL 3375: Neuropharmacology	03/15/07	15:00	16:30	GS
DeFranco	Donald	Lecture	Transcription regulation	MSMPHL 2360: Biology of Signal Transduction	04/12/07	9:00	10:30	GS
Eiseman	Julie	Lecture	Drug Metabolism and Biotransformation I	MSMPHL 2310: Principles of Pharm.	03/21/07	16:00	17:25	GS
Eiseman	Julie	Lecture	Drug Metabolism and Biotransformation II	MSMPHL 2310: Principles of Pharm.	03/28/07	16:00	17:25	GS

FAC LAST NAME	FAC FIRST NAME	ACTIVITY TYPE	ACTIVITY TITLE	COURSE/PROGRAM TITLE	DATE	START TIME	END TIME	STUDENT LEVEL
Freeman	Bruce	Lecture	Nitric oxide, cGMP and vascular/CNS signaling	INTBP 2000: Foundations of Biomedical Science	10/03/06	9:00	9:55	GS
Freeman	Bruce	Lecture	Nitric oxide, redox reactions and inflammatory signaling	INTBP 2000: Foundations of Biomedical Science	10/03/06	10:00	11:00	GS
Freeman	Bruce	Small Group	Jon Beckel	MSMPHL 3320: Journal Club	04/17/07	12:00	13:00	GS
Freeman	Bruce	Small Group	Jon Beckel	MSMPHL 2350: Research Seminar	04/20/07	12:00	13:00	GS
Friedman	Peter	Small Group	Mike Hezel	MSMPHL 3320: Journal Club	05/08/07	12:00	13:00	GS
Friedman	Peter	Small Group	Mike Hezel	MSMPHL 2350: Research Seminar	05/11/07	12:00	13:00	GS
Furey	William	Lecture	Lecture – Overview of X-ray crystallography	MSCBIO 2050: Laboratory Methods for Computational Biologists	01/22/07	15:00	16:00	GS
Furey	William	Lecture	Lecture and Lab – Introduction to crystallization methods and set up crystallization of lysozyme	MSCBIO 2050: Laboratory Methods for Computational Biologists	01/23/07	14:00	16:30	GS
Furey	William	Lecture	Lecture – X-ray data analysis and structure determination	MSCBIO 2050: Laboratory Methods for Computational Biologists	01/29/07	15:00	16:00	GS
Furey	William	Lecture	Lecture – X-ray data analysis and structure determination	MSCBIO 2050: Laboratory Methods for Computational Biologists	01/29/07	15:00	17:00	GS
Furey	William	Lecture	Computational Lab – on X-ray data analysis	MSCBIO 2050: Laboratory Methods for Computational Biologists	01/30/07	14:00	16:30	GS
Furey	William	Lecture	Lab – Fish out crystals and collect X-ray diffraction data	MSCBIO 2050: Laboratory Methods for Computational Biologists	02/01/07	14:00	15:30	GS
Furey	William	Lecture	Lecture – Lysozyme structure analysis review	MSCBIO 2050: Laboratory Methods for Computational Biologists	02/05/07	15:00	16:00	GS

FAC LAST NAME	FAC FIRST NAME	ACTIVITY TYPE	ACTIVITY TITLE	COURSE/PROGRAM TITLE	DATE	START TIME	END TIME	STUDENT LEVEL
Furey	William	Lecture	Lecture – X-ray wrap-up	MSCBIO 2050: Laboratory Methods for Computational Biologists	02/06/07	14:00	16:30	GS
Furey	William	Lecture	Lecture – X-ray wrap-up	MSCBIO 2050: Laboratory Methods for Computational Biologists	02/06/07	14:00	15:30	GS
Galbiati	Ferruccio	Lecture	Pharmacology of Diuretics	MSMPHL 3360: MOLECULAR PHARMACOLOGY	11/16/06	10:00	11:30	GS
Galbiati	Ferruccio	Exam	Exam	MSMPHL 3360: MOLECULAR PHARMACOLOGY	12/12/06	10:00	11:30	GS
Galbiati	Ferruccio	Small Group	Janine Bartholomew	MSMPHL 3320: Journal Club	12/14/06	12:00	13:00	GS
Galbiati	Ferruccio	Small Group	Janine Bartholomew	MSMPHL 2350: Research Seminar	12/15/06	12:00	13:00	GS
Galbiati	Ferruccio	Lecture	Signaling and Muscular Dystrophy	MSMPHL 2360: Biology of Signal Transduction	02/06/07	9:00	10:30	GS
Hershberger	Pamela	Lecture	Vitamin D Therapy of Cancer	MSCMP 3710 and MSPHL 3310 Cancer Biology and Therapeutics	11/15/06	14:00	15:00	GS
Hu	Jing	Small Group	Pete McDonald	MSMPHL 3320: Journal Club	09/28/06	12:00	13:00	GS
Hu	Jing	Small Group	Pete McDonald	MSMPHL 2350: Research Seminar	09/29/06	12:00	13:00	GS
Hu	Jing	Lecture	Chemoprevention of Cancer	MSCMP 3710 and MSPHL 3310 Cancer Biology and Therapeutics	12/08/06	14:00	15:00	GS
Jackson	Edwin	Lecture	Introduction to Pharmacology	MSMPHL 3375: Neuropharmacology	01/08/07	15:00	16:30	GS
Jackson	Edwin	Small Group	Alison Groeger	MSMPHL 3320: Journal Club	03/13/07	12:00	13:00	GS
Jackson	Edwin	Small Group	Alison Groeger	MSMPHL 2350: Research Seminar	03/16/07	12:00	13:00	GS
Jiang	Yu	Lecture	New Therapies: Targeting mTOR	MSCMP 3710 and MSPHL 3310 Cancer Biology and Therapeutics	11/03/06	14:00	15:00	GS

FAC LAST NAME	FAC FIRST NAME	ACTIVITY TYPE	ACTIVITY TITLE	COURSE/PROGRAM TITLE	DATE	START TIME	END TIME	STUDENT LEVEL
Jiang	Yu	Small Group	Miranda Sarachine	MSMPHL 3320: Journal Club	12/07/06	12:00	13:00	GS
Jiang	Yu	Small Group	Miranda Sarachine	MSMPHL 2350: Research Seminar	12/08/06	12:00	13:00	GS
Jiang	Yu	Lecture	Drug Administration and Absorption	MSMPHL 2310: Principles of Pharm.	01/03/07	16:00	17:25	GS
Jiang	Yu	Lecture	Drug Distribution and Elimination	MSMPHL 2310: Principles of Pharm.	01/10/07	16:00	17:25	GS
Jiang	Yu	Small Group	Problem solving techniques for current ethical challenges	INTBP 2290: Scientific Ethics Break-out Session	05/14/07	10:15	11:30	GS
Jiang	Yu	Small Group	Mentor and trainee guidelines & collaborative research	INTBP 2290: Scientific Ethics Break-out Session	05/16/07	10:15	11:30	GS
Jiang	Yu	Small Group	Peer review, authorship and publication issues	INTBP 2290: Scientific Ethics Break-out Session	05/21/07	10:15	11:30	GS
Jiang	Yu	Small Group	Record keeping and data presentation	INTBP 2290: Scientific Ethics Break-out Session	05/23/07	10:15	11:30	GS
Jiang	Yu	Small Group	Use of humans as research subjects	INTBP 2290: Scientific Ethics Break-out Session	06/04/07	10:15	11:30	GS
Jiang	Yu	Small Group	Use of Animals in Research	INTBP 2290: Scientific Ethics Break-out Session	06/06/07	10:15	11:30	GS
Jiang	Yu	Small Group	Intellectual property and patents	INTBP 2290: Scientific Ethics Break-out Session	06/11/07	10:15	11:30	GS
Jiang	Yu	Small Group	Responding to violations of research integrity; Conflicts of Interest in Academia	INTBP 2290: Scientific Ethics Break-out Session	06/13/07	10:15	11:30	GS
Lakoski	Joan	Small Group	Dev Chandra	MSMPHL 3320: Journal Club	09/14/06	12:00	13:00	GS
Lakoski	Joan	Small Group	Dev Chandra	MSMPHL 2350: Research Seminar	09/15/06	12:00	13:00	GS
Lakoski	Joan	Small Group	Professional Development	MSELECT 5971 Professional Development Course	05/30/07	14:00	16:00	GS
Lazo	John	Exam	Exam	MSMPHL 3360: MOLECULAR PHARMACOLOGY	10/10/06	10:00	11:30	GS

FAC LAST NAME	FAC FIRST NAME	ACTIVITY TYPE	ACTIVITY TITLE	COURSE/PROGRAM TITLE	DATE	START TIME	END TIME	STUDENT LEVEL
Lazo	John	Exam	Exam	MSMPHL 3360: MOLECULAR PHARMACOLOGY	11/09/06	10:00	11:30	GS
Lazo	John	Lecture	Multi-Drug Resistance	MSCMP 3710 and MSPHL 3310 Cancer Biology and Therapeutics	11/17/06	14:00	15:00	GS
Lazo	John	Lecture	Drug Resistance: Non-MDR Mechanisms	MSCMP 3710 and MSPHL 3310 Cancer Biology and Therapeutics	12/01/06	14:00	15:00	GS
Lazo	John	Exam	FINAL EXAM	MSCMP 3710 and MSPHL 3310 Cancer Biology and Therapeutics	12/11/06	14:00	15:00	GS
Lazo	John	Lecture	Protein phosphatases	MSMPHL 2360: Biology of Signal Transduction	02/27/07	9:00	10:30	GS
Lazo	John	Small Group	Pierre Queiroz de Oliveira	MSMPHL 3320: Journal Club	05/01/07	12:00	13:00	GS
Lazo	John	Small Group	Pierre Queiroz de Oliveira	MSMPHL 2350: Research Seminar	05/04/07	12:00	13:00	GS
Levitan	Edwin	Lecture	Ca	INTBP 2000: Foundations of Biomedical Science	12/11/06	9:00	9:55	GS
Levitan	Edwin	Lecture	Ca	INTBP 2000: Foundations of Biomedical Science	12/11/06	10:00	11:00	GS
Levitan	Edwin	Lecture	neurosecretion	INTBP 2000: Foundations of Biomedical Science	12/12/06	9:00	9:55	GS
Levitan	Edwin	Small Group	Yi Zhou	MSMPHL 3320: Journal Club	01/16/07	12:00	13:00	GS
Levitan	Edwin	Lecture	Anticholinesterases	MSMPHL 3375: Neuropharmacology	01/18/07	15:00	16:30	GS
Levitan	Edwin	Lecture	Pharmacokinetics	MSMPHL 2310: Principles of Pharm.	01/31/07	16:00	17:25	GS
Levitan	Edwin	Lecture	Dose - Response Relationships	MSMPHL 2310: Principles of Pharm.	02/06/07	16:00	17:25	GS
Levitan	Edwin	Lecture	Regulation receptor sensitivity	MSMPHL 2360: Biology of Signal Transduction	02/08/07	9:00	10:30	GS

FAC LAST NAME	FAC FIRST NAME	ACTIVITY TYPE	ACTIVITY TITLE	COURSE/PROGRAM TITLE	DATE	START TIME	END TIME	STUDENT LEVEL
Levitan	Edwin	Lecture	Exocytosis and Endocytosis	MSMPHL 2360: Biology of Signal Transduction	02/13/07	9:00	10:30	GS
Levitan	Edwin	Small Group	Dave Werner	MSMPHL 3320: Journal Club	04/03/07	12:00	13:00	GS
Levitan	Edwin	Small Group	Dave Werner	MSMPHL 2350: Research Seminar	04/06/07	12:00	13:00	GS
Levitan	Edwin	Small Group	Nicole Kotchey	MSMPHL 3320: Journal Club	04/10/07	12:00	13:00	GS
Levitan	Edwin	Small Group	Nicole Kotchey	MSMPHL 2350: Research Seminar	04/13/07	12:00	13:00	GS
Nichols	Mark	Lecture	Reproduction and contraception I	MSMPHL 3360: MOLECULAR PHARMACOLOGY	10/03/06	10:00	11:30	GS
Nichols	Mark	Lecture	Reproduction and contraception II	MSMPHL 3360: MOLECULAR PHARMACOLOGY	10/05/06	10:00	11:30	GS
Palladino	Michael	Small Group	John Caltagarone	MSMPHL 3320: Journal Club	09/07/06	12:00	13:00	GS
Palladino	Michael	Small Group	John Caltagarone	MSMPHL 2350: Research Seminar	09/08/06	12:00	13:00	GS
Palladino	Michael	Small Group	Controlled proteolysis of nascent polypeptides in rat liver cell fractions. II. Location of the polypeptides in rough microsomes	INTBP 2005 Foundations Conference	11/10/06	13:00	15:00	GS
Palladino	Michael	Small Group	Decay of Endoplasmic Reticulum-Localized mRNA's During the Unfolded Protein Response.	INTBP 2005 Foundations Conference	11/14/06	13:00	15:00	GS
Palladino	Michael	Small Group	Fusion of Cells by Flipped SNARE's	INTBP 2005 Foundations Conference	11/17/06	13:00	15:00	GS
Palladino	Michael	Small Group	Interaction of Tyrosine-Based Sorting Signals with Clathrin-Associated Protiens.	INTBP 2005 Foundations Conference	11/21/06	13:00	15:00	GS
Palladino	Michael	Small Group	LRP6 Holds the Key to the Entry of Anthrax Toxin.	INTBP 2005 Foundations Conference	12/01/06	13:00	15:00	GS

FAC LAST NAME	FAC FIRST NAME	ACTIVITY TYPE	ACTIVITY TITLE	COURSE/PROGRAM TITLE	DATE	START TIME	END TIME	STUDENT LEVEL
Palladino	Michael	Small Group	Cloning of genomic and complementary DNA from Shaker, a putative potassium channel gene from Drosophila. Science.	INTBP 2005 Foundations Conference	12/05/06	13:00	15:00	GS
Palladino	Michael	Small Group	Systematic analysis of genes required for synapse structure and function.	INTBP 2005 Foundations Conference	12/08/06	13:00	15:00	GS
Palladino	Michael	Small Group	The Principle of gating charge movement in a voltage-dependent K+ channel.	INTBP 2005 Foundations Conference	12/12/06	13:00	15:00	GS
Palladino	Michael	Lecture	Epilepsy and Anticonvulsants	MSMPHL 3375: Neuropharmacology	02/22/07	15:00	16:30	GS
Palladino	Michael	Lecture	Neurodegeneration - Model systems	MSMPHL 3375: Neuropharmacology	03/12/07	15:00	16:30	GS
Palladino	Michael	Exam	Final exam	MSMPHL 3375: Neuropharmacology	04/19/07	15:00	16:30	GS
Romero	Guillermo	Lecture	Glucose homeostasis I	MSMPHL 3360: MOLECULAR PHARMACOLOGY	09/12/06	10:00	11:30	GS
Romero	Guillermo	Lecture	Glucose homeostasis II	MSMPHL 3360: MOLECULAR PHARMACOLOGY	09/14/06	10:00	11:30	GS
Romero	Guillermo	Lecture	Introduction to Signal Transduction	INTBP 2000: Foundations of Biomedical Science	09/15/06	9:00	9:55	GS
Romero	Guillermo	Lecture	Receptor Structure and Function I	INTBP 2000: Foundations of Biomedical Science	09/15/06	10:00	11:00	GS
Romero	Guillermo	Lecture	Receptor Structure and Function II	INTBP 2000: Foundations of Biomedical Science	09/18/06	9:00	9:55	GS
Romero	Guillermo	Lecture	Receptor Structure and Function III	INTBP 2000: Foundations of Biomedical Science	09/18/06	10:00	11:00	GS
Romero	Guillermo	Lecture	Receptor Tyrosine Kinases I	INTBP 2000: Foundations of Biomedical Science	09/28/06	9:00	9:55	GS

FAC LAST NAME	FAC FIRST NAME	ACTIVITY TYPE	ACTIVITY TITLE	COURSE/PROGRAM TITLE	DATE	START TIME	END TIME	STUDENT LEVEL
Romero	Guillermo	Lecture	Receptor Tyrosine Kinases	INTBP 2000: Foundations of Biomedical Science	09/28/06	10:00	11:00	GS
Romero	Guillermo	Lecture	GPCR	MSMPHL 2360: Biology of Signal Transduction	01/11/07	9:00	10:30	GS
Romero	Guillermo	Lecture	Serine-Threonine Kinases I	MSMPHL 2360: Biology of Signal Transduction	01/30/07	9:00	10:30	GS
Romero	Guillermo	Lecture	Serine-Threonine Kinases II	MSMPHL 2360: Biology of Signal Transduction	02/01/07	9:00	10:30	GS
Romero	Guillermo	Lecture	MAP Kinase	MSMPHL 2360: Biology of Signal Transduction	02/20/07	9:00	10:30	GS
Romero	Guillermo	Lecture	Exam	MSMPHL 2360: Biology of Signal Transduction	02/22/07	9:00	10:30	GS
Romero	Guillermo	Lecture	Lipid Kinases and Lipases	MSMPHL 2360: Biology of Signal Transduction	03/29/07	9:00	10:30	GS
Romero	Guillermo	Lecture	Exam Handed Out	MSMPHL 2360: Biology of Signal Transduction	04/24/07	9:00	10:30	GS
Romero	Guillermo	Lecture	Pharmacology	MSTP Introduction to Moleculary Medicine	06/26/07	17:00	19:00	GS
Romero	Guillermo	Lecture	Pharmacology	MSTP Introduction to Moleculary Medicine	06/28/07	17:00	19:00	GS
Sharlow	Elizabeth	Lecture	Drug Discovery – INTRO Targets and validation	MSMPHL 3360: MOLECULAR PHARMACOLOGY	10/12/06	10:00	11:30	GS
Siegfried	Jill	Lecture	Lung Cancer	MSCMP 3710 and MSPHL 3310 Cancer Biology and Therapeutics	10/04/06	14:00	15:00	GS
Siegfried	Jill	Lecture	Hormone Therapy of Cancer	MSCMP 3710 and MSPHL 3310 Cancer Biology and Therapeutics	11/20/06	14:00	15:00	GS
Siegfried	Jill	Small Group	Neil Bhola	MSMPHL 3320: Journal Club	01/09/07	12:00	13:00	GS
Siegfried	Jill	Small Group	Neil Bhola	MSMPHL 2350: Research Seminar	01/12/07	12:00	13:00	GS

FAC LAST NAME	FAC FIRST NAME	ACTIVITY TYPE	ACTIVITY TITLE	COURSE/PROGRAM TITLE	DATE	START TIME	END TIME	STUDENT LEVEL
Siegfried	Jill	Lecture	Signaling and oncogenesis	MSMPHL 2360: Biology of Signal Transduction	04/03/07	9:00	10:30	GS
Sobol	Robert	Lecture	DNA Repair Mechanisms	MSCMP 3710 and MSPHL 3310 Cancer Biology and Therapeutics	09/25/06	14:00	15:00	GS
Sobol	Robert	Lecture	DNA damage and repair	INTBP 2000: Foundations of Biomedical Science	10/16/06	9:00	9:55	GS
Sobol	Robert	Lecture	DNA damage and repair	INTBP 2000: Foundations of Biomedical Science	10/16/06	10:00	11:00	GS
Sobol	Robert	Lecture	Genome Stability I	INTBP 2000: Foundations of Biomedical Science	10/17/06	9:00	9:55	GS
Sobol	Robert	Lecture	Genome Stability II	INTBP 2000: Foundations of Biomedical Science	10/17/06	10:00	11:00	GS
Sobol	Robert	Lecture	Targeting DNA repair pathways to enhance therapeutic efficacy	MSCMP 3710 and MSPHL 3310 Cancer Biology and Therapeutics	10/23/06	14:00	15:00	GS
Sobol	Robert	Small Group	Greg Gan	MSMPHL 3320: Journal Club	10/26/06	12:00	13:00	GS
Sobol	Robert	Small Group	Greg Gan	MSMPHL 2350: Research Seminar	10/27/06	12:00	13:00	GS
Vogt	Andreas	Lecture	Drug Discovery Module IV High Content Screening	MSMPHL 3360: MOLECULAR PHARMACOLOGY	10/26/06	10:00	11:30	GS
Vogt	Andreas	Lecture	Signaling and drug discovery	MSMPHL 2360: Biology of Signal Transduction	02/15/07	9:00	10:30	GS
Wang	Qiming	Lecture	Protein Kinases and Phosphatases I	INTBP 2000: Foundations of Bio Scie	09/26/06	9:00	9:55	GS
Wang	Qiming	Lecture	Protein Kinases and Phosphatases II	INTBP 2000: Foundations of Biomedical Science	09/26/06	10:00	11:00	GS
Wang	Qiming	Lecture	Pharmacology of Antihypertensive Drugs	MSMPHL 3360: MOLECULAR PHARMACOLOGY	11/21/06	10:00	11:30	GS
Wang	Qiming	Small Group	Dora Pene-Dumitrescu	MSMPHL 3320: Journal Club	11/30/06	12:00	13:00	GS

FAC LAST NAME	FAC FIRST NAME	ACTIVITY TYPE	ACTIVITY TITLE	COURSE/PROGRAM TITLE	DATE	START TIME	END TIME	STUDENT LEVEL
Wang	Qiming	Small Group	Dora Pene-Dumitrescu	MSMPHL 2350: Research Seminar	12/01/06	12:00	13:00	GS
Wood	Richard	Lecture	Male Histology	MSCBMP 2870: Histology	04/04/07	8:30	9:30	GS
Yalowich	Jack	Lecture	Antibiotics I	MSMPHL 3360: MOLECULAR PHARMACOLOGY	09/05/06	10:00	11:30	GS
Yalowich	Jack	Lecture	Antibiotics II	MSMPHL 3360: MOLECULAR PHARMACOLOGY	09/07/06	10:00	11:30	GS
Yalowich	Jack	Lecture	Principles of Cancer Chemotherapy I	MSCMP 3710 and MSPHL 3310 Cancer Biology and Therapeutics	10/18/06	14:00	15:00	GS
Yalowich	Jack	Lecture	Principles of Cancer Chemotherapy II	MSCMP 3710 and MSPHL 3310 Cancer Biology and Therapeutics	10/20/06	14:00	15:00	GS
Yalowich	Jack	Lecture	Alkylating Agents II: Oxazaphosphorines	MSCMP 3710 and MSPHL 3310 Cancer Biology and Therapeutics	11/10/06	14:00	15:00	GS
Yalowich	Jack	Lecture	Antifolates	MSCMP 3710 and MSPHL 3310 Cancer Biology and Therapeutics	11/13/06	14:00	15:00	GS
Yalowich	Jack	Lecture	Topoisomerase Inhibitors	MSCMP 3710 and MSPHL 3310 Cancer Bio and Therapeutics	11/29/06	14:00	15:00	GS
Yalowich	Jack	Lecture	Drug Transport	MSMPHL 2310: Principles of Pharm.	02/20/07	16:00	17:25	GS
Yalowich	Jack	Lecture	Drug Resistance	MSMPHL 2310: Principles of Pharm.	02/21/07	16:00	17:25	GS
Zhang	Lin	Small Group	Hypothesis Generation & Testing	INTBP 2005 Foundations Conference	08/29/06	13:00	15:00	GS
Zhang	Lin	Small Group	Proceedings of the National Academy of Sciences	INTBP 2005 Foundations Conference	09/01/06	13:00	15:00	GS
Zhang	Lin	Small Group	Reprogramming Control of an Allosteric Signaling Switch Through Modular Recombination.	INTBP 2005 Foundations Conference	09/05/06	13:00	15:00	GS

FAC LAST NAME	FAC FIRST NAME	ACTIVITY TYPE	ACTIVITY TITLE	COURSE/PROGRAM TITLE	DATE	START TIME	END TIME	STUDENT LEVEL
Zhang	Lin	Small Group	A Myristoyl/Phosphotyrosine Switch Regulates c-Abl.	INTBP 2005 Foundations Conference	09/08/06	13:00	15:00	GS
Zhang	Lin	Small Group	Functional organization of the yeast proteome by systematic analysis of protein complexes	INTBP 2005 Foundations Conference	09/12/06	13:00	15:00	GS
Zhang	Lin	Small Group	Dual signaling is differentially activated by different active states of the metabotropic glutamate receptor 1α	INTBP 2005 Foundations Conference	09/19/06	13:00	15:00	GS
Zhang	Lin	Small Group	New Insights into the Role of Conserved, Essential Residues in the GTP Binding/GTP Hydrolytic Cycle of Large G Proteins.	INTBP 2005 Foundations Conference	09/22/06	13:00	15:00	GS
Zhang	Lin	Small Group	Discrete Microdomains with High Concentration of cAMP in Stimulated Rat Neonatal Cardiac Myocytes	INTBP 2005 Foundations Conference	09/26/06	13:00	15:00	GS
Zhang	Lin	Small Group	An Allosteric Mechanism for Activation of the Kinase Domain of Epidermal Growth Factor Receptor.	INTBP 2005 Foundations Conference	09/29/06	13:00	15:00	GS
Zhang	Lin	Small Group	Responsible Conduct Workshop	INTBP 2005 FoundationsConference	10/03/06	13:00	15:00	GS
Zhang	Lin	Lecture	Cell cycle	INTBP 2000: Foundations of Biomedical Science	10/31/06	9:00	9:55	GS
Zhang	Lin	Lecture	Cell cycle	INTBP 2000: Foundations of Biomedical Science	10/31/06	10:00	11:00	GS
Zhang	Lin	Lecture	p53 in anticancer therapy	MSCMP 3710 and MSPHL 3310 Cancer Biology and Therapeutics	11/08/06	14:00	15:00	GS
Zhang	Lin	Lecture	Apoptotic response to Stress	MSMPHL 2360: Biology of Signal Transduction	03/15/07	9:00	10:30	GS

FAC LAST NAME	FAC FIRST NAME	ACTIVITY TYPE	ACTIVITY TITLE	COURSE/PROGRAM TITLE	DATE	START TIME	END TIME	STUDENT LEVEL
Zhang	Lin	Small Group	Alex Bank	MSMPHL 3320: Journal Club	03/27/07	12:00	13:00	GS
Zhang	Lin	Small Group	Alex Bank	MSMPHL 2350: Research Seminar	03/30/07	12:00	13:00	GS

Medical Student Committee Activities

FAC LAST NAME	FAC FIRST NAME	COMMITTEE NAME:	COMMITTEE ROLE	SERVICE START DATE	SERVICE END DATE
DeFranco	Donald	Course Design Group - Cell Tissue and Physiology	Member	07/01/06	06/30/07
DeFranco	Donald	Dean's Applicant Interviewer	Member	07/01/06	06/30/07
deGroat	William	Course Design Group - Neuroscience	Member	07/01/06	06/30/07
Friedman	Peter	Promotions	Member	07/01/06	06/30/07
Yalowich	Jack	Curriculum	Member	07/01/06	06/30/07
Yalowich	Jack	Promotions	Member	07/01/06	06/30/07
Yalowich	Jack	Retention Committee	Member	07/01/06	06/30/07
Yalowich	Jack	UMETC	Member	07/01/06	06/30/07

Medical Student Administrative Activities

FAC LAST NAME	FAC FIRST NAME	ACTIVITY TYPE	COURSE / CLERKSHIP	SERVICE START DATE	SERVICE END DATE	DEGREE PROGRAM	MEDICAL STUDENT LEVEL
DeFranco	Donald	Course Director	Cell Biology & Physiology	07/01/06	06/30/07	MS	MS-1
Yalowich	Jack	Course Director	Pharmacology	07/01/06	06/30/07	MS	MS-2

Graduate Student Administrative Activities

FAC LAST NAME	FAC FIRST NAME	ACTIVITY TYPE	COURSE / PROGRAM TITLE	SERVICE START DATE	SERVICE END DATE
Altschuler	Daniel	GS Course Director	INTBP 2000: Foundations of Biomedical Science	08/28/06	12/16/06
Altschuler	Daniel	GS Course Director	INTBP 2005: Foundations of Biomedical Science Conf.	08/28/06	12/16/06
Bisello	Alessandro	GS Course Director	MSPHL 2310: Principles of Pharmacology	01/03/07	4/28/07
DeFranco	Donald	GS Program Director	Molecular Pharmacology	07/01/06	06/30/07
Defranco	Donald	GS Course Director	MSMPHL 3320: Journal Club	08/28/06	12/16/06
Defranco	Donald	GS Course Director	MSPHL 2350: Research Seminar	08/28/06	12/16/06
Defranco	Donald	GS Course Director	MSPHL 2350: Research Seminar	01/03/07	04/28/07
Defranco	Donald	GS Course Director	MSPHL 3320: Journal Club	01/03/07	04/28/07
Galbiati	Ferruccio	GS Course Director	MSPHL 3360: MOLECULAR PHARMACOLOGY	08/28/06	12/16/06
Jiang	Yu	GS Course Director	MSPHL 2310: Principles of Pharmacology	01/03/07	4/28/07
Lazo	John	GS Course Director	MSPHL 3360: MOLECULAR PHARMACOLOGY	08/28/06	12/16/06
Palladino	Michael	GS Course Director	MSMPHL 3375: Neuropharmacology	01/03/07	4/28/07
Romero	Guillermo	GS Course Director	MSMPHL 2360: Biology of Sig Transduc	01/03/07	04/28/07
Yalowich	Jack	GS Course Director	MSPHL 3310/MSCMP 3710: CANCER BIOLOGY AND THERAPEUTICS	08/28/06	12/16/06

Graduate Student Ph.D. Mentoring Activities

FAC LAST NAME	FAC FIRST NAME	ACTIVITY TYPE	STUDENT NAME
DeFranco	Donald	PhD Mentor	Caltagarone, John
Freeman	Bruce	PhD Mentor	Groeger, Alison
Galbiati	Ferruccio	PhD Mentor	Bartholomew, Janine\
Galbiati	Ferruccio	PhD Mentor	Hezel, Michael
Lazo	John	PhD Mentor	McDonald, Peter
Lazo	John	PhD Mentor	Tomko, Robert
Lazo	John	PhD Mentor	Bansal, Pallavi
Lazo	John	PhD Mentor	Kitchens, Carolyn
Lazo	John	PhD Mentor	Queiroz de Oliveira, Pierre
Lazo	John	PhD Mentor	Wang, Yan
Levitan	Edwin	PhD Mentor	Zhou, Yi
Palladino	Michael	PhD Mentor	Kotchey, Nicole
Siegfried	Jill	PhD Mentor	Dulak, Austin
Wood	Richard	PhD Mentor	Gan,Gregory
Zhang	Lin	PhD Mentor	Bank, Alex

Graduate Student Lab Supervision Activities, Other Than Primary Ph.D. Mentoring

FAC LAST NAME	FAC FIRST NAME	PROGRAM	PERIOD START DATE	PERIOD END DATE	STUDENT WEEKS IN LAB:	STUDENT NAME
Conrads	Thomas	IBGP	01/01/07	03/31/07	10	Bateman, Nicholas
Galbiati	Ferruccio	IBGP	09/15/06	12/31/06	10	Furda, Amy
Levitan	Edwin	IBGP	01/01/07	03/31/07	10	Wong, Man Yan
Singh	Shivendra	IBGP	09/15/06	12/31/06	10	Panjarian, Shoghag
Sobol	Robert	IBGP	07/01/06	09/15/06	10	Goellner, Eva
Wang	Qiming	IBGP	09/15/06	12/31/06	10	Macneil, Courtney

FAC LAST NAME	FAC FIRST NAME	PROGRAM	PERIOD START DATE	PERIOD END DATE	STUDENT WEEKS IN LAB:	STUDENT NAME
Wood	Richard	PIMB	11/27/06	12/22/06	4	Liu, Xi
Zhang	Lin	IBGP	01/01/07	03/31/2007	10	Goellner, Eva

Graduate Program Committee Activities

FAC LAST NAME	FAC FIRST NAME	COMMITTEE NAME	COMMITTEE ROLE	SERVICE START DATE	SERVICE END DATE
DeFranco	Donald	PIMB-Academic Affairs	Chair	07/03/06	07/02/07
DeFranco	Donald	PIMB-Steering	Member	07/09/06	07/08/07
DeFranco	Donald	Graduate Council	Member	07/01/06	06/30/07
DeFranco	Donald	IBGP Steering Committee	Member	07/01/06	06/30/07
Furey	William	MBSB-Oversight & Evaluations	Member	07/01/06	06/30/07
Galbiati	Ferruccio	IBGP- Recruiting	Member	07/01/06	06/30/07
Palladino	Michael	IBGP-SURP (Recruiting Subcommittee)	Member	07/01/06	06/30/07
Zhang	Lin	IBGP PRC Admissions Subcommittee	Member	07/01/06	06/30/07

Graduate Program Comprehensive / Dissertation Committee Activities

FAC LAST NAME	FAC FIRST NAME	STUDENT NAME	COMMITTEE TYPE	COMMITTEE ROLE	SERVICE START DATE	SERVICE END DATE
Altschuler	Daniel	Bartholomew	Dissertation	Member	08/23/06	6/30/07
Altschuler	Daniel	Linnoila	Dissertation	Member	07/01/06	6/30/07
Altschuler	Daniel	Wang, Yan	Comprehensive	Member	07/01/06	6/27/07
Bisello	Alessandro	Dulak	Comprehensive	Member	07/01/06	6/30/07
Bisello	Alessandro	Groeger	Comprehensive	Member	07/01/06	6/30/07
DeFranco	Donald	Bartholomew	Dissertation	Chair	08/23/06	6/30/07
DeFranco	Donald	Caltagarone	Dissertation	Member	07/01/06	6/30/07
DeFranco	Donald	Erazo	Dissertation	Member	10/20/06	6/30/07
DeFranco	Donald	Gan	Dissertation	Chair	07/01/06	6/30/07
DeFranco	Donald	Kotchey	Comprehensive	Chair	07/01/06	6/30/07
DeFranco	Donald	Linnoila	Dissertation	Chair	07/01/06	6/30/07
DeFranco	Donald	McDonald	Dissertation	Chair	07/01/06	6/30/07
DeFranco	Donald	Tomko	Dissertation	Chair	07/01/06	6/30/07
deGroat	William	Chandra	Dissertation	Member	07/01/06	6/30/07
deGroat	William	Hezel	Comprehensive	Chair	08/24/06	8/24/06
Freeman	Bruce	Kliment	Comprehensive	Member	06/07/07	06/07/07
Freeman	Bruce	Queiroz De Oliveira	Comprehensive	Member	07/11/06	07/11/06
Freeman	Bruce	Queiroz De Oliveira	Dissertation	Chair	07/12/06	6/30/2007
Freeman	Bruce	Sarachine	Dissertation	Chair	01/03/07	06/30/07
Galbiati	Ferruccio	Bartholomew	Dissertation	Member	08/23/06	6/30/07
Galbiati	Ferruccio	Kotchey	Comprehensive	Member	07/01/06	6/30/07

FAC LAST NAME	FAC FIRST NAME	STUDENT NAME	COMMITTEE TYPE	COMMITTEE ROLE	SERVICE START DATE	SERVICE END DATE
Jiang	Yu	Bank	Dissertation	Member	08/29/06	6/30/07
Jiang	Yu	Dulak	Comprehensive	Member	07/01/06	6/30/07
Jiang	Yu	McDonald	Dissertation	Member	07/01/26	6/30/07
Jiang	Yu	Queiroz De Oliveira	Dissertation	Member	07/12/06	6/30/2007
Lakoski	Joan	Chandra	Dissertation	Chair	07/01/06	6/30/07
Lazo	John	Groeger	Comprehensive	Chair	07/01/06	6/30/07
Lazo	John	McDonald	Dissertation	Member	07/01/06	6/30007
Lazo	John	Queiroz De Oliveira	Dissertation	Member	07/12/06	6/30/2007
Lazo	John	Tomko	Dissertation	Member	07/01/06	6/30/07
Levitan	Edwin	Beckel	Dissertation	Chair	07/01/06	6/30/07
Levitan	Edwin	Sarachine	Comprehensive	Member	07/11/06	07/11/06
Levitan	Edwin	Werner, David	Dissertation	Chair	07/01/06	6/30/07
Nichols	Mark	Caltagarone	Dissertation	Member	07/01/06	6/30/07
Nichols	Mark	Kitchens	Comprehensive	Member	07/01/06	6/30/07
Nichols	Mark	Sarachine	Dissertation	Member	01/03/07	06/30/07
Palladino	Michael	Caltagarone	Dissertation	Member	07/01/06	6/30/07
Palladino	Michael	Chandra	Dissertation	Member	07/01/06	6/30/07
Palladino	Michael	Hezel	Comprehensive	Member	08/24/06	8/24/06
Palladino	Michael	Iyer	Comprehensive	Member	07/01/06	6/30/07
Palladino	Michael	Kotchey	Comprehensive	Member	07/01/06	6/30/07
Romero	Guillermo	Groeger	Comprehensive	Member	07/01/06	6/30/07
Romero	Guillermo	Linnoila	Dissertation	Member	07/01/06	6/30/07
Romero	Guillermo	Sarachine	Dissertation	Member	01/03/07	06/30/07
Siegfried	Jill	Bhola	Dissertation	Chair	01/03/07	6/30/07

FAC LAST NAME	FAC FIRST NAME	STUDENT NAME	COMMITTEE TYPE	COMMITTEE ROLE	SERVICE START DATE	SERVICE END DATE
Siegfried	Jill	Mburu	Comprehensive	Member	08/04/06	08/04/06
Siegfried	Jill	Mburu	Dissertation	Member	09/07/06	06/30/07
Singh	Shivendra	Leeman	Comprehensive	Chair	10/24/06	10/24/06
Singh	Shivendra	Leeman	Dissertation	Member	01/03/07	06/30/07
Sobol	Robert	Bank	Dissertation	Chair	08/29/06	6/30/07
Wang	Qiming	McDonald	Dissertation	Member	07/01/06	6/30/2007
Wood	Richard	Bartoli	Dissertation	Member	02/21/07	6/30/07
Wood	Richard	Constantinescu	Dissertation	Member	12/06/06	6/30/07
Wood	Richard	Gan	Dissertation	Member	07/01/06	6/30/07
Wood	Richard	Queiroz De Oliveira	Comprehensive	Chair	07/11/06	07/11/06
Yalowich	Jack	Caltagarone	Dissertation	Chair	07/01/06	6/30/07
Yalowich	Jack	Pene-dumitrescu	Dissertation	Chair	10/23/06	06/30/07
Zhang	Lin	Bank	Dissertation	Member	08/29/06	6/30/07
Zhang	Lin	Bhola	Dissertation	Member	01/03/07	6/30/07
Zhang	Lin	Dulak	Comprehensive	Chair	07/01/06	6/30/07
Zhang	Lin	Gan	Dissertation	Member	07/01/06	6/30/07
Zhang	Lin	Queiroz De Oliveira	Comprehensive	Member	07/11/06	07/11/06
Zhang	Lin	Queiroz De Oliveira	Dissertation	Member	07/12/06	6/30/2007

Teaching Awards

Don DeFranco, Ph.D.
Professor

Instructor, Frontiers in Reproductive Biology Course, Marine Biology Laboratory, Woods Hole, MA
Vice-Chair, Medical School Curriculum Committee

John Lazo, Ph.D.
Professor

The Dean's Teaching Excellence Award, The Warren Alpert Medical School of Brown University, 2007

Post-doctoral Fellows

Name	Lab
Susan Abbatiello	Conrads
Hiroyuki Achiwa	Lazo
Veronica Alonso	Friedman
Juan Ardura	Friedman
Debra Artim	Degroat
Lesley Ashmore	Palladino
Lihua Bai	Eiseman
Xiaochun Bai	Jiang
Laura Baker	Freeman
Pallavi Bansal	Lazo
Ajaykumar Bommareddy	Singh
Gustavo Bonacci	Freeman
Krishnamoorth Chandrasekhar	Furey
Jun Chen	Wang
Peng Cheng	Nichols
Marsha Cole	Freeman
Crissy Dudgeon	Zhang
Drew Dudgeon	Lazo
Timothy Feinstein	Vilardaga
Jianxia Guo	Zhang
Eun-Ryeong Hahm	Singh
Daniel Hochbaum	Altschuler
Kyoungja Hong	Altschuler
Stacey Hrizo	Palladino
Shunqian Jin	Yalowich
Leonel Joannas	Altschuler
Florenta Kullmann	Degroat
Heini Kansanen	Freeman
Nicholas Khoo	Freeman
Piotr Kos	Palladino
Fumito Koizumi	Lazo
Luis Leiva-Vega	Romero
Hua Li	Zhang
Dongzhu Ma	Jiang
Masanao Nakashima	Lazo

Lakshminarasi Pasupulati	Furey
Anna Powolny	Singh
Ilva Putzier	Levitan
Brian Reese	Lazo
Tanja Rudolph	Freeman
Volker Rudolph	Freeman
Ely Sebastian	Friedman
Mineaki Seki	Wood
Bing Shen	Roppolo
Kunwar Singh	Singh
Maria Soares	Lazo
Gyun Jee Song	Bisello
Silvia Stan	Singh
Keiichi Takata	Wood
Ram Trivedi	Sobol
Jaya Vatsyayan	Singh
Peng Wang	Zhang
Tao Wang	UPCI
Renaud Warin	Singh
Irene Wolf	Defranco
Steven Woodcock	Freeman
Xiang Xu	Zhang
Gonghong Yan	Jiang
Hanqing Ye	Altschuler
Yongbei Yu	Degroat
Fang Zhang	Lazo
Chao-Ming Zhou	Levitan
Fangdong Zou	Zhang
Huafei Zou	Jiang

Faculty Data

Current Faculty

Primary Faculty

Name	Position
Daniel Altschuler	Associate Professor
Palaniappa Arjunan	Instructor
Paul Baker	Research Assistant Professor
Alessandro Bisello	Assistant Professor
Thomas Conrads	Visiting Associate Professor
William de Groat	Professor
Donald Defranco	Professor
Julie Eiseman	Research Associate Professor
Melanie Flint	Research Instructor
Bruce Freeman	Professor and Chairman
Peter Friedman	Professor
William Furey	Professor
Daniela Galbiati	Research Instructor
Ferruccio Galbiati	Associate Professor
Jing Hu	Assistant Professor
Pamela Hershberger	Research Assistant Professor
Yu Jiang	Associate Professor
Edwin Jackson	Professor
Paul Johnston	Research Associate Professor
Yung Kim	Research Instructor
Edwina Kinchington	Research Instructor
Lynn Knowles	Research Instructor
Joan Lakoski	Professor
John Lazo	Professor
Edwin Levitan	Professor
Elena Makhina	Research Assistant Professor
Mark Nichols	Research Assistant Professor
Alicia Palladino	Research Instructor
Michael Palladino	Assistant Professor
Fernando Ribeiro Neto	Research Assistant Professor
Guillermo Romero	Associate Professor
James Roppolo	Research Associate Professor
Francisco Schopfer	Research Assistant Professor
Adrian Sculptoreanu	Research Assistant Professor
Dinara Shakiryanova	Research Assistant Professor
Elizabeth Sharlow	Research Assistant Professor
Jill Siegfried	Professor
Shivendra Singh	Professor
Robert Sobol Jr.	Assistant Professor
Harish Srinivas	Research Instructor
Sanjay Srivastava	Research Assistant Professor
Laura Stabile	Research Assistant Professor
Jean Pierre Vilardaga	Assistant Professor
Andreas Vogt	Research Assistant Professor
Bin Wang	Research Instructor
Qiming Wang	Assistant Professor
Birgitte Wittschieben	Research Instructor

John Wittschieben	Research Instructor
Richard Wood	Professor
Dong Xiao	Research Instructor
Jack Yalowich	Associate Professor
Lin Zhang	Associate Professor

Secondary Faculty

Name	Position	Primary Department
Susan Amara	Professor	Neurobiology
Carlos Batthyany	Adjunct Instructor	Adjunct
Christopher Bakkenist	Assistant Professor	Radiation Oncology
Aaron Barchowsky	Associate Professor	Env. Occup. Health
Philip Bauer	Assistant Professor	Surgery
Lori Birder	Associate Professor	Medicine
Robert Branch	Professor	Medicine
Clifton Callaway	Associate Professor	Emergency Medicine
Jane Cavanaugh	Adj. Res. Assistant Professor	Adjunct
Jun Chen	Professor	Neurology
Merrill Egorin	Professor	Medicine
John Fernstrom	Professor	Psychiatry
Mitchell Fink	Professor	Critical Care Medicine
William Fleming, Jr.	Adjunct Professor	Adjunct
Gerald Gebhart	Professor	Anesthesiology
Jennifer Grandis	Professor	Otolaryngology
Gregg Homanics	Associate Professor	Anesthesiology
Daniel Johnson	Associate Professor	Medicine
Valerian Kagan	Professor	Env. Occup. Health
Anthony Kanai	Associate Professor	Medicine
Yong Lee	Professor	Surgery
Chester Mathis	Professor	Neurology
James Perel	Professor	Psychiatry
Ruth Perez	Assistant Professor	Neurology
Michael Pezzone	Assistant Professor	Medicine
Bruce Pitt	Professor	Env. Occup. Health
Rafael Radi,	Adj. Professor	Adjunct
Homero Rubbo	Adj. Professor	Adjunct
William Bruce Sneddon	Adj. Assistant Professor	Adjunct
George Somogyi	Adj. Research Assoc. Professor	Adjunct
Richard Steinman	Associate Professor	Medicine
Changfeng Tai	Assistant Professor	Urology
Pei Tang	Associate Professor	Anesthesiology
Marni Brisson Tierno	Adj. Research Asst Professor	Adjunct
Gonzalo Torres	Assistant Professor	Neurobiology
Wen Xie	Associate Professor	Pharm. Sciences
Yan Xu	Professor	Anesthesiology
Naoki Yoshimura	Professor	Urology

New Faculty

Rafael Radi, M.D.
Adjunct Professor

Departamento de Bioquímica. Facultad de Medicina, Universidad de la República

Homero Rubbo, Ph.D.
Adjunct Professor

Departamento de Bioquímica. Facultad de Medicina, Universidad de la República

Dinara Shakiryanova, PhD
Research Assistant Professor

Prior Position and Institution: Postdoctoral Research Associate, Department of Pharmacology, University of Pittsburgh

Jean-Pierre Vilardaga, PhD
Assistant Professor

Prior Position and Institution: Assistant Professor, Department of Medicine, Harvard Medical School, Massachusetts General Hospital

Bin Wang, PhD
Research Instructor

Prior Position and Institution: Postdoctoral Research Associate, Department of Pharmacology, University of Pittsburgh

Membership in Professional Societies

Bruce Freeman, Ph.D.
Professor and Chair
American Association for the Advancement of Science
American Chemical Society
American Heart Association
American Physiological Society
American Society for Cell and Molecular Biology
American Thoracic Society
Biochemical Society
Society for Free Radical Biology and Medicine

Daniel Altschuler, Ph.D.
Associate Professor
The Endocrine Society

Palaniappa Arjunan, Ph.D.
Research Instructor
American Crystallographic Association
Pittsburgh Diffraction Society

Paul Baker, Ph.D.
Research Assistant Professor
American Diabetes Association
Society for Free Radical Biology and Medicine

Alessandro Bisello
Assistant Professor
American Society for Bone & Mineral Research

Alicia Celotto, Ph.D.
Research Instructor
Genetics Society of America
Society of Neuroscience

Thomas Conrads, Ph.D.
Visiting Associate Professor
American Society for Mass Spectrometry
American Association for Cancer Research
Human Proteome Organization
American Society of Pharmacology and Experimental Therapeutics

Donald DeFranco, Ph.D.
Professor
American Association for the Advancement of Science (AAAS)
American Society of Cell Biology (ASCB)
Endocrine Society
Society for Neuroscience

W. Chet de Groat, Ph.D.
Professor
Rho Chi Pharmaceutical Honor Society
Philadelphia Physiological Society
American Association for the Advancement of Science
Sigma Xi
American Society for Pharmacology and Experimental Therapeutics
Society for Neuroscience
Pittsburgh Neuroscience Society
New York Academy of Sciences
Urodynamics Society
International Brain Research Organization
American Gastroenterological Association
International Medical Society of Paraplegia
Society for Basic Urologic Research
Mid-Atlantic Pharmacology Society
American Motility Society
International Continence Society
The American Autonomic Society

The Dana Alliance for Brain Initiatives
International Society for Autonomic Neuroscience
International Spinal Cord Society

Julie Eiseman, Ph.D.
Research Associate Professor
American Association for Cancer Research
FASEB
American Association for the Advancement of Science
Society of Toxicology

Peter Friedman, Ph.D.
Professor
American Physiological Society
American Society for Biochemistry and Molecular Biology
American Society for Bone and Mineral Research
American Society of Nephrology
American Society of Pharmacology & Experimental Therapeutics
Biophysical Society
Endocrine Society
International Society of Nephrology
Salt & Water Club
Society of General Physiologists
British Society for Endocrinology
American Chemical Society

Melanie Flint, Ph.D.
Research Instructor
American Society for Mass Spectrometry
Society of Toxicology
Society of Toxicologists
American Association of Immunologists.

William Furey, Ph.D.
Professor
American Crystallographic Association
Pittsburgh Diffraction Society
New York Academy of Sciences
American Association for the Advancement of Science

Ferruccio Galbiati, Ph.D.
Associate Professor
American Society of Pharmacology & Experimental Therapeutics
American Society of Cell Biology

Pamela Hershberger
Research Assistant Professor
American Association for Cancer Research
National Lung Cancer Partnership

Jing Hu, Ph.D.
Assistant Professor
American Heart Association
American Association for Cancer Research

Yu Jiang, Ph.D.
Associate Professor
American Society for Microbiology
American Society for Pharmacology and Experimental Therapeutics
American Society of Genetics

Edwin Jackson, Ph.D.
Professor
American College of Clinical Pharmacology
American Federation for Clinical Research
American Heart Association
American Society of Hypertension
American Society for Pharmacology and Experimental Therapeutics
Council for High Blood Pressure Research
International Society for Heart Research

Paul Johnston, Ph.D.
Research Associate Professor
Society for Biomolecular Sciences

Lynn Knowles, Ph.D.
Research Instructor
American Society for Nutrition
American Association for Cancer Research

John Lazo, Ph.D.
Allegheny Foundation Professor
American Society for Pharmacology and Experimental Therapeutics
American Association for Cancer Research
American Chemical Society
American Society of Biochemistry and Molecular Biology
American Association for the Advancement of Science
New York Academy of Sciences

Edwina Lerner Kinchington, Ph.D.
Research Instructor
American Association of Cancer Research
Women in Cancer Research
National Lung Cancer Partnership

Edwin Levitan, Ph.D.
Professor
Society for Neuroscience
Biophysical Society
AHA basic science council
Society of General Physiologists

Elena Makhina, Ph.D.
Research Assistant Professor
Biophysical Society

Mark Nichols, Ph.D.
Research Assistant Professor
American Association for Advancement of Science
Genetics Society of America (GSA)
The Endocrine Society
American Association of Cancer Researchers (AACR)

Michael Palladino, Ph.D.
Assistant Professor
Genetics Society of America
Society for Neuroscience
American Society for Pharmacology and Experimental Therapeutics
Pittsburgh Neuroscience Society

Guillermo Romero, Ph.D.
Associate Professor
American Society for Pharmacology and Experimental Therapeutics
American Diabetes Association
American Society of Cell Biology

James Roppolo, Ph.D.
Research Assistant Professor
American Association for the Advancement of Science
Society for Neuroscience
The New York Academy of Sciences

Francisco Schopfer, Ph.D.
Research Assistant Professor
American Heart Association
Society for Free Radical Biology and Medicine

Adrian Sculptoreanu, Ph.D.
Research Assistant Professor
Biophysical Society
Neuroscience Society
American Physiological Society

Dinara Shakiryanova, Ph.D.
Research Instructor
Society for Neuroscience

Elizabeth Sharlow, Ph.D.
Research Instructor
American Association for Cancer Research

Jill Siegfried, Ph.D.
Professor
American Association for Cancer Research
American Association for the Advancement of Science
International Association for the Study of Lung Cancer
American Society for Pharmacology and Experimental Therapeutics
Society for Executive Leadership in Academic Medicine
Women Against Lung Cancer: Alliance for Education and Research
National Lung Cancer Partnership

Shivendra Singh, Ph.D.
Professor
American Society for Pharmacology and Experimental Therapeutics
American Society for Biochemistry and Molecular Biology
Society of Toxicology
International Society for the Study of Xenobiotics
American Association for Cancer Research

Robert Sobol, Ph.D.
Assistant Professor
American Association for the Advancement of Science
American Association for Cancer Research
American Society for Microbiology
American Society for Cell Biology
Environmental Mutagen Society
American Cancer Society

Laura Stabile, Ph.D.
Research Assistant Professor
National Lung Cancer Partnership
American Association for Cancer Research
Sigma Xi Scientific Honorary Society
Association for Women in Science
Association of Molecular Biology and Biochemistry
RNA Society
The Endocrine Society

Andreas Vogt, Ph.D.
Research Assistant Professor
American Association for Cancer Research
American Chemical Society
Deutsche Pharmazeutische Gesellschaft
Society of Biomolecular Screening

Q. Jane Wang, Ph.D.
Assistant Professor
American society for Pharmacology and Experimental Therapeutics
American Association for Cancer Research
American Association for the Advancement of Science

John Wittschieben, Ph.D.
Research Instructor
2007 Mammalian DNA Repair Gordon Research Conference, February 2007: "Role of DNA polymerase zeta subunit Rev3L for cell proliferation in adult mice".

Dong Xiao, Ph.D.
Research Instructor
American Association for Cancer Research

Jack Yalowich, Ph.D.
Associate Professor
New York Academy of Sciences
Sigma Xi
American Association for Cancer Research
American Society for Pharmacology and Experimental Therapeutics

Lin Zhang, Ph.D.
Associate Professor
American Association for Cancer Research (AACR)
American Society of Human Genetics (ASHG)
American Association for the Advancement of Science (AAAS)

Three Year Bibliography

Bruce Freeman, Ph.D.
Professor and Chair

Rudolph V, Rudolph TK, Freeman BA. Copper Trafficking and Extracellular Superoxide Dismutase Activity. Kinky Hair, Kinky Vessels. Hypertension. 2008 Sep 2. [Epub ahead of print] No abstract available.

Rudolph V, Rudolph TK, Schopfer FJ, Bonacci G, Lau D, Szoecs K, Klinke A, Meinertz T, Freeman BA, Baldus S. Bivalirudin decreases NO bioavailability by vascular immobilization of myeloperoxidase. J Pharmacol Exp Ther. 2008 Aug 13. [Epub ahead of print]

Ferreira AM, Ferrari M, Trostchansky A, Batthyány C, Souza JM, Alvarez MN, López GV, Baker PR, Schopfer FJ, O'Donnell V, Freeman BA, Rubbo H. Macrophage activation induces formation of the anti-inflammatory lipid cholesteryl-nitrolinoleate.
Biochem J. 2008 Aug 1. [Epub ahead of print]

Li Y, Zhang J, Schopfer FJ, Martynowski D, Garcia-Barrio MT, Kovach A, Suino-Powell K, Baker PR, Freeman BA, Chen YE, Xu HE. Molecular recognition of nitrated fatty acids by PPAR gamma. Nat Struct Mol Biol. 2008 Aug;15(8):865-7. Epub 2008 Jul 6.

Rudolph V, Rudolph TK, Freeman BA. Blood pressure regulation: role for neutrophils?
Blood. 2008 May 15;111(10):4840.

Ichikawa T, Zhang J, Chen K, Liu Y, Schopfer FJ, Baker PR, Freeman BA, Chen YE, Cui T. Nitroalkenes suppress lipopolysaccharide-induced signal transducer and activator of transcription signaling in macrophages: a critical role of mitogen-activated protein kinase phosphatase 1. Endocrinology. 2008 Aug;149(8):4086-94. Epub 2008 May 8.

Freeman BA, Baker PR, Schopfer FJ, Woodcock SR, Napolitano A, d'Ischia M. Nitro-fatty acid formation and signaling. J Biol Chem. 2008 Jun 6;283(23):15515-9. Epub 2008 Feb 19. Review. No abstract available.

Turell L, Botti H, Carballal S, Ferrer-Sueta G, Souza JM, Durán R, Freeman BA, Radi R, Alvarez B. Reactivity of sulfenic acid in human serum albumin. Biochemistry. 2008 Jan 8;47(1):358-67. Epub 2007 Dec 14.

Baker, LMS, PRS Baker, F Golin-Bisello, FJ Schopfer, M Fink, SR Woodcock, BP Branchaud, R Radi, BA Freeman. Nitro-fatty acid reaction with glutathione and cysteine: kinetic analysis of thiol alkylation by a Michael addition reaction. J Biol Chem, in press 2007.

Villacorta L, J Zhang, M T Garcia-Barrio, X Chen, BA Freeman, YE Chen, T Cui. Nitro-linoleic Acid Inhibits Vascular Smooth Muscle Cell Proliferation via the Keap1/Nrf2 Signaling Pathway. Am J Physiol Heart Circ Physiol, Jul;293(1):H770-6, 2007.

Tórtora V, C Quijano, BA Freeman, R. Radi and L. Castro. Mitochondrial aconitase reaction with nitric oxide, S-nitrosoglutathione and peroxynitrite: Mechanisms and relative contributions to aconitase inactivation. Free Rad. Biol & Medicine (2007), Free Rad. Biol & Medicine 42, 1045-1088, 2007.

Hsu HC, T Zhou, H Kim, S Barnes, P Yang, Q Wu, J Zhou, BA Freeman, M Luo and JD Mountz. Production of a novel class of polyreactive pathogenic autoantibodies in BXD2 mice causes glomerulonephritis and arthritis. Arthritis Rheum, 54(1): 343-55, 2006.

Wright MM, FJ Schopfer, PR Baker, V Vidyasagar, P Powell, P Chumley, KE Iles, BA Freeman, A Agarwal. Fatty acid transduction of nitric oxide signaling: nitrolinoleic acid potently activates endothelial heme oxygenase 1 expression. Proc Nat Acad Sci USA. 103 (11): 4299-304, 2006.

Batthyany C, FJ Schopfer, PR Baker, R Duran, LM Baker, Y Huang, C Cervenansky, BP Branchaud, BA Freeman. Reversible post-translational modification of proteins by nitrated fatty acids in vivo. J Biol Chem. 281(29): 20450-20463, 2006.

Cui, T, F Schopfer, J Zhang, K Chen, T Ichigawa, PRS BAKER, C Batthyany, BK Chacko, X Feng, R Patel, A Agarwal, BA Freeman, Y Chen. Nitrated fatty acids: Endogenous anti-inflammatory signaling mediators. J Biol Chem 281: 35686-35698, 2006.

Baldus S, K Müllerleile, P Chumley, D Steven, V Rudolph, GK Lund, H-J Staude, A Stork, R Köster, J Kähler, C Weiss, T Münzel, T Meinertz, BA Freeman, T Heitzer. Inhibition of xanthine oxidase improves myocardial contractility in patients with ischemic cardiomyopathy. Free Rad. Biol. & Medicine 41 (2006) 1282–1288.

Daniel Altschuler, Ph.D.
Associate Professor

Hong K, Lou L, Gupta S, Ribeiro-Neto F, Altschuler DL. A novel Epac-Rap-PP2A signaling module controls cAMP-dependent Akt regulation. J Biol Chem. 2008 Aug 22;283(34):23129-38. Epub 2008 Jun 12.

Hochbaum D, Hong K, Barila G, Ribeiro-Neto F, Altschuler DL. Epac, in synergy with cAMP-dependent protein kinase (PKA), is required for cAMP-mediated mitogenesis.
J Biol Chem. 2008 Feb 22;283(8):4464-8. Epub 2007 Dec 6.

Palaniappa Arjunan, Ph.D.
Research Instructor

Kale S, Arjunan P, Furey W, Jordan F. A dynamic loop at the active center of the Escherichia coli pyruvate dehydrogenase complex E1 component modulates substrate utilization and chemical communication with the E2 component.
J Biol Chem. 2007 Sep 21;282(38):28106-16. Epub 2007 Jul 17.

A Thiamin-bound, pre-decarboxylation reaction intermediate analogue in the pyruvate dehydrogenase E1 subunit induces large-scale disorder-to-order transformations in the enzyme and reveals novel structural features in the covalently bound adduct., P. Arjunan, M. Sax, A. Brunskill, K. Chandrasekhar, N. Nemeria, S. Zhang, F. Jordan and W. Furey. ***J.Biol.Chem***, 281, 15296-15303 (2006).

Active-site changes in the pyruvate dehydrogenase multienzyme complex E1 apoenzyme component from *Escherichia coli* observed at 2.32 Å resolution., K. Chandrasekhar, P.Arjunan, M.Sax, N.Nemeria, F.Jordan, W.Furey. *Acta Cryst,* D62, 1382-1386 (2006).

Paul Baker, Ph.D.
Research Assistant Professor

Li Y, Zhang J, Schopfer FJ, Martynowski D, Garcia-Barrio MT, Kovach A, Suino-Powell K, Baker PR, Freeman BA, Chen YE, Xu HE. Molecular recognition of nitrated fatty acids by PPAR gamma. Nat Struct Mol Biol. 2008 Aug;15(8):865-7. Epub 2008 Jul 6.

Ferreira AM, Ferrari M, Trostchansky A, Batthyány C, Souza JM, Alvarez MN, López GV, Baker PR, Schopfer FJ, O'Donnell V, Freeman BA, Rubbo H. Macrophage activation induces formation of the anti-inflammatory lipid cholesteryl-nitrolinoleate.
Biochem J. 2008 Aug 1. [Epub ahead of print]

Ichikawa T, Zhang J, Chen K, Liu Y, Schopfer FJ, Baker PR, Freeman BA, Chen YE, Cui T. Nitroalkenes suppress lipopolysaccharide-induced signal transducer and activator of transcription signaling in macrophages: a critical role of mitogen-activated protein kinase phosphatase 1. Endocrinology. 2008 Aug;149(8):4086-94. Epub 2008 May 8.

Freeman BA, Baker PR, Schopfer FJ, Woodcock SR, Napolitano A, d'Ischia M. Nitro-fatty acid formation and signaling. J Biol Chem. 2008 Jun 6;283(23):15515-9. Epub 2008 Feb 19. Review. No abstract available.

Baker, LMS, PRS Baker, F Golin-Bisello, FJ Schopfer, M Fink, SR Woodcock, BP Branchaud, R Radi, BA Freeman. Nitro-fatty acid reaction with glutathione and cysteine: kinetic analysis of thiol alkylation by a Michael addition reaction. J Biol Chem, in press 2007.

Wright, M, Schopfer, FJ, Baker, PRS, Vidyasagar, V, Powell, P, Chumley, P, Isles, KI, Freeman, BA and Agarwal, A. Fatty acid transduction of nitric oxide signaling: Nitrolinoleic acid potently activates endothelial heme oxygenase-1 expression. Proc. Natl. Acad. Sci. USA (2006) 103(11):4299-4304.

Batthyany, C, Schopfer, FJ, Baker PRS, Duran, R, Baker LMS, Huang, Y,, Cervenansky, C, Branchaud, BP and Freeman, BA. Reversible post-translational modification of proteins by nitrated fatty acids in vivo. J. Biol. Chem. (2006) 281(29):20450-20463.

Cui, T, Schopfer, FJ, Zhang, J, Chen, K, Ichikawa, T, Baker, PRS, Batthyany, C, Chacko, BK, Feng, X, Patel, RP, Agarwal, A, Freeman, BA and Chen, YE. Nitrated fatty acids: endogenous anti-inflammatory signaling mediators J. Biol. Chem. (2006) 281(47):35686-35698.

Alessandro Bisello
Assistant Professor

Wheeler D, Garrido JL, Bisello A, Kim YK, Friedman PA, Romero G. Regulation of parathyroid hormone type 1 receptor dynamics, traffic, and signaling by the Na+/H+ exchanger regulatory factor-1 in rat osteosarcoma ROS 17/2.8 cells. Mol Endocrinol. 2008 May;22(5):1163-70. Epub 2008 Jan 17.

Wang B, Bisello A, Yang Y, Romero GG, Friedman PA. NHERF1 regulates parathyroid hormone receptor membrane retention without affecting recycling.
J Biol Chem. 2007 Dec 14;282(50):36214-22. Epub 2007 Sep 19.

Horwitz M, Tedesco MB, M Sereika SM, Garcia-Ocana A, Bisello A, Hollis BW, Gundberg C, Stewart AF. Safety and Tolerability of Subcutaneous PTHrP(1-36) in Healthy Human Volunteers: A Dose Escalation Study. Osteoporosis International. 2006; 17:225-30.

Ke Chen, Fanghong Li, Ji Li, Hongbo Cai, Steven Strom, Alessandro Bisello, David E. Kelley, Miriam Friedman-Einat, Gregory A. Skibinski, Mark A. McCrory, Alexander J. Szalai, Allan Z. Zhao. Induction of Leptin Resistance through Direct Interaction of C-Reactive Protein with Leptin. Nature Medicine 2006; 12:425-32.

Syme CA, Zhang L, Bisello A. Caveolin-1 Regulates Cellular Trafficking and Function of the Glucagon-like Peptide 1 Receptor. Molecular Endocrinology 2006; 20:3400-11.

Fiaschi-Taesch N, Sicari BM, Ubriani K, Bigatel T, Takane KK, Cozar-Castellano I, Bisello A, Law B, Stewart AF. Cellular mechanism through which parathyroid hormone-related protein induces proliferation in arterial smooth muscle cells: definition of an arterial smooth muscle PTHrP/p27kip1 pathway. Circ Res. 2006; 99:933-42.

Alicia Celotto, Ph.D.
Research Instructor

Seigle JL, Celotto AM, Palladino MJ. Degradation of functional triose phosphate isomerase protein underlies sugarkill pathology. Genetics. 2008 Jun;179(2):855-62. Epub 2008 May 5.

Alicia M. Celotto, Adam C. Frank, Jacquelyn L. Seigle and Michael J. Palladino. (2006) Drosophila model of human inherited TPI deficiency glycolytic enzymopathy. Genetics. 174(3): 1237-46.

Alicia M. Celotto, Adam C. Frank, Steven W. McGrath, Tim Fergestad, Wayne A. Van Voorhies, Karolyn F. Buttle, Carmen A. Mannella and Michael J. Palladino. (2006) Mitochondrial Encephalomyopathy in Drosophila. The Journal of Neuroscience. 26(3): 810-820.

Thomas Conrads, Ph.D.
Visiting Associate Professor

Abbatiello SE, Pan YX, Zhou M, Wayne AS, Veenstra TD, Hunger SP, Kilberg MS, Eyler JR, Richards NG, Conrads TP. Mass spectrometric quantification of asparagine synthetase in circulating leukemia cells from acute lymphoblastic leukemia patients.
J Proteomics. 2008 Apr 30;71(1):61-70. Epub 2007 Dec 5.

Mi L, Xiao Z, Hood BL, Dakshanamurthy S, Wang X, Govind S, Conrads TP, Veenstra TD, Chung FL. Covalent binding to tubulin by isothiocyanates. A mechanism of cell growth arrest and apoptosis. J Biol Chem. 2008 Aug 8;283(32):22136-46. Epub 2008 Jun 3.

Bowen, C., Stuart, S., Ju, J. H., Blonder, J., Conrads, T. P., Veenstra, T. D. and Gelman, E. P. (2007) NKX3.1 Homeodomain Protein Stimulates Formation of the Topoisomerase I/DNA Complex and Interacts with Topoisomerase I to Mediate DNA Repair, Cancer Res. 67, 455-464.

Kong, L., Saavedra, J. E., Buzard, G. S., Xu, X., Hood, B. L., Conrads, T. P., Veenstra, T. D., and Keefer, L. K. (2006) Deamidation of peptides in aerobic nitric oxide solution by a nitrosative pathway, Nitric Oxide: Biology and Chemistry 14, 144-151.

Ali, I. U., Xiao, Z., Malone, W., Smith, M., Conrads, T. P., Veenstra, T. D., Greenwald, P., Luke, B. T. and McLarty, J. W. (2006) Plasma Proteomic Profiling: Search for Lung Cancer Diagnostic and Early Detection Markers, Oncol. Report 15, 1367-1372.

Kim, B.-J., Hood, B. L., Aragon, R. A., Hardwick, J. P., Conrads, T. P., Veenstra, T. D. and Song, B. J. (2006) Increased oxidation and degradation of cytosolic proteins in alcohol-exposed mouse liver and hepatoma cells, Proteomics 6, 1250-1260.

Yang, H., Yu, L. R., Yi, M., Lucas, D. A., Lukes, L., Lancaster, M., Chan, K. C., Issaq, H. J., Stephens, R. M., Conrads, T. P., Veenstra, T. D., and Hunter, K. W. (2006) Parallel Analysis of Transcript and Translation

Profiles: Identification of Metastasis-related Signal Pathways Differentially Regulated by Drug and Genetic Modifications, J. Proteome Res. 5, 1555-1567.

Meng, Z., Camalier, C. E., Lucas, D. A., Veenstra, T. D., Beck, G. R., and Conrads, T. P. (2006) Probing Early Growth Response 1 interacting proteins at the active promoter in osteoblast cells using oligoprecipitation and mass spectrometry, J. Proteome Res. 5, 1931-1939.

Murphy, S., Larrivée, B., Pollet, I., Craig, K. S., Williams, D. E., Huang, X. H., Abbott, M., Wong, F., Curtis, C., Conrads, T. P., Veenstra, T. D., Puri, M., Hsiang, Y., Roberge, M., Andersen, R. J., Karsan, A. (2006) Identification of Sokotrasterol Sulfate as a Novel Pro-angiogenic Steroid, Circ. Res. 99, 257-265.

Chertova, E., Chertov, O., Coren, L. V., Roser, J. D., Turbey, C. M., Bess Jr., J. Sowder II, R. C., Barsov, E., Hood, B. L., Fisher, R. J., Conrads, T. P., Veenstra, T. D., Lifson, J. D., and Ott, D. E. (2006) Proteomic and Biochemical Analysis of Purified Human Immunodeficiency Virus Type 1 Produced from Infected Monocyte-Derived Macrophages, J. Virol. 80, 9039-9052.

Zhou, M., Prieto, D. A., Lucas, D. A., Chan, K. C., Issaq, H. J., Veenstra, T. D. and Conrads, T. P. (2006) Characterization of the SELDI Protein Chip Serum Retentate, J. Proteome Res. 5, 2207-2216.

Go E. P., Wikoff W., Shen Z., O'Maille G., Morita H., Conrads T. P., Nordstrom A., Trauger S. A., Uritboonthai W., Lucas D., Chan K.C., Veenstra T. D., Lewicki H., Oldstone M. B., Schneemann A., Siuzdak G. (2006) Mass Spectrometry Reveals Specific and Global Molecular Transformations during Viral Infection, J. Proteome Res. 5, 2405-2416.

Waybright, T. J., Van, Q. N., Muschik, G. M., Conrads, T. P., Veenstra, T. D. and Issaq, H. J. (2006) LC-MS in Metabonomics: Optimization of Experimental Conditions for the Analysis of Metabolites in Human Urine, J. Liq. Chromatogr. Relat. Technol. 29, 2475-2497.

Habermann, J. K., Roblick, U. J., Luke, B. T., Prieto, D. A., Finlay, W. J. J., Podust, V. N., Roman, J. M., Oevermann, E., Schiedeck, T., Homann, N., Duchrow, M., Conrads, T. P., Veenstra, T. D., Burt, S. K., Bruch, H.-P., Auer, G., and Ried, T. (2006) Increased serum levels of complement C3a anaphylatoxin indicate the presence of colorectal tumors, Gastroenterology 131, 1020-1029.

Moon, K. H., Hood, B. L., Kim, B.-J., Hardwick, J. P., Conrads, T. P., and Veenstra, T. D. and Song, B. J. (2006) Inactivation of Oxidized and S-nitrosylated Mitochondrial Proteins in Alcoholic Fatty Liver of Rats, Hepatology 44, 1218-1230.
Stockwin, L. H., Blonder, J., Bumke, M. A., Lucas, D. A., Chan, K. C., Conrads, T. P., Issaq, H. J., Veenstra, T. D., Newton, D. L., and Rybak, S. M. (2006) Proteomic Analysis of the Plasma Membrane from Hypoxia-Adapted Malignant Melanoma, J. Proteome Res. 5, 2996-3007.

Rastgar, F. J., Najafi, Z., Malekzadeh, R., Conrads, T. P., Ziaee, A. A., Abnet, C., Yazdznbod, M., Karkhane, A. A. and Salekdeh, G. H. (2006) Identification of squamous cell carcinoma associated proteins by proteomics and loss of beta tropomyosin expression in esophageal cancer, World J. Gastroenterol. 12, 7104-7112.

Ritt, D., Zhou, M., Conrads, T. P., Veenstra, T. D., and Morrison, D. K. (2006) CK2 is a Component of the KSR1 Complex that Facilitates Raf-1 Activation, Curr. Biol.17, 1-6.
Xiao, Z., Camalier, C. E., Nagashima, K., Chan, K. C., Lucas, D. A., de la Cruz, J., Gignac, M., Lockett, S., Veenstra, T. D., Conrads, T. P., and Beck, G. R. Jr. (2006) Analysis of the Extracellular Matrix Vesicle Proteome in Mineralizing Murine Osteoblasts, J. Cell. Physiol. 210, 325-335.

Conrads, T. P., Hussey, G., Hood, B. L., Zhang, C., Guo, L., Michejda, C. J., Veenstra, T. D., and Keay, S. K. (2006) CKAP4/p63 is a Receptor for the Frizzled-8 Protein-related Antiproliferative Factor from Interstitial Cystitis Patients, J. Biol. Chem. 281, 37836-37843.

Feng, Y., Yuan, J. H., Maloid, S. C., Fisher, R., Copeland, T. D., Longo, D. L., Conrads, T. P., Veenstra, T. D., Ferris, A., Hughes, S., Dimitrov, D. S., and Ferris, D. K. (2006) Pole-like Kinase 1-mediated Phosphorylation of the GTP-binding Protein Ran is Important for Bipolar Spindle Formation, Biochem. Biophys. Res. Commun. 349, 144-152.

Donald DeFranco, Ph.D.
Professor

Ho Y, Samarasinghe R, Knoch ME, Lewis M, Aizenman E, Defranco DB. Selective Inhibition of MAPK Phosphatases by Zinc Accounts for ERK1/2-dependent Oxidative Neuronal Cell Death. Mol Pharmacol. 2008 Jul 17. [Epub ahead of print]

Wolf IM, Heitzer MD, Grubisha M, DeFranco DB. Coactivators and nuclear receptor transactivation. J Cell Biochem. 2008 Aug 1;104(5):1580-6.

Zhang Y, Aizenman E, DeFranco DB, Rosenberg PA. (2007) Intracellular zinc release, 12-lipoxygenase activation and MAPK dependent neuronal and oligodendroglial death. Molecular Medicine, in press.

Deklebab B, Witchel SF, DeFranco DB. (2007) TNF-alpha and glucocorticoid receptor interaction in L6 muscle cells; a cooperative downregulation of myosin heavy chain. Steroids, in press.
Ho Y, Logue ES, Callaway CW, DeFranco DB. (2007) Different mechanisms regulating ERK activation in distinct brain regions following global ischemia and reperfusion. Neuroscience, 145, 248-255.

Heitzer M, DeFranco DB. (2007) Hic-5/ARA55 a prostate stroma-specific AR coactivator. Steroids 72, 218-220

Heitzer MD, DeFranco DB. (2006) Mechanism of action of Hic-5/ARA55, a LIM domain-containing nuclear receptor coactivator. Mol. Endocrinol., 20, 56-64.

Luo Y, DeFranco DB. (2006) Opposing roles for ERK1/2 in neuronal oxidative toxicity: distinct mechanisms of ERK1/2 action at early versus late phases of oxidative stress. J. Biol. Chem., 281, 16436-16442.

Heitzer MD, DeFranco DB. (2006) Hic-5/ARA55 a LIM domain-containing nuclear receptor coactivator expressed in prostate stromal cells. Cancer Res., 66, 7326-7333.

Gore AC, Attardi B, DeFranco DB. (2006) Glucocorticoid repression of the reproductive axis: Effects on GnRH and gonadotropin subunit mRNA levels Mol. Cell. Endocrinol., 256, 40-48.

Jiang H, Poirier MA, Liang Y, Pei Z, Weiskittel CE, Smith WW, DeFranco DB, Ross CA. (2006) Depletion of CBP is directly linked with cellular toxicity caused by mutant huntingtin. Neurobiol Dis., 23, 543-551.

Heitzer MD, DeFranco DB. (2006) Hic-5, an adaptor-like nuclear receptor coactivator. Nuclear Receptor Signaling 4, e019

Witchell S, DeFranco DB. (2006) Mechanisms of Disease: regulation of glucocorticoid hormone and receptor levels-impact on the metabolic syndrome. Nature Clinical Practice: Endocrinology and Metabolism, 2, 621-631.

Rasar M, DeFranco DB, Hammes SR. (2006) Paxillin regulates steroid-triggered meiotic resumption by enhancing an all-or-none feed-forward kinase loop. J Biol. Chem., 281, 39455-39464.

Lu NZ, Wardell SE, Burnstein KL, DeFranco D, Fuller PJ, Giguere V, Hochberg RB, McKay L, Renoir JM, Weigel NL, Wilson EM, McDonnell DP, Cidlowski JA. (2006) International Union of Pharmacology. LXV. The pharmacology and classification of the nuclear receptor superfamily: glucocorticoid, mineralocorticoid, progesterone, and androgen receptors. Pharmacol Rev. 58, 782-797.

W. Chet de Groat, Ph.D.
Professor

Yoshiyama M, de Groat WC. The Role of Vasoactive Intestinal Polypeptide and Pituitary Adenylate Cyclase-Activating Polypeptide in the Neural Pathways Controlling the Lower Urinary Tract. J Mol Neurosci. 2008 Aug 2. [Epub ahead of print]

Masuda N, Masuda H, Matsuyoshi H, Chancellor MB, de Groat WC, Yoshimura N.
Effects of intrathecal injection of a hyperpolarization-activated channel (I(h)) inhibitor ZD7288 on bladder function in urethane-anesthetized rats. Neurourol Urodyn. 2008 Jul 18. [Epub ahead of print]

Tai C, Wang J, Chancellor MB, Roppolo JR, de Groat WC. Influence of temperature on pudendal nerve block induced by high frequency biphasic electrical current. J Urol. 2008 Sep;180(3):1173-8. Epub 2008 Jul 18.

Sculptoreanu A, Aura Kullmann F, de Groat WC. Neurokinin 2 receptor-mediated activation of protein kinase C modulates capsaicin responses in DRG neurons from adult rats. Eur J Neurosci. 2008 Jun;27(12):3171-81.

Miyazato M, Sasatomi K, Hiragata S, Sugaya K, Chancellor MB, de Groat WC, Yoshimura N. Suppression of detrusor-sphincter dysynergia by GABA-receptor activation in the lumbosacral spinal cord in spinal cord-injured rats.
Am J Physiol Regul Integr Comp Physiol. 2008 Jul;295(1):R336-42. Epub 2008 May 21.

Fowler CJ, Griffiths D, de Groat WC. The neural control of micturition. Nat Rev Neurosci. 2008 Jun;9(6):453-66. Review.

Miyazato M, Kaiho Y, Kamo I, Chancellor MB, Sugaya K, de Groat WC, Yoshimura N.
Effect of duloxetine, a norepinephrine and serotonin reuptake inhibitor, on sneeze-induced urethral continence reflex in rats. Am J Physiol Renal Physiol. 2008 Jul;295(1):F264-71. Epub 2008 May 14.

Chancellor MB, Fowler CJ, Apostolidis A, de Groat WC, Smith CP, Somogyi GT, Roger Aoki K. Drug Insight: biological effects of botulinum toxin A in the lower urinary tract.
Nat Clin Pract Urol. 2008 Jun;5(6):319-28. Epub 2008 May 6. Review.

Yoshiyama M, de Groat WC. Effects of intrathecal administration of pituitary adenylate cyclase activating polypeptide on lower urinary tract functions in rats with intact or transected spinal cords. Exp Neurol. 2008 Jun;211(2):449-55. Epub 2008 Mar 7.

Tai C, Wang J, Shen B, Wang X, Roppolo JR, de Groat WC. Hindlimb movement in the cat induced by amplitude-modulated stimulation using extra-spinal electrodes. J Neural Eng. 2008 Jun;5(2):111-24. Epub 2008 Mar 26.

Furuta A, Kita M, Suzuki Y, Egawa S, Chancellor MB, de Groat WC, Yoshimura N.
Association of overactive bladder and stress urinary incontinence in rats with pudendal nerve ligation injury.
Am J Physiol Regul Integr Comp Physiol. 2008 May; 294(5):R1510-6. Epub 2008 Mar 12.

Yu Y, de Groat WC. Sensitization of pelvic afferent nerves in the in vitro rat urinary bladder-pelvic nerve preparation by purinergic agonists and cyclophosphamide pretreatment. Am J Physiol Renal Physiol. 2008 May;294(5):F1146-56.Epub 2008 Mar 5.

Kullmann FA, Artim DE, Birder LA, de Groat WC. Activation of muscarinic receptors in rat bladder sensory pathways alters reflex bladder activity. J Neurosci. 2008 Feb 20;28(8):1977-87.

Miyazato M, Sasatomi K, Hiragata S, Sugaya K, Chancellor MB, de Groat WC, Yoshimura N. GABA receptor activation in the lumbosacral spinal cord decreases detrusor overactivity in spinal cord injured rats. J Urol. 2008 Mar;179(3):1178-83.

Tai C, Shen B, Wang J, Chancellor MB, Roppolo JR, de Groat WC. Inhibitory and excitatory perigenital-to-bladder spinal reflexes in the cat. Am J Physiol Renal Physiol. 2008 Mar;294(3):F591-602. Epub 2007 Dec 26.

Sugaya, K. et al. Bladder volume dependent excitatory and inhibitory functions of the pelvic nerve on bladder activity in rats. Biomedical Research, in press.

Yamane, H., Sculptoreanu, A., de Groat, W.C. Effects of ralfinamide, a Na+ channel blocker, on firing properties of nociceptive dorsal root ganglion neurons of adult rats. Experimental Neurology, in press.

Saitoh, C., Kitada, C., Uchida, W., Chancellor, M.B., de Groat, W.C., Yoshimura, N. The differential contractile responses to capsaicin and anandamide in muscle strips isolated from the rat urinary bladder. European Journal of Pharmacology, in press.

Prantil, R.L., Jankowski, R.J., Kaiho, Y., de Groat, W.C., Chancellor, M.B., Yoshimura, N., Vorp, D.A. Ex vivo biomechanical properties of the female urethra in a rat model of birth trauma. American Journal of Physiology, 292: F1229-F1237, 2007.

Yoshiyama, M., de Groat, W.C. Role of spinal metabotropic glutamate receptors in regulation of lower urinary tract function in the decerebrate unanesthetized rat. Neuroscience Letters, 420: 18-22, 2007.

Masuda, H., Ogawa, T., Kihara, K., Chancellor, M.B., de Groat, W.C., Yoshimura, N. Effects of anesthesia on the nitrergic pathway during the micturition reflex in rats. BJU International, 100(1): 175-180, 2007.

Beckel, J.M., Kanai, A., Lee, S.J., de Groat, W.C., Birder, L.A. Expression of functional nicotinic acetylcholine receptors in rat urinary bladder epithelial cells. American Journal of Physiology, 290: F103-F110, 2006.

Chang, H.Y., Cheng, C-L., Chen, J-J., Peng, C-W., de Groat, W.C. Reflexes evoked by electrical stimulation of afferent axons in the pudendal nerve under empty and distended bladder conditions in urethane-anesthetized rats. Journal of Neuroscience Methods, 150: 80-89, 2006.

Tai, C., Smerin, S.E., de Groat, W.C., Roppolo, J.R. Pudendal-to-bladder reflex in chronic spinal cord injured cat. Experimental Neurology, 197: 225-234, 2006.

Ishihama, H., Momota, Y., Yanase, H., Xiaojun, W., de Groat, W.C., Kawatani, M. Activation of alpha1D adrenergic receptors in the rat urothelium facilitates the micturition reflex. Journal of Urology, 175: 358-364, 2006.

Wu, H.Y., de Groat, W.C. Maternal separation uncouples reflex from spontaneous voiding in rat pups. Journal of Urology, 175: 1148-1151, 2006.

Liu, J., Tai, C., de Groat, W.C., Peng, X-M., Mata, M., Fink, D.J. Release of GABA from sensory neurons transduced with a GAD67-expressing vector occurs by non-vesicular mechanisms. Brain Research, 1073: 297-304, 2006.

Jankowski, R.J., Prantil, R.L., Chancellor, M.B., de Groat, W.C., Huard, J., and Vorp, D.A. Biomechanical characterization of the urethral musculature. American Journal of Physiology, 290: F1127-F1134, 2006.

Ruan, H.-Z., Birder, L.A., Xiang, Z., Chopra, B., Buffington, T., Tai, C., Roppolo, J.R., de Groat, W.C., Burnstock, G. Expression of P2X and P2Y receptors in the intramural parasympathetic ganglia of the cat urinary bladder. American Journal of Physiology, 290: F1143-F1152, 2006.

Zhang, X., Roppolo, J.R., de Groat, W.C., Tai, C. Simulation analysis of conduction block in myelinated axons induced by high-frequency biphasic rectangular pulses. IEEE Transactions on Biomedical Engineering, 53: 1433-1436, 2006.

Masuda, H., Hayashi, Y., Chancellor, M.B., Kihara, K., de Groat, W.C., de Miguel, F., Yoshimura, N. Roles of peripheral and central nicotinic receptors in the micturition reflex in rats. Journal of Urology, 176: 374-379, 2006.

Chang, H-Y., Cheng, C-L., Chen, J-J., de Groat, W.C. Roles of glutamatergic and serotonergic mechanisms in reflex control of the external urethral sphincter in urethane-anesthetized rats. American Journal of Physiology, 291: R224-234, 2006.

Tai, C., Miscik, C.L., Ungerer, T.D., Roppolo, J.R., de Groat, W.C. Suppression of bladder reflex activity in chronic spinal cord injured cats by activation of serotonin 5-HT1A receptors. Experimental Neurology, 199: 427-437, 2006.

Masuda, N., Hayashi, Y., Matsuyoshi, H., Chancellor, M.B., de Groat, W.C., Yoshimura, N. Characterization of hyperpolarization-activated current (Ih) in dorsal root ganglion neurons innervating rat urinary bladder. Brain Research, 1096: 40-52, 2006.

Peng, C-W., Chen, J-J., Chang, H-Y., de Groat, W.C., Cheng, C-L. External urethral sphincter activity in a rat model of pudendal nerve injury. Journal of Neurourology and Urodynamics, 25: 388-396, 2006.

Ogawa, T., Seki, S., Masuda, H., Igawa, Y., Nishizawa, O., Kuno, S., Chancellor, M.B., de Groat, W.C., Yoshimura, N. Dopaminergic mechanisms controlling urethral function in rats. Neurourology and Urodynamics, 25: 480-489, 2006.

Ng, Y-K., de Groat, W.C., Wu, H-Y. Muscarinic regulation of neonatal rat bladder spontaneous contractions. American Journal of Physiology, 291: R1049-R1059, 2006.

Yoshimura, N., Bennett, N.E., Hayashi, Y., Ogawa, T., Nishizawa, O., Chancellor, M., de Groat, W.C., Seki, S. Bladder overactivity and hyperexcitability of bladder afferent neurons after intrathecal delivery of nerve growth factor in rats. Journal of Neuroscience, 26:10847-10855, 2006.

Kamo, I., KaihoY., Canon, T., Chancellor, M.B., de Groat, W.C., Prantil, R.L., Vorp, D.A., Yoshimura, N.: Functional analysis of active urethral closure mechanisms under sneeze-induced stress conditions in a rat model of birth trauma. Journal of Urology, 176: 2711-2715, 2006.

Zhang, X., Roppolo, J.R., de Groat, W.C., Tai, C. Mechanisms of nerve conduction block induced by high-frequency biphasic electrical currents. IEEE Transactions on Biomedical Engineering, 53: 2445-2454, 2006.

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Beumer JH, Eiseman JL, Parise RA, Joseph E, Covey JM, Egorin MJ. Modulation of gemcitabine (2',2'-difluoro-2'-deoxycytidine) pharmacokinetics, metabolism, and bioavailability in mice by 3,4,5,6-tetrahydrouridine. Clin Cancer Res. 2008 Jun 1;14(11):3529-35.

Guo J, Parise RA, Joseph E, Egorin MJ, Lazo JS, Prochownik EV, Eiseman JL. Efficacy, pharmacokinetics, tisssue distribution, and metabolism of the Myc-Max disruptor, 10058-F4 [Z,E]-5-[4-ethylbenzylidine]-2-thioxothiazolidin-4-one, in mice. Cancer Chemother Pharmacol. 2008 May 29. [Epub ahead of print]

Zamboni WC, Jung LL, Strychor S, Joseph E, Zamboni BA, Fetterman SA, Sidone BJ, Burke TG, Curran DP, Eiseman JL. Plasma and tissue disposition of non-liposomal DB-67 and liposomal DB-67 in C.B-17 SCID mice. Invest New Drugs. 2008 Oct;26(5):399-406. Epub 2008 Feb 2.

Florian JA Jr, Eiseman JL, Parker RS. Nonlinear model predictive control for dosing daily anticancer agents using a novel saturating-rate cell-cycle model. Comput Biol Med. 2008 Mar;38(3):339-47. Epub 2008 Jan 28.

Parise RA, Beumer JH, Kangani CO, Holleran JL, Eiseman JL, Smith NF, Covey JM, Perrine SP, Egorin MJ. Liquid chromatography-mass spectrometric assay for quantitation of the short-chain fatty acid, 2,2-dimethylbutyrate (NSC 741804), in rat plasma. J Chromatogr B Analyt Technol Biomed Life Sci. 2008 Feb 1;862(1-2):168-74. Epub 2007 Dec 8.

Zamboni WC, Strychor S, Joseph E, Walsh DR, Zamboni BA, Parise RA, Tonda ME, Yu NY, Engbers C, Eiseman JL. Plasma, tumor, and tissue disposition of STEALTH liposomal CKD-602 (S-CKD602) and nonliposomal CKD-602 in mice bearing A375 human melanoma xenografts. Clin Cancer Res. 2007 Dec 1;13(23):7217-23.

Beumer JH, Eiseman JL, Parise RA, Florian JA Jr, Joseph E, D'Argenio DZ, Parker RS, Kay B, Covey JM, Egorin MJ. Plasma pharmacokinetics and oral bioavailability of 3,4,5,6-tetrahydrouridine, a cytidine deaminase inhibitor, in mice. Cancer Chemother Pharmacol. 2008 Aug;62(3):457-64. Epub 2007 Nov 15.

Beumer, J.H. Eiseman, J.L., Parise, R.A., Joseph, E., Holleran, J.L., Covey, J.M. and Egorin, M.J. " Pharmacokinetics, metabolism and oral bioabailability of the DNA methyltransferase inhibitor, 5-fluoro-2'-deoxycytidine in mice." Clinical Cancer Research, 2006, in press

Ramanathan, R.K., Trump, D.L., Eiseman, J.L., Balani, C.P., Agarwala, S.S., Zuhowski, E.G., Lan, J., Potter, D.M., Ivy, S.P., Ramalingam, S., Brufsky, A.M., Wong, M.K., Tutchko, S., and Egorin, M.J. "Phase I Pharmacokinetic-Pharmacodynamic Study of 17-(Allylamino)-17-Demethoxygeldanamycin (17AAG, NSC 330507), A Novel Inhibitor of Heat Shock Protein 90, in Patients With Refractory Advanced Cancers." Clinical Cancer Research, 2006, in press

Eiseman, J.L., Guo, J., Ramanathan, R.K., Belani, C.P., Solit, D. B., Scher, H.I., Ivy, S. P., Zuhowski, E.G. and Egorin, M.J. "Evaluation of Plasma Insulin-like Growth Factor Binding Protein 2 (IGFBP-2) and Her-2 Extracellular Domain (Her-2 ECD) as Biomarkers for 17-Allylamino-17-demethoxygeldanamycin (17-AAG) Treatment of Adult Patients with Advanced Solid Tumors ." Clinical Cancer Research, 2006, in press.

Beumer, J.H., Joseph, E., Egorin, M.J., Covey, J.M. and Eiseman, J.L. "Quantitiative determination of zebularine (NSC 309132), a DNA methyltransferase inhibitor, and three metabolites in murine plasma by high-performance liquid chrmomatography coupled with on-line radioactivity detection." J. Chromatogr. B Analyt.Technol.Biomed. Life Sci, 2006, 83:147-155.

Beumer, J.H. Joseph, E., Egorin, M.J., Parker, R.S., D'argenio, D.Z., Covey, J.M., and Eiseman, J.L. "A mass balance and disposition study of the DNA methyltransferase inhibitor, zebularine (NSC 309132) and three of its metabolites in mice." Clinical Cancer Research, 2006, 12:5826-5833.

Melanie Flint, Ph.D.
Research Instructor

Flint MS, Baum A, Chambers WH, Jenkins FJ (2007). Identifying molecular mechanisms involved in DNA damage and repair in 3T3 cells following stress hormone exposure. Psychoneuroendocrinology. 32(5):470-9.

Yang T, MS Flint, K Webb, and Chambers WH (2006). CD161:ClrB interactions mediate activation of enhanced lysis of tumor target cells following NK cell:DC co-culture. Immunol Res. 36 (1-3): 43-50

Peter Friedman, Ph.D.
Professor

Sebastian EM, Suva LJ, Friedman PA. Differential effects of intermittent PTH(1-34) and PTH(7-34) on bone microarchitecture and aortic calcification in experimental renal failure. Bone. 2008 Aug 9. [Epub ahead of print]

Wang B, Yang Y, Friedman PA. Na/H Exchange Regulatory Factor 1, a Novel AKT-associating Protein, Regulates Extracellular Signal-regulated Kinase Signaling through a B-Raf-Mediated Pathway. Mol Biol Cell. 2008 Apr;19(4):1637-45. Epub 2008 Feb 13.

Wheeler D, Garrido JL, Bisello A, Kim YK, Friedman PA, Romero G. Regulation of parathyroid hormone type 1 receptor dynamics, traffic, and signaling by the Na+/H+ exchanger regulatory factor-1 in rat osteosarcoma ROS 17/2.8 cells. Mol Endocrinol. 2008 May;22(5):1163-70. Epub 2008 Jan 17.

Sneddon WB, Friedman PA 2007 ß-arrestin-dependent parathyroid hormone-stimulated ERK activation and PTH1R internalization. Endocrinology, In press.

Sneddon WB, Yang Y, Ba, J., Harinstein LM, and Friedman PA. Extracellular signal-regulated kinase activation by parathyroid hormone in distal tubule cells. Am. J. Physiol: 2007. 292: F1028-F1034.

Srivisinan R, Wolfe D, Huang S, Krisky D, Fink D, Friedman PA, deGroat WC, and Glorioso J. A platform for drug discovery: selective vector replication to identify ion channel antagonists. Nature Methods Accepted, 2007.

Friedman PA, and Goodman WG. PTH(1-84) / PTH(7-84): a balance of power. Am J Physiol Renal Physiol 290: F975-F984, 2006.

Weinman EJ, Hall RA, Friedman PA, Liu-Chen LY, and Shenolikar S. The association of NHERF adaptor proteins with G protein-coupled receptors and receptor tyrosine kinases. Annu Rev Physiol 68: 491-505, 2006.

William Furey, Ph.D.
Professor

Matei E, Furey W, Gronenborn AM. Solution and crystal structures of a sugar binding site mutant of cyanovirin-N: no evidence of domain swapping. Structure. 2008 Aug 6;16(8):1183-94.

Kale S, Ulas G, Song J, Brudvig GW, Furey W, Jordan F. Efficient coupling of catalysis and dynamics in the E1 component of Escherichia coli pyruvate dehydrogenase multienzyme complex. Proc Natl Acad Sci U S A. 2008 Jan 29;105(4):1158-63. Epub 2008 Jan 23.

A Dynamic Loop at the Active Center of the Escherichia coli Pyruvate Dehydrogenase Complex E1 Component Modulates Substrate Utilization and Chemical Communication with the E2 Component. S. Kale, P. Arjunan, W. Furey & F. Jordan, J. Biol. Chem., in press, 2007. Shake-and-Bake on the Grid. R. Miller, N. Shah, M. Green, W. Furey, and C. Weeks, J. Applied Crystallography, 2007.

A Thiamin-Bound, Pre-decarboxylation Reaction Intermediate Analogue in the Pyruvate Dehydrogenase E1 Subunit Induces Large-Scale Disorder-to-Order Transformations in the Enzyme and Reveals Novel Structural Features in the Covalently Bound Adduct. P. Arjunan, M. Sax, A. Brunskill, K. Chandrasekhar, N. Nemeria, S. Zhang, F. Jordan & W. Furey, *J. Biol. Chem*. 281, 15296-15303, 2006.

Active Site Changes in the Pyruvate Dehydrogenase Multienzyme Complex E1 Apoenzyme Component from *Escherichia coli* Observed at 2.32 Å Resolution. K. Chandrasekhar, P. Arjunan, M. Sax, N. Nemeria, F. Jordan & W. Furey, *Acta Cryst D*, 62, 1382-1386, 2006.

Ferruccio Galbiati, Ph.D.
Associate Professor

Volonte D, McTiernan CF, Drab M, Kasper M, Galbiati F. Caveolin-1 and caveolin-3 form heterooligomeric complexes in atrial cardiac myocytes that are required for doxorubicin-induced apoptosis. Am J Physiol Heart Circ Physiol. 2008 Jan;294(1):H392-401. Epub 2007 Nov 2.

Fecchi, K., Volonte, D., Schmeck, K., and Galbiati, F. 2006. Spatial and temporal regulation of GLUT4 translocation by flotillin-1 and caveolin-3 in skeletal muscle cells. FASEB J., 20 (6), 705-757.

Dasari, A., Bartholomew, J.N., Volonte, D., and Galbiati F. 2006. Oxidative stress induces premature senescence by stimulating caveolin-1 gene transcription through p38 MAPK/Sp1-mediated activation of two GC-rich promoter elements. Cancer Research, 66 (22), 10805-10814.

Pamela Hershberger
Research Assistant Professor

Parise, R.A., Egorin, M.J., Kanterewicz, B., Taimi, M., Petkovich, M., Lew, A.M., Chuang, S.S., Nichols, M., El-Hefnawy, T., and Hershberger, P.A. CYP24, the enzyme that catabolizes the anti-proliferative agent vitamin D, is increased in lung cancer. Int. J. Cancer, 2006, 119:1819-1828.

Jing Hu, Ph.D.
Assistant Professor

Hu J, Straub J, Xiao D, Singh SV, Yang H, Sonenberg N and Vatsyayan J. Phenethyl isothiocyanate, a cancer chemopreventive constituent of cruciferous vegetables, inhibits cap-dependent translation by regulating level and phosphorylation of 4E-BP1. Cancer Research (In press).

Edwin Jackson, Ph.D.
Professor

Jackson EK, Mi Z. Sitagliptin augments sympathetic enhancement of the renovascular effects of angiotensin II in genetic hypertension. Hypertension. 2008 Jun;51(6):1637-42. Epub 2008 Apr 28.

Tofovic SP, Zhang X, Zhu H, Jackson EK, Rafikova O, Petrusevska G. 2-Ethoxyestradiol is antimitogenic and attenuates monocrotaline-induced pulmonary hypertension and vascular remodeling.Vascul Pharmacol. 2008Apr-Jun;48(4-6):174-83. Epub 2008 Feb 13.

Su Y, Huang X, Raskovalova T, Zacharia L, Lokshin A, Jackson E, Gorelik E. Cooperation of adenosine and prostaglandin E(2) (PGE (2)) in amplification of cAMP-PKA signaling and immunosuppression. Cancer Immunol Immunother. 2008 Nov;57(11):1611-23. Epub 2008 Mar 8.

Ren J, Mi Z, Jackson EK. Assessment of nerve stimulation-induced release of purines from mouse kidneys by tandem mass spectrometry. J Pharmacol Exp Ther. 2008 Jun;325(3):920-6. Epub 2008 Mar 5.

Dubey RK, Jackson EK, Gillespie DG, Zacharia LC, Wunder D, Imthurn B, Rosselli M. Medroxyprogesterone abrogates the inhibitory effects of estradiol on vascular smooth muscle cells by preventing estradiol metabolism. Hypertension. 2008 Apr;51(4):1197-202. Epub 2008 Feb 7.

Jackson EK, Gillespie DG, Zhu C, Ren J, Zacharia LC, Mi Z. Alpha2-adrenoceptors enhance angiotensin II-induced renal vasoconstriction: role for NADPH oxidase and RhoA. Hypertension. 2008 Mar;51(3):719-26. Epub 2008 Feb 4.

Jackson EK, Mi Z. Regulation of renal ectophosphodiesterase by protein kinase C and sodium diet. J Pharmacol Exp Ther. 2008 Apr;325(1):210-6. Epub 2008 Jan 25.

Sonalker PA, Tofovic SP, Bastacky SI, Jackson EK. Chronic noradrenaline increases renal expression of NHE-3, NBC-1, BSC-1 and aquaporin-2. Clin Exp Pharmacol Physiol. 2008 May;35(5-6):594-600. Epub 2007 Dec 26.

Dubey, R.K., Imthurn, B., and Jackson, E.K.: 2-Methoxyestradiol - A potential treatment for multiple proliferative disorders. Endocrinology (In Press), 2007.

Forman, M.B., and Jackson, E.K.: Importance of tissue perfusion in STEMI patients undergoing reperfusion strategies: Role of adenosine. Clinical Cardiology (In Press), 2007.

Jackson, E.K., Mi, Z., and Dubey, R.K.: The extracellular cAMP-adenosine pathway significantly contributes to the in vivo production of adenosine. Journal of Pharmacology and Experimental Therapeutics 320: 117-123, 2007.

Jackson, T.C., Mi, Z., Bastacky, S.I., McHale, T., Melhem, M.F., Sonalker, P.A., Tofovic, S.P., and Jackson, E.K.: PPARα agonists improve renal preservation in kidneys subjected to chronic in vitro perfusion: Interaction with mannitol. Transplant International 20: 277-290, 2007.

Zhang, X., Jia, Y., Jackson, E.K., and Tofovic, S.P.: 2-Methoxyestradiol and 2-ethoxyestradiol retard the progression of renal disease in aged, obese, diabetic ZSF1 rats. Journal of Cardiovascular Pharmacology 49: 56-63, 2007.

Jackson, E.K.,Gillespie, D.G., and Jackson, T.C.: Phospholipase C and Src Modulate Angiotensin II–Induced Cyclic AMP Production in Preglomerular Microvascular Smooth-Muscle Cells from Spontaneously Hypertensive Rats. Journal of Cardiovascular Pharmacology 49; 106-110, 2007.

Jackson, E.K., Ren, J, Zacharia, L.C., and Mi, Z. Characterization of renal ecto-phosphodiesterase. Journal of Pharmacology and Experimental Therapeutics 321: 810-815, 2007.

Jackson, E.K., Mi, Z., Zacharia, L.C., Tofovic, S.P., and Dubey, R.K.: The pancreatohepatorenal cAMP-adenosine mechanism. Journal of Pharmacology and Experimental Therapeutics 321: 799-809, 2007.

Funakoshi, H, Zacharia, L.C., Tang, Z., Zhang, J., Lee, L.L., Good, J.C., Herrmann, D.E., Higuchi, Y., Koch, W.J., Jackson, E.K., Chan, T.O., and Feldman, A.M. A1 Adenosine receptor up-regulation accompanies decreasing myocardial adenosine levels in mice with left ventricular dysfunction. Circulation 115: 2307 - 2315, 2007.

Sonalker, P.A. and Jackson, E.K. Norepinephrine, via β-adrenoceptors, regulates BSC-1 expression in thick ascending limb cells. Hypertension 49: 1351 - 1357, 2007.

Bhanu, N.V., Aerbajinai, W., Gantt, N.M., Jackson, E.K., Goh, S.-H., Lee, Y.T., and Miller, J.L.: Cl-IB-MECA inhibits human erythropoiesis. British Journal of Haematology doi:10.1111/j.1365-2141.2007.

Raskovalova, T., Lokshin, A., Huang, X., Zarour, H., Jackson, E.K., and Gorelik, E.: Adenosine-mediated inhibition of cytokine production and cytotoxic activity of human anti-melanoma specific CD8+ and CD4+ T cells. Cancer Reserch (In Press) 2007.

Wu, X., Drabek, T., Tisherman, S.A., Henchir, J., Stezoski, S.W., Culver, S., Stezoski, J. Jackson, E.K., Garman, R., and Kochanek, P.M.: Emergency preservation and resuscitation with profound hypothermia, oxygen, and glucose allows reliable neurological recovery after 3 h of cardiac arrest from rapid exsanguination in dogs. Journal of Cerebral Blood Flow and Metabolism (In Press) 2007.

Tofovic, S.P., Salah, E.M., Zhang, M., Jackson, E.K., and Melham, M.: Early renal injury induced by caffeine consumption in obese (fa-facp), diabetic ZAF1 rats. Renal Failure (In Press) 2007.

Sachse, K.T., Jackson, E.K., Wisniewski, S.R., Gillespie, D.G., Puccio, A.M., Clark, R.S.B, Dixon, C.E., and Kochanek, P.M.: Increases in cerebrospinal fluid caffeine concentration are associated with favorable outcome after severe traumatic brain injury in humans. Journal of Cerebral Blood Flow and Metabolism (In Press) 2007.

Jackson, E.K., Dubinion, J.H., and Mi, Z.: Effects of dipeptidyl peptidase IV inhibition on arterial blood pressure. Clinical and Experimental Pharmacology and Physiology (In Press) 2007.

Sonalker, P.A., Tofovic, S.P., and Jackson, E.K.: Cellular distribution of the renal bumetanide-sensitive Na-K-2Cl cotransporter BSC-1 in the outer strip of inner medulla during the development of hypertension in the spontaneously hypertensive rat. Clinical and Experimental Pharmacology and Physiology (In Press) 2007.

Jackson, E.K.: Confirmation of the pivotal role of Gs" in renin release. American Journal of Physiology – Renal Physiology 292: F26, 2007.

Kochanek, P.M., Vagni, V.A., Janesko, K.L., Washington, C.B., Crumrine, P.K., Garman, R.H., Jenkins, L.W., Clark, R.S.B., Homanics, G.E., Dixon, C.E., Schnermann, J., and Jackson, E.K.: Adenosine A1 receptor knockout mice develop lethal status epilepticus after experimental traumatic brain injury. Journal of Cerebral Blood Flow and Metabolism 26: 565-575, 2006.

Dubinion, J.H., Mi, Z., Zhu, C., Gao, L., and Jackson, E.K.: PP-fold peptide receptors and angiotensin II-induced renal vasoconstriction. Hypertension 47: 545-551, 2006.

Weiqun, Y., Zacharia, L.C., Jackson, E.K., and Apodaca, G.: Adenosine receptor expression and function in bladder uroepithelium. American Journal of Physiology - Cell Physiology 291: 254-265, 2006.

Jackson, E.K., Zacharia, L.C., Zhang, M., Gillepspie, D.G., Zhu, C., and Dubey, R.K.: cAMP-adenosine pathway in the proximal tubule. Journal of Pharmacology and Experimental Therapeutics 317: 1219-1229, 2006.

Dubinion, J.H., Mi, Z., and Jackson, E.K.: Role of renal sympathetic nerves in regulating renovascular responses to angiotensin II in spontaneously hypertensive rats. Journal of Pharmacology and Experimental Therapeutics 317: 1330-1336, 2006.

Lokshin, A., Raskovalova, T., Huang, X., Zacharia, L.C., Jackson, E.K., and Gorelik, E.: Adenosine-mediated inhibition of the cytotoxic activity and cytokine production by Ly49D activated NK cells: Involvement of protein kinase A (PKA) type I. Cancer Research 66: 7758-7765, 2006.

Barchiesi, F., Jackson, E.K., Finerle, J., and Dubey, R.K.: 2-Methoxyestradiol, an endogenous 17β-estradiol metabolite, inhibits neointima formation and smooth muscle cell growth via double blockade of cell cycle. Circulation Research 99266-274, 2006.

Zacharia, L.C., Jackson, E.K., Kloosterboer, H.J., Imthurn, B., and Dubey, R.K.: Conversion of tibolone to 7α-methyl-thinyl estradiol using GC-MS and LC-MS: Interpretation and clinical implications. Menopause 13: 926-934, 2006.

Ohta, A., Gorelik, E., Prasad, S. J., Ronchese, F., Lukashev, D., Wong, M.K.K., Huang, X., Caldwell, S., Liu, K., Smith, P., Chen, J-F., Jackson, E.K., Apasov, S., Abrams, S., and Sitkovsky, M.: A2A adenosine receptor protects tumors from anti-tumor T cells. Proceedings of the National Academy of Sciences of the United States of American 103: 13132-13137, 2006.

Tofovic, S.P., Zhang, X., Jackson, E.K., Dacic, S., and Petrusevaska, G.: 2-Methoxyestradiol mediates protective effects of estradiol in monocrotaline-induced pulmonary hypertension. Vascular Pharmacology 45: 358-367, 2006.

Arendash, G.W., Schleif, W., Rezai-zadeh, K., Jackson, E.K., Zacharia, L.C., Cracchiolo, J.R., Shippy, D., and Tan, J.: Caffeine Protects Alzheimer's Mice Against Cognitive Impairment and Reduces Brain Aβ Production. Neuroscience 142: 941-952, 2006.

Yu Jiang, Ph.D.
Associate Professor

Ma D, Bai X, Guo S, Jiang Y. The switch I region of Rheb is critical for its interaction with FKBP38. J Biol Chem. 2008 Jul 25. [Epub ahead of print]

He F, Zhang Q, Kuruba R, Gao X, Li J, Li Y, Gong W, Jiang Y, Xie W, Li S. Upregulation of decorin by FXR in vascular smooth muscle cells. Biochem Biophys Res Commun. 2008 Aug 8;372(4):746-51. Epub 2008 Jun 2.

Yu S, Franceschi RT, Luo M, Zhang X, Jiang D, Lai Y, Jiang Y, Zhang J, Xiao G. Parathyroid hormone increases activating transcription factor 4 expression and activity in osteoblasts: requirement for osteocalcin gene expression. Endocrinology. 2008 Apr;149(4):1960-8. Epub 2008 Jan 10.

Yu S, Jiang Y, Galson DL, Luo M, Lai Y, Lu Y, Ouyang HJ, Zhang J, Xiao G. General transcription factor IIA-gamma increases osteoblast-specific osteocalcin gene expression via activating transcription factor 4 and runt-related transcription factor 2. J Biol Chem. 2008 Feb 29;283(9):5542-53. Epub 2008 Jan 2.

Bai X, Ma D, Liu A, Shen X, Wang QJ, Liu Y, Jiang Y. Rheb activates mTOR by antagonizing its endogenous inhibitor, FKBP38. Science. 2007 Nov 9;318(5852):977-80.

Singha UK, Jiang Y, Yu S, Luo M, Lu Y, Zhang J, Xiao G. Rapamycin inhibits osteoblast proliferation and differentiation in MC3T3-E1 cells and primary mouse bone marrow stromal cells. J Cell Biochem. 2007 May 21; [Epub ahead of print].

Yan, C, Shen, X and Jiang, Y (2006). Rapamycin Activates the Tap42-associated phosphatases by abrogating their association with Tor complex 1. EMBO J. 25(15):3546-55.

Qu C. Altomonte, J. He, J. Su, D. Perdomo, G. Tze, T. Baliga, S. Jiang, Y. and Dong, H. (2006) Fibrates downregulate Foxo1 expression and ameliorate hypertriglyceridemia in high fructose diet-fed hamsters. Am J Physiol Endocrinol Metab. [Epub ahead of print].
Hasinoff BB, Wu X, Begleiter A, Guziec LJ, Guziec F Jr, Giorgianni A, Yang S, Jiang Y, Yalowich JC. Structure-activity study of the interaction of bioreductive benzoquinone alkylating agents with DNA topoisomeraseII. Cancer Chemother Pharmacol. 2006 57(2):221-33.

Liu H, Liu ZQ, Chen CX, Magill S, Jiang Y, Liu YJ. (2006). Inhibitory regulation of EGF receptor degradation by sorting nexin 5. Biochem Biophys Res Commun. 7;342(2):537-46.

Paul Johnston, Ph.D.
Research Assocaite Professor

Johnston PA, Soares KM, Shinde SN, Foster CA, Shun TY, Takyi HK, Wipf P, Lazo JS. Development of a 384-Well Colorimetric Assay to Quantify Hydrogen Peroxide Generated by the Redox Cycling of Compounds in the Presence of Reducing Agents. Assay Drug Dev Technol. 2008 Aug 12. [Epub ahead of print]

Brisson-Tierno M*, Johnston PA*, Foster C, Skoko JJ, Shun TY, Lazo JS. (2007) Development and Optimization of high-throughput in vitro protein phosphatase screening assays for drug discovery. * Authors contributed equally to this work. Nature Protocols. 2:1134-44.

Johnston PA, Foster CA, Shun TY, Skoko JJ, Shinde S, Wipf P, and Lazo JS. (2007) Development and Implementation of a 384-well Homogeneous Fluorescence Intensity HTS Assay to Identify Mitogen-Activated Protein Kinase Phosphatase-1 Dual Specificity Protein Phosphatase Inhibitors. Assays and Drug. Discovery Technologies. In Press.

Arnold DM, Foster C, Huryn DM, Lazo JS, Johnston PA, Wipf P. (2007) Synthesis and Biological Activity of a Focused Library of Mitogen-activated Protein Kinase Phosphatase Inhibitors. Chem. Biol. Drug Des. 69:23-30.

Edwina Kinchington, Ph.D.
Research Instructor

Mitchell, J.L, Trible, R.P., Emert-Sedlack, L.A., Weis, D.D., Lerner, E.C., Applen, J.J., Sefton, B.M., Smithgall, T.E., and Engen, J.R. Functional Characterization and conformational analysis of the Herpesvirus saimiri Tip-C484 protein. Journal of Molecular Biology. 2007 Mar 2;366(4):1282-93

Hochrein, J.M., Lerner, E.C., Schiavone, A.P., Smithgall, T.E., and Engen, J.R. An examination of dynamics crosstalk between SH2 and SH3 domains by hydrogen/deuterium exchange and mass spectrometry. Protein Science, 15: 65-73, 2006.

Eisfeld, A.J., Turse, S.E., Jackson, S.A., Lerner, E.C., and Kinchington, P.R. Phosphorylation of the varicella-zoster virus (VZV) major transcriptional regulatory protein IE62 by the VZV open reading frame 66 protein kinase. J. Virology. 80: 1710-1723, 2006.

Hochrein, J.M., Wales, T.M., Lerner, E.C., Schiavone, A.P., Smithgall, T.E., and Engen, J.R. Conformational features of the full-length HIV and SIV Nef proteins determined by Mass Spectrometry. Biochemistry. 45: 7733-7739, 2006.

Chong, Y.P., Chan, A.S., Chan, K.C., Williamson, N.A., Lerner, E.C., Smithgall, T.E., Bjorge, J.D., Fujita, D.J., Purcell, A.W., Scholz, G., Mulhern, T.D., and Cheng, H.C. C-terminal SRC kinase-homologous kinase (CHK) – a unique inhibitor inactivating multiple active conformations of SRC-family tyrosine kinases. J. Biol. Chem. 281:32988-32999, 2006.

Joan M. Lakoski, Ph.D.
Professor

Keyser DJ, Lakoski JM, Lara-Cinisomo S, Schultz DJ, Williams VL, Zellers DF, Pincus HA. Advancing institutional efforts to support research mentorship: a conceptual framework and self-assessment tool. Acad Med. 2008 Mar;83(3):217-25.

Cavanaugh, J.E., Jaumotte, J.D., Lakoski, J.M., Zigmond, M.J. Neuroprotective Role of ERK1/2 and ERK5 in a Dopaminergic Cell Line Under Basal Conditions and in Response to Oxidative Stress. J. Neuro. Res. 84:1367-1375, 2006.

John Lazo, Ph.D.
Allegheny Foundation Professor

Sharlow ER, Leimgruber S, Yellow-Duke A, Barrett R, Wang QJ, Lazo JS. Development, validation and implementation of immobilized metal affinity for phosphochemicals (IMAP)-based high-throughput screening assays for low-molecular-weight compound libraries. Nat Protoc. 2008;3(8):1350-63.

Johnston PA, Soares KM, Shinde SN, Foster CA, Shun TY, Takyi HK, Wipf P, Lazo JS.
Development of a 384-Well Colorimetric Assay to Quantify Hydrogen Peroxide Generated by the Redox Cycling of Compounds in the Presence of Reducing Agents. Assay Drug Dev Technol. 2008 Aug 12. [Epub ahead of print]

de Oliveira PE, Tomko RJ Jr, Lazo JS. Is a step backwards in S-phase-targeted chemotherapy a step forward? Mol Interv. 2008 Jun;8(3):137-40. No abstract available.

Guo J, Parise RA, Joseph E, Egorin MJ, Lazo JS, Prochownik EV, Eiseman JL. Efficacy, pharmacokinetics, tisssue distribution, and metabolism of the Myc-Max disruptor, 10058-F4 [Z,E]-5-[4-ethylbenzylidine]-2-thioxothiazolidin-4-one, in mice. Cancer Chemother Pharmacol. 2008 May 29. [Epub ahead of print]

Lazo JS.Rear-view mirrors and crystal balls: a brief reflection on drug discovery.
Mol Interv. 2008 Apr;8(2):60-3. No abstract available.

Vogt A, McDonald PR, Tamewitz A, Sikorski RP, Wipf P, Skoko JJ 3rd, Lazo JS. A cell-active inhibitor of mitogen-activated protein kinase phosphatases restores paclitaxel-induced apoptosis in dexamethasone-protected cancer cells. Mol Cancer Ther. 2008 Feb;7(2):330-40. Epub 2008 Feb 1.

Brisson, M., Foster, C., Wipf, P., Joo, B., Tomko, R.J., Nguyen, T. and Lazo, J.S. Independent mechanistic inhibition of Cdc25 phosphatases by a natural product caulibugulone. Molec Pharm. 71:184-192, 2007.

Arnold, D.M., Foster, C., Huryn D.M., Lazo, J.S., Johnston, P.A., and Wipf, P. Synthesis and biological activity of a focused library of mitogen-activated protein kinase phosphatase inhibitors. Chem Biol Drug Des. 69:23-30, 2007.

Bansal, P., and Lazo, J.S. Induction of Cdc25B regulates cell cycle resumption after genotoxic stress. Cancer Res. 67:3356-3363, 2007.

Montoya, S.E., Thiels, E., Card, J.P., and Lazo, J.S. Astrogliosis and behavioral changes in mice lacking the neutral cysteine protease bleomycin hydrolase. Neuroscience. 146:890-900, 2007.

Panchal, R.G., Ruthel, G. Brittingham, K.C., Lane, D., Kenny, T.A., Gussio, R., Lazo, J.S., and Bavari, S. Chemical genetic screening identifies critical pathways in anthrax lethal toxin-induced pathogenesis. Chem Biol. 14:245-55, 2007.

Vogt, A., and Lazo, J.S. Implementation of high-content assay for inhibitors of mitogen-activated protein kinase phosphatases. Methods. 42:268-277, 2007.

Towne, C.F., York, I.A., Watkin, L.B., Lazo, J.S., and Rock, K.L. Analysis of the role of bleomycin hydrolase in antigen presentation and the generation of CD8 T cell responses. J Immunol. 178:6923-30, 2007.

Achiwa, H., and Lazo, J.S. PRL-1 tyrosine phosphatase regulates c-Src levels, adherence, and invasion in human lung cancer cells. Cancer Res. 67:643-50, 2007.

Tierno, M.B., Johnston, P.A., Foster, C., Skoko, J.J., Shinde, S.N., Shun, T. Y., and Lazo, J.S. Development and optimization of high-throughput in vitro protein phosphatase screening assays. Nature Protocols. 2:1134-1144, 2007.

Lazo, J.S., Brady, L.S., and Dingledine, R.J. Building a pharmacological lexicon: small molecule discovery in academia. Mol Pharmacol. 72:1-7, 2007.

Johnston, P.A., Foster, C.A., Shun, T.Y., Skoko, J., Shinde, S., Wipf, P., and Lazo, J.S. Development and implementation of a 384-well homogeneous fluorescence intensity HTS assay to identify MKP-1 dual specificity protein phosphatase inhibitors. Assay Drug Develop Technol. 5:319-32, 2007.

Lazo, J.S., Skoko, J.S., Werner, S., Mitasev, B., Bakan, A., Koizumi, F., Yellow-Duke, A. Bahar, I., and Brummond, K.M. Structurally unique inhibitors of human mitogen-activated protein kinase phosphatase-1 identified in a pyrrole carboxamide library. J Pharmacol Expt Therap. 322:940-947, 2007.

Guo, J. Parise, R.A., Joseph, E., Lan, J. Pan, S., Joo, B. Egorin, M.J., Wipf, P., Lazo, J.S., and Eiseman, J.I. Pharmacology and antitumor activity of a quinolinedione Cdc25 phosphatase inhibitor DA3003-1 (NSC 663284). Anticancer Res. In Press, 2007.

Wang, H., Hammoudeh, D.I., Follis, A.V., Reese, B.E., Lazo, J.S., Metallo, S.J., and Prochownik, E.V. Improved low molecular weight myc-max inhibitors. Molec Cancer Therp. In Press, 2007.

Srivastava, S.K., Bansal, P., Oguri, T., Lazo, J.S., and Singh, S.V. Cdc25B phosphatase is essential for benzo[a]pyrene-7,8-diol-9,10-epoxide induced neoplastic transformation. Cancer Res. In Press, 2007

Wipf, P., Graham, T.H., Vogt, A. Sikorski, R., Ducruet, A., and Lazo, J.S. Cellular Analysis of disorazole C1 and structure-activity relationship of analogs of the natural product. Chemical Biology & Drug Design. 67:66-73, 2006.

Lazo, J.S., Nunes, R., Skoko, J.J., Queiroz de Oliveira, P.E., Vogt, A., and Wipf, P. Novel benzofuran inhibitors of human mitogen-activated protein kinase phosphatase-1. Bioorg Med Chem. 14:5643-5650, 2006.

Cossy, J., Belotti, D., Brisson, M., Skoko, J.J., Wipf, P. and Lazo, J.S. Biological evaluation of newly synthesized quinoline-5,8-quinones as Cdc25B inhibitors. Bioorg Med Chem. 14:6283-6387, 2006.

Edwin Levitan, Ph.D.
Professor

Shakiryanova D, Levitan ES. Prolonged presynaptic posttetanic cyclic GMP signaling in Drosophila motoneurons. Proc Natl Acad Sci U S A. 2008 Sep 9;105(36):13610-3. Epub 2008 Sep 2.

Wong MY, Shakiryanova D, Levitan ES. Presynaptic Ryanodine Receptor-CamKII Signaling is Required for Activity-dependent Capture of Transiting Vesicles. J Mol Neurosci. 2008 Jul 1. [Epub ahead of print]

Levitan ES. Signaling for vesicle mobilization and synaptic plasticity. Mol Neurobiol. 2008 Feb;37(1):39-43. Epub 2008 Apr 30. Review.

Shakiryanova D, Klose MK, Zhou Y, Gu T, Deitcher DL, Atwood HL, Hewes RS, Levitan ES. Presynaptic ryanodine receptor-activated calmodulin kinase II increases vesicle mobility and potentiates neuropeptide release. J Neurosci. 2007 Jul 18;27(29):7799-806.

Levitan ES, Lanni F, Shakiryanova D. In vivo imaging of vesicle motion and release at the Drosophila neuromuscular junction. Nat Protoc. 2007;2(5):1117-25.

Singer-Lahat, D., Sheinin, A., Chikvashvili, D., Tsuk, S., Greitzer, D., Friedrich, R., Feinshreiber, L., Ashery, U., Benveniste,M., Levitan, E.S., and Lotan, I. K+ channel facilitation of exocytosis by dynamic interaction with syntaxin. J. Neurosci. 2007 Feb 14;27(7):1651-8
Redman, P.T., He, K., Hartnett, K.A., Jefferson, B.S., Hu, L., Rosenberg, P.A., Levitan, E.S., and Aizenman, E. Apoptotic surge of potassium currents is mediated by p38 phosphorylation of Kv2.1. Proc Natl Acad Sci U S A. 2007 Feb 27;104(9):3568-73.

Pal, S., Takimoto, K., Aizenman, E., and Levitan, E.S. Apoptotic surface delivery of K^+ channels. Cell Death and Diff. 13: 661-667, 2006.

Sturman, D.A., Shakiryanova, D., Hewes, R.S., Deitcher, D.L., and Levitan, E.S. Nearly neutral secretory vesicles in Drosophila nerve terminals. Biophysical J. 90:L45-47, 2006.

Zhou, C., Ziegler, C., Birder, L.A., Stewart, A.F.R., and Levitan, E.S. Angiotensin II and stretch activate NADPH oxidase to destabilize cardiac Kv4.3 channel mRNA. Circ. Res. 98:1040-1047, 2006.

Hahn, J., Kullmann, P.H.M., Horn, J.P., and Levitan, E.S. D2 autoreceptors chronically enhance dopamine neuron pacemaker activity. J. Neurosci. 26:5240-5247, 2006.

Shakiryanova, D., Tully, A., and Levitan, E.S. Activity-dependent synaptic capture of transiting peptidergic vesicles. Nature Neuroscience 9:896-900, 2006.

Kula E., Levitan, E.S., Pyza, E., and Rosbash, M. PDF cycling in the dorsal protocerebrum of the Drosophila brain is not necessary for circadian clock function. J Biol Rhythms. 21:104-117, 2006.

Grishin, A., Li, H., Levitan, E.S., Zaks-Makhina, E. Identification of GRIF-1 (TRAK2) as a trafficking factor for the K+ channel Kir2.1. J. Biol. Chem. 281: 30104-30111, 2006.

Salvador-Recatala, V., Kim, Y., Zaks-Makhina, E., and Levitan, E.S. Voltage-gated K^+ channel block by catechol derivatives: defining nonselective and selective pharmacophores. JPET 319: 758-764, 2006.

Redman, P.T., Jefferson, B.S., Ziegler, C.B., Mortensen, O.V., Torres, G.E., Levitan, E.S., and Aizenman, E. A vital role for Kv channels in dopamine transporter-mediated 6-hydroxydopamine neurotoxicity. Neurosci. 143:1-6, 2006.

Elena Makhina, Ph.D.
Research Assistant Professor

Grishin A, Li H, Levitan ES, Zaks-Makhina E. 2006. Identification of gamma-aminobutyric acid receptor-interacting factor 1 (TRAK2) as a trafficking factor for the K+ channel Kir2.1. J. Biol. Chem., 2006, 281:30104-11.

Salvador-Recatala V, Kim Y, Zaks-Makhina E, Levitan ES. Voltage-gated K+ channel block by catechol derivatives: defining nonselective and selective pharmacophores. J Pharmacol Exp Ther. 2006, 319:758-64.

Mark Nichols, Ph.D.
Assistant Professor

Parise RA, Egorin MJ, Kanterewicz B, Taimi M, Petkovich M, Lew AM, Chuang SS, Nichols M, El-Hefnawy T, and Hershberger PA. (2006) CYP24, the enzyme that catabolizes the anti-proliferative agent vitamin D, is increased in lung cancer. Intl. J Cancer, 119:1819-28.

Michael J. Palladino, Ph.D.
Assistant Professor

Langhans MT, Palladino MJ. Cleavage of Mispaired Heteroduplex DNA Substrates by Numerous Restriction Enzymes. Curr Issues Mol Biol. 2008 May 19;11(1):1-12. [Epub ahead of print]

Seigle JL, Celotto AM, Palladino MJ. Degradation of functional triose phosphate isomerase protein underlies sugarkill pathology.
Genetics. 2008 Jun;179(2):855-62. Epub 2008 May 5.

Fergestad T, Olson L, Patel KP, Miller R, Palladino MJ, Ganetzky B. Neuropathology in Drosophila mutants with increased seizure susceptibility. Genetics. 2008 Feb;178(2):947-56. Epub 2008 Feb 1.

Paul, Sarah M., Michael J. Palladino, and Greg. J. Beitel (2007). A pump-independent function of the Na,K-ATPase is required for epithelial junction function and tracheal tube-size control. Development, 134(1):147-55.

Tim Fergestad, Barry Ganetzky and Michael J. Palladino (2006). Neuropathology Drosophila Membrane Excitability Mutants. Genetics 172:1031-1042.

Alicia M. Celotto, Adam C. Frank, Steven W. McGrath, Timothy J. Fergestad, Wayne A. Van Voorhies, Karolyn Buttle, Carmen A. Mannella and Michael J. Palladino (2006). Mitochondrial Encephalomyopathies in Drosophila. Journal of Neuroscience. 26(3): 810-820.

Alicia M. Celotto, Adam C. Frank, Jacquelyn L. Seigle, Michael J. Palladino (2006). Drosophila model of human inherited TPI deficiency glycolytic enzymopathy. Genetics, 174: 1237-1246.

Guillermo Romero, Ph.D.
Associate Professor

Wheeler D, Garrido JL, Bisello A, Kim YK, Friedman PA, Romero G. Regulation of parathyroid hormone type 1 receptor dynamics, traffic, and signaling by the Na+/H+ exchanger regulatory factor-1 in rat osteosarcoma ROS 17/2.8 cells. Mol Endocrinol. 2008 May;22(5):1163-70. Epub 2008 Jan 17.

David Wheeler, W. Bruce Sneddon, Bin Wang, Peter A. Friedman, and Guillermo Romero. NHERF-1 and the cytoskeleton regulate the traffic and membrane dynamics of G-protein-coupled receptors. E-pub ahead of print J. Biol. Chem., Jun 2007; doi:10.1074/jbc.M701544200

Yang Z., Asico, L.D., Yu, P., Wang, Z., Jones, J.E., Escano, C.S., Wang, X., Quinn, M.T., Sibley, D.R., Romero, G.G., Felder, R.A., and Jose, P.A. D5 dopamine receptor regulation of reactive oxygen species production, NADPH oxidase, and blood pressure. Am J Physiol Regul Integr Comp Physiol. 290:R96-R104, 2006.

James Roppolo, Ph.D.
Research Assistant Professor

Tai C, Wang J, Chancellor MB, Roppolo JR, de Groat WC. Influence of temperature on pudendal nerve block induced by high frequency biphasic electrical current.
J Urol. 2008 Sep;180(3):1173-8. Epub 2008 Jul 18.

Tai C, Wang J, Shen B, Wang X, Roppolo JR, de Groat WC. Hindlimb movement in the cat induced by amplitude-modulated stimulation using extra-spinal electrodes.
J Neural Eng. 2008 Jun;5(2):111-24. Epub 2008 Mar 26.

Tai C, Shen B, Wang J, Chancellor MB, Roppolo JR, de Groat WC. Inhibitory and excitatory perigenital-to-bladder spinal reflexes in the cat. Am J Physiol Renal Physiol. 2008 Mar;294(3):F591-602. Epub 2007 Dec 26.

Wang J, Shen B, Roppolo JR, de Groat WC, Tai C. Influence of frequency and temperature on the mechanisms of nerve conduction block induced by high-frequency biphasic electrical current. J Comput Neurosci. 2008Apr;24(2):195-206.Epub 2007Aug 8.

Changfeng Tai, Jicheng Wang, Xianchun Wang, William C. de Groat, and James R. Roppolo, “Bladder inhibition and voiding induced by pudendal nerve stimulation in chronic spinal cord injured cats”, Neurourology and Urodynamics, 2007, in press.

Kanai A, Roppolo JR, Ikeda Y, Zabbarova I, Changfeng Tai, Birder L, Griffiths D, de Groat W, Fry C, “Origin of spontaneous activity in neonatal and adult rat bladders and its enhancement by stretch and muscarinic agonists”. American Journal of Physiology Renal Physiology, 2007, in press.

Huai-Zhen Ruan, Lori, A. Birder, Zhenghua Xiang, Bikramjit Chopra, Tony Buffington, Changfeng Tai, James R. Roppolo, William C. de Groat and Geoffrey Burnstock, “Expression of P2X and P2Y receptors in the intramural parasympathetic ganglia of the cat urinary bladder.” American Journal of Physiology (Renal Physiology), 290(5): F1143-F1152, 2006.

Xu Zhang, James R. Roppolo, William C. de Groat and Changfeng Tai, "Mechanism of nerve conduction block induced by high-frequency biphasic electrical currents", IEEE Transactions on Biomedical Engineering, Vol. 53, NO. 12, PP2445-2454, 2006.

Changfeng Tai, Cynthia Miscik, Timothy Ungerer, James Roppolo, and William de Groat, "Suppression of bladder reflex activity in chronic spinal cord injured cats by activation of serotonin 5-HT1A receptors", Experimental Neurology, Vol. 199, PP427-437, 2006.

Xu Zhang, James R. Roppolo, William C. de Groat and Changfeng Tai, "Simulation analysis of conduction block in myelinated axons induced by high-frequency biphasic rectangular pulses", IEEE Transactions on Biomedical Engineering, Vol. 53, No.7, PP1433-1436, 2006.

Changfeng Tai, James R. Roppolo and William C. de Groat, "Spinal reflex control of micturition after spinal cord injury", Restorative Neurology and Neuroscience, Vol.24, No.2, PP69-78, 2006.

Changfeng Tai, Stanley E. Smerin, William C. de Groat and James R. Roppolo, "Pudendal-to-bladder reflex in chronic spinal cord injured cat", Experimental Neurology, Vol.197, PP225-234, 2006.

Francisco Schopfer, Ph.D.
Research Assistant Professor

Rudolph V, Rudolph TK, Schopfer FJ, Bonacci G, Lau D, Szoecs K, Klinke A, Meinertz T, Freeman BA, Baldus S. Bivalirudin decreases NO bioavailability by vascular immobilization of myeloperoxidase. J Pharmacol Exp Ther. 2008 Aug 13. [Epub ahead of print]

Ferreira AM, Ferrari M, Trostchansky A, Batthyány C, Souza JM, Alvarez MN, López GV, Baker PR, Schopfer FJ, O'Donnell V, Freeman BA, Rubbo H. Macrophage activation induces formation of the anti-inflammatory lipid cholesteryl-nitrolinoleate. Biochem J. 2008 Aug 1. [Epub ahead of print]

Li Y, Zhang J, Schopfer FJ, Martynowski D, Garcia-Barrio MT, Kovach A, Suino-Powell K, Baker PR, Freeman BA, Chen YE, Xu HE. Molecular recognition of nitrated fatty acids by PPAR gamma. Nat Struct Mol Biol. 2008 Aug;15(8):865-7. Epub 2008 Jul 6.

Ichikawa T, Zhang J, Chen K, Liu Y, Schopfer FJ, Baker PR, Freeman BA, Chen YE, Cui T. Nitroalkenes suppress lipopolysaccharide-induced signal transducer and activator of transcription signaling in macrophages: a critical role of mitogen-activated protein kinase phosphatase 1. Endocrinology. 2008 Aug;149(8):4086-94. Epub 2008 May 8.

Freeman BA, Baker PR, Schopfer FJ, Woodcock SR, Napolitano A, d'Ischia M.
Nitro-fatty acid formation and signaling. J Biol Chem. 2008 Jun 6;283(23):15515-9. Epub 2008 Feb 19. Review. No abstract available.

Baker, LMS, PRS Baker, F Golin-Bisello, FJ Schopfer, M Fink, SR Woodcock, BP Branchaud, R Radi, BA Freeman. Nitro-fatty acid reaction with glutathione and cysteine: kinetic analysis of thiol alkylation by a Michael addition reaction. J Biol Chem, 2007.

Batthyany, C., Schopfer, F. J., Baker, P. R., Duran, R., Baker, L. M., Huang, Y., Cervenansky, C., Braunchaud, B. P., and Freeman, B. A. Reversible post-translational modification of proteins by nitrated fatty acids in vivo J Biol Chem; 281: 20450-63; 2006.

Wright, M. M., Schopfer, F. J., Baker, P. R., Vidyasagar, V., Powell, P., Chumley, P., Iles, K. E., Freeman, B. A., and Agarwal, A. Fatty acid transduction of nitric oxide signaling: nitrolinoleic acid potently activates endothelial heme oxygenase 1 expression Proc Natl Acad Sci U S A 103: 4299-304; 2006.

Cui, T., Schopfer, F.J., Zhang, J., Chen, K., Ichikawa, T., Baker, P.R., Batthyany, C., Chacko, B.K., Feng, X., Patel, R.P., Agarwal, A., Freeman, B.A., Chen, Y.E. Nitrated fatty acids: Endogenous anti-inflammatory signaling mediators. J Biol Chem; 281: 35686-706; 2006.

Adrian Sculptoreanu, Ph.D.
Research Assistant Professor

Sculptoreanu A, Aura Kullmann F, de Groat WC. Neurokinin 2 receptor-mediated activation of protein kinase C modulates capsaicin responses in DRG neurons from adult rats. Eur J Neurosci. 2008 Jun;27(12):3171-81.

Yamane H, de Groat WC, Sculptoreanu A. Effects of ralfinamide, a Na+ channel blocker, on firing properties of nociceptive dorsal root ganglion neurons of adult rats. Exp Neurol. 2007 Nov;208(1):63-72. Epub 2007 Jul 19.

Srinivasan R, Huang S, Chaudhry S, Sculptoreanu A, Krisky D, Cascio M, Friedman PA, de Groat WC, Wolfe D, Glorioso JC. An HSV vector system for selection of ligand-gated ion channel modulators. Nat Methods. 2007 Sep;4(9):733-9. Epub 2007 Aug 5.

Dinara Shakiryanova, Ph.D.
Research Instructor

Shakiryanova D, Levitan ES. Prolonged presynaptic posttetanic cyclic GMP signaling in Drosophila motoneurons. Proc Natl Acad Sci U S A. 2008 Sep 9;105(36):13610-3. Epub 2008 Sep 2.

Wong MY, Shakiryanova D, Levitan ES. Presynaptic Ryanodine Receptor-CamKII Signaling is Required for Activity-dependent Capture of Transiting Vesicles. J Mol Neurosci. 2008 Jul 1. [Epub ahead of print]

Shakiryanova D, Klose MK, Zhou Y, Gu T, Deitcher DL, Atwood HL, Hewes RS, Levitan ES. Presynaptic ryanodine receptor-activated calmodulin kinase II increases vesicle mobility and potentiates neuropeptide release. J Neurosci. 2007 Jul 18;27(29):7799-806.

Levitan ES, Lanni F, Shakiryanova D. In vivo imaging of vesicle motion and release at the Drosophila neuromuscular junction. Nat Protoc. 2007;2(5):1117-25.

Shakiryanova, D, Klose, MK, Zhou, Y, Gu, T, Deitcher, DL, Atwood, HL, Hewes, RS, Levitan, ES. Presynaptic Ryanodine Receptor-activated Calmodulin Kinase II Increases Vesicle Mobility and Potentiates Neuropeptide Release. (2007) Journal of Neuroscience.

Shakiryanova D,Tully A, Levitan ES. Activity-dependent synaptic capture of transiting peptidergic vesicles. (2006) Nature Neuroscience 9(7), 896-900.

Sturman DA, Shakiryanova D, Hewes RS, Deitcher DL, Levitan ES. Nearly neutral secretory vesicles in Drosophila nerve terminals. (2006) Biophysical Journal 90(6), L45-L47.

Elizabeth Sharlow, Ph.D.
Research Instructor

Sharlow ER, Leimgruber S, Yellow-Duke A, Barrett R, Wang QJ, Lazo JS. Development, validation and implementation of immobilized metal affinity for phosphochemicals (IMAP)-based high-throughput screening assays for low-molecular-weight compound libraries. Nat Protoc. 2008;3(8):1350-63.

Shah PP, Myers MC, Beavers MP, Purvis JE, Jing H, Grieser HJ, Sharlow ER, Napper AD, Huryn DM, Cooperman BS, Smith AB 3rd, Diamond SL. Kinetic characterization and molecular docking of a novel, potent, and selective slow-binding inhibitor of human cathepsin L. Mol Pharmacol. 2008 Jul;74(1):34-41. Epub 2008 Apr 10.

Ramanathan RK, Kirkpatrick DL, Egorin MJ, Friedland D, Belani CP, Green SB, Chow HH S, Cordova CA, Stratton SP, Sharlow ER, Baker A, and T Dragovich. 2007. A Phase I, Pharmacokinetic and Pharmacodynamic Study of PX-12, a Novel Inhibitor of Thioredoxin-1, in Patients with Advanced Solid Tumors. Clinical Cancer Research 13: 2109 – 2014.

Jill Siegfried, Ph.D.
Professor

Palma MD, Domchek SM, Stopfer J, Erlichman J, Siegfried JD, Tigges-Cardwell J, Mason BA, Rebbeck TR, Nathanson KL. The relative contribution of point mutations and genomic rearrangements in BRCA1 and BRCA2 in high-risk breast cancer families. Cancer Res. 2008 Sep 1;68(17):7006-14. Epub 2008 Aug 14.

Traynor AM, Schiller JH, Stabile LP, Kolesar JM, Eickhoff JC, Dacic S, Hoang T, Dubey S, Marcotte SM, Siegfried JM. Pilot study of gefitinib and fulvestrant in the treatment of post-menopausal women with advanced non-small cell lung cancer. Lung Cancer. 2008 Aug 11. [Epub ahead of print]

Stabile LP, Rothstein ME, Keohavong P, Jin J, Yin J, Land SR, Dacic S, Luong TM, Kim KJ, Dulak AM, Siegfried JM. Therapeutic targeting of human hepatocyte growth factor with a single neutralizing monoclonal antibody reduces lung tumorigenesis. Mol Cancer Ther. 2008 Jul;7(7):1913-22.

Wilson DO, Weissfeld JL, Fuhrman CR, Fisher SN, Balogh P, Landreneau RJ, Luketich JD, Siegfried JM. The Pittsburgh Lung Screening Study (PLuSS): Outcomes within 3 years of a first CT Scan. Am J Respir Crit Care Med. 2008 Jul 17. [Epub ahead of print]

Koppikar P, Choi SH, Egloff AM, Cai Q, Suzuki S, Freilino M, Nozawa H, Thomas SM, Gooding WE, Siegfried JM, Grandis JR. Combined inhibition of c-Src and epidermal growth factor receptor abrogates growth and invasion of head and neck squamous cell carcinoma. Clin Cancer Res. 2008 Jul 1;14(13):4284-91.

Wilson DO, Weissfeld JL, Balkan A, Schragin JG, Fuhrman CR, Fisher SN, Wilson J, Leader JK, Siegfried J, Shapiro SD, Sciurba FC. Association of Radiographic Emphysema and Airflow Obstruction with Lung Cancer. Am J Respir Crit Care Med. 2008 Jun 19. [Epub ahead of print]

Seethala RR, Gooding WE, Handler PN, Collins B, Zhang Q, Siegfried JM, Grandis JR.
Immunohistochemical analysis of phosphotyrosine signal transducer and activator of transcription 3 and epidermal growth factor receptor autocrine signaling pathways in head and neck cancers and metastatic lymph nodes. Clin Cancer Res. 2008 Mar 1;14(5):1303-9. Erratum in: Clin Cancer Res. 2008 Apr 1;14(7):2247.

Yue W, Sun Q, Dacic S, Landreneau RJ, Siegfried JM, Yu J, Zhang L. Downregulation of Dkk3 activates beta-catenin/TCF-4 signaling in lung cancer. Carcinogenesis. 2008 Jan;29(1):84-92. Epub 2007 Nov 28.

Zhang, W, Weissfeld, JL, Romkes, J, Land, SR, Grandis, JR, Siegfried, JM.. Association of the EGFR Intron 1 CA Repeat Length with Lung Cancer Risk. Molecular Carcinogenesis, 46(5): 372-380, 2007.

Myerberg, M.M., Latoche, J.D., McKenna, E.E., Stabile, L.P., Siegfried, J.M., Feghali-Bostwick, C.A., Pilewski, J.M. HGF and other fibroblast secretions modulate the phenotype of human bronchial epithelial cells. Am. J. Physiol. Lung Cell Mol Physiol, 292: L1352-L1360, 2007.

Liu, X, Carlisle, DL, Swick, MC, Gaither Davis, A, Grandis, JR, Siegfried, JM. Gastrin-releasing peptide activates Akt through the epidermal growth factor receptor pathway and abrogates the effects of gefitinib. Experimental Cell Research 313:1361-1372, 2007.

Zhang, Q., Bhola, N.E., Lui, V.W.Y., Siwak, D.R., Thomas, S.M., Gubish, C.T., Siegfried, J.M., Mills, G.B., Shin, D., Grandis, J.R. Antitumor mechanisms of combined gastrin-releasing peptide receptor and epidermal growth factor receptor targeting in head and neck cancer. Mol Cancer Ther 6(4): 1414-1424, 2007.

Liu, Y., Gao, W., Siegfried, J.M., Weissfeld, J.L., Luketich, J.D., Keohavong, P. Promoter Methylation of RASSF1A and DAPK and mutations of K-ras, p53, and EGFR in lung tumors from smokers and never-smokers. BMC Cancer 3: 7-74, 2007.

Yidiz, P.B., Shyr, Y., Rahman, J.S.M., Wardwell, N.R., Zimmerman, L.J., Shakhtour, B., Gray, W. H., Chen, S., Li, M., Roder, H., Liebler, D.C., Bigbee, W.L., Siegfried, J.M., Weissfeld, J.L., Gonzalez, A.L., Ninan, M., Johnson, D.H., Carbone, D.P., Caprioli, R. M., Massion, P.P. Diagnostic accuracy of MALDI mass spectrometric analysis of unfractionated serum in lung cancer. In press, Journal of Thoracic Oncology.

Yue, W., Dacic, S., Sun, Q., Landreneau, L., Guo, M., Zhou, W., Siegfried, J.M., Yu, J., Zhang, L. Frequent inactivation of RAMP2, EFEMP1 and Dutt1 in lung cancer by promoter hypermethylation. In Press, Clinical Cancer Research.

Gao, W.M., Romkes, M., Siegfried, J.M., Luketich, J.D., Keohavong, P. Polymorphisms in DNA repair genes XPD and XRCC1 and p53 mutations in lung carcinomas of never-smokers. Molecular Carcinogenesis, 45: 828-832, 2006.

Stabile, L.P., Lyker, J.S., Land, S.R., Dacic, Sanja, Zamboni, B.A., Siegfried, J.M. Transgenic mice overexpressing hepatocyte growth factor in the airways show increased susceptibility to lung cancer. Carcinogenesis 27: 1547-55, 2006.

Zhang, Q., Thomas, S.M., Lui, V.W.Y., Xi, S., Siegfried, J.M., Fan, H., Smithgall, T., Mills, G., Grandis, J.R. Phosphorylation of TNF-converting enzyme by Gastrin-releasing peptide induces amphiregulin release and EGFR activation. Proc. National Acad. Science. 103: 6901-6906, 2006.

Liu, Y., Lan, Q., Siegfried, J.M., Luketich, J.D., Keohavong, P. Aberrant Promoter Methylation of p16 and MGMT Genes in Lung Tumors from Smoking and Never-Smoking Lung Cancer Patients. Neoplasia 8: 46-51, 2006.

Carlisle, D., Xuwan, L., Hopkins, T.M., Swick, MC., Dhir, R., Siegfried, J.M. Nicotine Activates Cell Signaling Pathways through Muscle-type and Neuronal nicotinic Acetylcholine Receptors in Non-small Cell Lung Cancer Cells. In Press, Pulmonary Pharmacology and Therapeutics, 2006.

Kelloff GJ, Lippman SM, Dannenberg AJ, Sigman CC, Pearce HL, Reid BJ, Szabo E, Jordan VC, Spitz MR, Mills GB, Papadimitrakopoulou VA, Lotan R, Aggarwal BB, Bresalier RS, Kim J, Arun B, Lu KH, Thomas ME, Rhodes HE, Brewer MA, Follen M, Shin DM, Parnes HL, Siegfried JM, Evans AA, Blot WJ, Chow WH, Blount PL, Maley CC, Want KK, Lam S, Lee JJ, Dubinett SM, Engstrom PF, Meyskens FL Jr., O'Shaughnessy J, Hawk ET, Levin B, Nelson WG, Hong WK. AACR Task Force on Cancer Prevention. Progress in Chemoprevention Drug Development: the Promise of Molecular Biomarkers for Prevention of Intraepithelial Neoplasia and Cancer—a Plan to Move Forward. Clinical Cancer Research 12: 3661-97, 2006.

Zhang, W, Stabile, LP, Keohavong, P, Romkes, M, Grandis, JR, Traynor, AM, Siegfried, JM. Mutation and Polymorphism in the EGFR-TK Domain Associated with Lung Cancer. Journal of Thoracic Oncology 7:635-647, 2006.

Thomas, SM, Bhola, NE, Zhang, Q, Contrucci, SC, Wentzel, AL, Freilino, ML, Gooding, WE, Siegfried, JM, Chan DC, Grandis, JR. Cross-talk between G protein-coupled receptor and epidermal growth factor receptor signaling pathways contributes to growth and invasion of head and neck squamous cell carcinoma. Cancer Research, 66(24): 11831-9, 2006.

Shivendra Singh, Ph.D.
Professor

Xiao D, Powolny AA, Singh SV. Benzyl isothiocyanate targets mitochondrial respiratory chain to trigger ros-dependent apoptosis in human breast cancer cells. J Biol Chem. 2008 Sep 3. [Epub ahead of print]

Antosiewicz J, Ziolkowski W, Kar S, Powolny AA, Singh SV. Role of Reactive Oxygen Intermediates in Cellular Responses to Dietary Cancer Chemopreventive Agents.
Planta Med. 2008 Jul 31. [Epub ahead of print]

Powolny AA, Singh SV. Multitargeted prevention and therapy of cancer by diallyl trisulfide and related Allium vegetable-derived organosulfur compounds. Cancer Lett. 2008 Jun 23. [Epub ahead of print]

Chen J, Deng F, Singh SV, Wang QJ. Protein kinase D3 (PKD3) contributes to prostate cancer cell growth and survival through a PKCepsilon/PKD3 pathway downstream of Akt and ERK 1/2. Cancer Res. 2008 May 15;68(10):3844-53.

Hahm ER, Arlotti JA, Marynowski SW, Singh SV. Honokiol, a constituent of oriental medicinal herb magnolia officinalis, inhibits growth of PC-3 xenografts in vivo in association with apoptosis induction. Clin Cancer Res. 2008 Feb 15;14(4):1248-57.

Powolny AA, Singh SV. Plumbagin-induced Apoptosis in Human Prostate Cancer Cells is Associated with Modulation of Cellular Redox Status and Generation of Reactive Oxygen Species. Pharm Res. 2008 Sep;25(9):2171-80. Epub 2008 Jan 23.

Xiao D, Singh SV. z-Guggulsterone, a constituent of Ayurvedic medicinal plant Commiphora mukul, inhibits angiogenesis in vitro and in vivo. Mol Cancer Ther. 2008 Jan;7(1):171-80.

Stan SD, Kar S, Stoner GD, Singh SV. Bioactive food components and cancer risk reduction. J Cell Biochem. 2008 May 1;104(1):339-56. Review.
PMID: 18092339 [PubMed - indexed for MEDLINE]

Xiao, H., and Singh, S.V.: p53 regulates cellular responses to environmental carcinogen benzo[a]pyrene-7,8-diol-9,10-epoxide in human lung cancer cells. Cell Cycle, In Press, 2007.

Singh, S.V., Choi, S., Zeng, Y., Hahm, E., and Xiao, D.: Guggulsterone-induced apoptosis in human prostate cancer cells is caused by reactive oxygen intermediate-dependent activation of c-Jun NH2-terminal kinase. Cancer Res., In Press, 2007.

Xiao, D., and Singh, S.V.: Phenethyl isothiocyanate inhibits angiogenesis in vitro and ex vivo. Cancer Res., 67: 2239-2246, 2007.

Herman-Antosiewicz, A., Stan S.D., Hahm, E.R., Xiao, D., and Singh, S.V.: Activation of a novel ataxia-telangiectasia mutated and Rad3 related/checkpoint kinase 1-dependent prometaphase checkpoint in cancer cell by diallyl trisulfide, a promising cancer chemopreventive constituent of processed garlic. Mol. Cancer Ther., 6: 1249-1261, 2007.

Hu, J., Straub, J., Xiao, D., Singh, S.V., Yang, H.S., Sonenberg, N., and Vatsyayan, V.: Phenethyl isothiocyanate, a cancer chemopreventive constituent of cruciferous vegetables, inhibits cap-dependent translation by regulating level and phosphorylation of 4E-BP1. Cancer Res., 67: 3569-3573, 2007.

Kim, Y.A., Xiao, D., Xiao, H., Powolny, A.A., Lew, K.L., Reilly, M.L., Zeng, Y., Wang, Z., and Singh, S.V.: Mitochondria-mediated apoptosis by diallyl trisulfide in human prostate cancer cells is associated with generation of reactive oxygen species and regulated by Bax/Bak. Mol. Cancer Ther., 6: 1599-1509, 2007.

Herman-Antosiewicz, A., Xiao, H., Lew, K.L., and Singh, S.V.: Induction of p21 protein protects against sulforaphane-induced mitotic arrest in LNCaP human prostate cancer cell line. Mol. Cancer Ther., 6: 1673-1681, 2007.

Xiao, D., and Singh, S.V.: Diallyl trisulfide, a constituent of processed garlic, inactivates Akt to trigger mitochondrial translocation of BAD and caspase-mediated apoptosis in human prostate cancer cells. Carcinogenesis, 27: 533-540, 2006.

Gong, H., Singh, S.V., Singh, S.P., Mu, Y., Lee, J.H., Saini, S.P.S., Toma, D., Ren, S., Kagan, V.E., Day, B.W., Zimniak, P., and Xie, W.: Orphan nuclear receptor PXR sensitizes oxidative stress responses in transgenic mice and cancerous cells. Mol. Endocrinol., 20: 279-290, 2006.

Antosiewicz, J., Herman-Antosiewicz, A., Marynowski, S.W., and Singh, S.V.: c-Jun NH_2-terminal kinase signaling axis regulates diallyl trisulfide-induced generation of reactive oxygen species and cell cycle arrest in human prostate cancer cells. Cancer Res., 66: 5379-5386, 2006.

Herman-Antosiewicz, A., Johnson, D.E., and Singh, S.V.: Sulforaphane causes autophagy to inhibit release of cytochrome *c* and apoptosis in human prostate cancer cells. Cancer Res., 66: 5828-5835, 2006.

Saavedra, J.E., Srinivasan, A., Buzard, G.S., Davies, K.M., Waterhouse, D.J., Inami, K., Wilde, T.C., Citro, M.L., Cuellar, M., Deschamps, J.R., Parrish, D., Shami, P.J., Findlay, V.J., Townsend, D.M., Tew, K.D., Singh, S., Jia, L., Ji, X., and Keefer, L.K.: PABA/NO as an anticancer lead: analogue synthesis, structure revision, solution chemistry, reactivity toward glutathione, and in vitro activity. J. Med. Chem., 49: 1157-1164, 2006.

Xiao, D., Li, M., Herman-Antosiewicz, A., Antosiewicz, J., Xiao, H., Lew, K.L., Zeng, Y., Marynowski, S.W., and Singh, S.V.: Diallyl trisulfide inhibits angiogenic features of human umbilical vein endothelial cells by causing Akt inactivation and down-regulation of VEGF and VEGF-R2. Nut. Cancer, 55: 94-107, 2006.

Xiao, D., Lew, K.L., Zeng, Y., Xiao, H., Marynowski, S.W., Dhir, R., and Singh, S.V.: Phenethyl isothiocyanate-induced apoptosis in PC-3 human prostate cancer cells is mediated by reactive oxygen species-dependent disruption of the mitochondrial membrane potential. Carcinogenesis, 27: 2223-2234, 2006.

Xiao, D., Lew, K.L., Kim, Y., Zeng, Y., Hahm, E., Dhir, R., and Singh, S.V.: Diallyl trisulfide suppresses growth of PC-3 human prostate cancer xenograft *in vivo* in association with induction of multidomain proapoptotic proteins Bax and Bak. Clin. Cancer Res., 15: 6836-6843, 2006.

Xiao, D., Vogel, V., and Singh, S.V.: Benzyl isothiocyanate-induced apoptosis in human breast cancer cells is initiated by reactive oxygen species and regulated by Bax and Bak. Mol. Cancer Ther., 5: 2931-2945, 2006.

Choi, S., Lew, K.L., Xiao, H., Herman-Antosiewicz, A., Xiao, D., Brown, C.K., and Singh, S.V.: D,L-Sulforaphane-induced cell death in human prostate cancer cells is regulated by inhibitor of apoptosis family proteins and Apaf-1. Carcinogenesis, In Press, 2006.

Robert Sobol, Ph.D.
Assistant Professor

Allen D, Herbert DC, McMahan CA, Rotrekl V, Sobol RW, Wilson SH, Walter CA.
Mutagenesis Is Elevated in Male Germ Cells Obtained from DNA Polymerase-beta Heterozygous Mice. Biol Reprod. 2008 Jul 23. [Epub ahead of print]

Kronenberg G, Harms C, Sobol RW, Cardozo-Pelaez F, Linhart H, Winter B, Balkaya M, Gertz K, Gay SB, Cox D, Eckart S, Ahmadi M, Juckel G, Kempermann G, Hellweg R, Sohr R, Hörtnagl H, Wilson SH, Jaenisch R, Endres M. Folate deficiency induces neurodegeneration and brain dysfunction in mice lacking uracil DNA glycosylase. J Neurosci. 2008 Jul 9;28(28):7219-30.

Trivedi RN, Wang XH, Jelezcova E, Goellner EM, Tang JB, Sobol RW. Human methyl purine DNA glycosylase and DNA polymerase beta expression collectively predict sensitivity to temozolomide. Mol Pharmacol. 2008 Aug;74(2):505-16. Epub 2008 May 13.

Sobol RW. CHIPping away at base excision repair. Mol Cell. 2008 Feb 29;29(4):413-5.

Kronenberg, G, Hamrs, C., Sobol, R.W., Cardozo-Pelaez, F., Winter, B., Balkaya, M., Gertz, K., Gay, S.B., Cox, D. Linhard, H., Eckart, S. Ahmadi, M., Juckel, G., Kempermann, G., Hellweg, R., Sobol R.W., "DNA polymerase ß null mouse embryonic fibroblasts harbor a homozygous null mutation in DNA polymerase iota" (2007) DNA Repair 6, 3-7.

Chiosea, S., Jelezcova, E., Chandran, U., Mantha, G., Sobol, R.W. and Dacic, S. "Dicer, A Component of the MicroRNA Machinery, marks precursor lesions in Lung Adenocarcinoma" (2007) Cancer Research, (In Press).

Pollack, I.F, Hamilton, R.L., Sobol, R.W., Burnham, J., Yates, A.J., Holmes, E.J., Zhou, T. and Finlay, J.L. "MGMT Expression Strongly Correlates with Outcome in Childhood Malignant Gliomas: Results from the CCG-945 Cohort" (2006) Journal of Clinical Oncology; 24, 3431;3437.

Chiosea, S., Jelezcova, E., Chandran, U., Acquafondata, M., McHale, T., Sobol, R.W. and Dhir, R. "Up-regulation of Dicer, A Component of the MicroRNA Machinery, in Prostate Adenocarcinoma" (2006) American Journal of Pathology; 169, 1812-1820.

Harish Srinivas, Ph.D.
Research Instructor

Xia D, Srinivas H, Ahn YH, Sethi G, Sheng X, Yung WK, Xia Q, Chiao PJ, Kim H, Brown PH, Wistuba II, Aggarwal B, Kurie JM. Mitogen-activated protein kinase kinase-4 promotes cell survival by decreasing PTEN expression through an NFkB-dependent pathway. J Biol Chem. 282(6):3507-3519, 2007.

Khatlani TS, Wislez M, Sun M, Srinivas H, Iwanaga K, Ma L, Hanna AE, Liu D, Girard L, Kim YH, Pollack JR, Minna JD, Wistuba II, Kurie JM. c-Jun N-terminal kinase is activated in non-small-cell lung cancer and neoplastic transformation in human bronchial epithelial cells. Oncogene. 2006 2007 Apr 19;26(18):2658-66.

Srinivas H, Xia D, Moore NL, Uray IP, Kim H, Ma L, Weigel NL Brown PH, and Kurie JM. Akt phosphorylates and suppresses the transactivation of retinoic acid receptor alpha. Biochem J. 395(3): 653-662, 2006.

Laura Stabile, Ph.D.
Research Assistant Professor

Traynor AM, Schiller JH, Stabile LP, Kolesar JM, Eickhoff JC, Dacic S, Hoang T, Dubey S, Marcotte SM, Siegfried JM. Pilot study of gefitinib and fulvestrant in the treatment of post-menopausal women with advanced non-small cell lung cancer. Lung Cancer. 2008 Aug 11. [Epub ahead of print]

Stabile LP, Rothstein ME, Keohavong P, Jin J, Yin J, Land SR, Dacic S, Luong TM, Kim KJ, Dulak AM, Siegfried JM. Therapeutic targeting of human hepatocyte growth factor with a single neutralizing monoclonal antibody reduces lung tumorigenesis. Mol Cancer Ther. 2008 Jul;7(7):1913-22.

Siegfried JM, Gubish CT, Rothstein ME, Queiroz De Oliveira PE, Stabile LP. Signaling pathways involved in cyclooxygenase-2 induction by hepatocyte growth factor in non-small cell lung cancer. Mol Pharmacol. 2007 Jun 5; [Epub ahead of print

Myerburg MM, Latoche JD, McKenna EE, Stabile LP, Siegfried JS, Feghali-Bostwick CA, Pilewski JM. Hepatocyte growth factor and other fibroblast secretions modulate the phenotype of human bronchial epithelial cells. Am J Physiol Lung Cell Mol Physiol. 2007 Jun;292(6):L1352-60.

Myerburg MM, Latoche JD, McKenna EE, Stabile LP, Siegfried JM, Feghali-Bostwick CA, Pilewski JM. HGF and other fibroblast secretions modulate the phenotype of human bronchial epithelial cells. In Press. Am J Physiol Lung. Jan 2007.

Zhang W, Stabile LP, Keohavong P, Romkes M, Grandis JR, Traynor AM, Siegfried JM. Mutation and polymorphism in the EGFR-TK domain associated with lung cancer. Journal of Thoracic Oncology. 2006. Sept; 1(7), 635- 647.

Stabile LP, Lyker JS, Land SR, Dacic S, Zamboni BA, Siegfried JM. Transgenic mice overexpressing the hepatocyte growth factor gene in the airways show increased susceptibility to lung cancer. Carcinogenesis. 2006 Aug; 27(8): 1547-1555.

Jean-Pierre Vilardaga, Ph.D.
Assistant Professor

Lohse MJ, Nikolaev VO, Hein P, Hoffmann C, Vilardaga JP, Bünemann M. Optical techniques to analyze real-time activation and signaling of G-protein-coupled receptors.
Trends Pharmacol Sci. 2008 Mar;29(3):159-65. Epub 2008 Feb 11. Review.

Vilardaga JP, Nikolaev VO, Lorenz K, Ferrandon S, Zhuang Z, Lohse MJ. Conformational cross-talk between alpha2A-adrenergic and mu-opioid receptors controls cell signaling. Nat Chem Biol. 2008 Feb;4(2):126-31. Epub 2008 Jan 13.

Lohse MJ, Bünemann M, Hoffmann C, Vilardaga JP, Nikolaev VO. Monitoring receptor signaling by intramolecular FRET. Curr Opin Pharmacol. 2007 Oct;7(5):547-53. Epub 2007 Oct 4. Review.

Dean T, Vilardaga JP, Potts JT Jr, Gardella TJ.Altered selectivity of parathyroid hormone (PTH) and PTH-related protein (PTHrP) for distinct conformations of the PTH/PTHrP receptor. Mol Endocrinol. 2008 Jan;22(1):156-66. Epub 2007 Sep 13.

Lohse MJ, Hoffmann C, Nikolaev VO, Vilardaga JP, Bünemann M. Kinetic analysis of G protein-coupled receptor signaling using fluorescence resonance energy transfer in living cells. Adv Protein Chem. 2007;74:167-88. Review.

Rochais F, Vilardaga JP, Nikolaev VO, Bünemann M, Lohse MJ, Engelhardt S. Real-time optical recording of beta1-adrenergic receptor activation reveals supersensitivity of the Arg389 variant to carvedilol. J Clin Invest. 2007 Jan;117(1):229-35.

Vilardaga JP. Switching modes for G protein-coupled receptor activation. Nat Chem Biol. 2006 Aug;2(8):395-6. No abstract available.

Nikolaev VO, Hoffmann C, Bünemann M, Lohse MJ, Vilardaga JP. Molecular basis of partial agonism at the neurotransmitter alpha2A-adrenergic receptor and Gi-protein heterotrimer. J Biol Chem. 2006 Aug 25;281(34):24506-11. Epub 2006 Jun 20.
PMID: 16787921 [PubMed - indexed for MEDLINE]

Andreas Vogt, Ph.D.
Research Assistant Professor

Lazo, J.S., Nunes, R., Skoko, J.J., Pierre E. Queiroz de Oliveira, P.E., Vogt, A., and Wipf, P. Novel Benzofuran Inhibitors of Human Mitogen-activated Protein Kinase Phosphatase-1. Bioorganic and Medicinal Chemistry 14, (16), 5643-5650 (2006)

Wipf, P., Graham, T.H., Vogt, A., Sikorski, R.P., Ducruet, A.P., and Lazo, J.S. (2006) Cellular analysis of Disorazole C1 and structure-activity relationship of analogs of the natural product. Chemical Biology & Drug Design 67, 66-73

Ohkanda,J., Strickland,C.L., Blaskovich,M.A., Carrico,D., Lockman,J.W., Vogt,A., Bucher,C.J., Sun,J., Qian,Y., Knowles,D., Pusateri,E.E., Sebti,S.M., and Hamilton,A.D. (2006). Structure-based design of imidazole-containing peptidomimetic inhibitors of protein farnesyltransferase. Org. Biomol. Chem. 4, 482-492.

Daniela Volonte, Ph.D.
Research Instructor

Volonte D, McTiernan CF, Drab M, Kasper M, Galbiati F. Caveolin-1 and caveolin-3 form heterooligomeric complexes in atrial cardiac myocytes that are required for doxorubicin-induced apoptosis. Am J Physiol Heart Circ Physiol. 2008 Jan;294(1):H392-401. Epub 2007 Nov 2.

Fecchi, Katia*, Volonte, Daniela*, Schmeck, Kevin, and Galbiati, Ferruccio. 2006. Spatial and temporal regulation of glut-4 translocation by flotillin-1 and caveolin-3 in skeletal muscle cells. FASEB J., Apr;20(6):705-7.

Arvind Dasari*, Janine N. Bartholomew*, Daniela Volonte, and Ferruccio Galbiati. 2006. Oxidative stress induces premature senescence by stimulating caveolin-1 gene transcription through p38 MAPK/Sp1-mediated activation of two GC-rich promoter elements. Cancer Research; 2006 Nov 15;66(22):10805-14.

Q. Jane Wang, Ph.D.
Assistant Professor

Sharlow ER, Leimgruber S, Yellow-Duke A, Barrett R, Wang QJ, Lazo JS. Development, validation and implementation of immobilized metal affinity for phosphochemicals (IMAP)-based high-throughput screening assays for low-molecular-weight compound libraries. Nat Protoc. 2008;3(8):1350-63.

Chen J, Deng F, Singh SV, Wang QJ. Protein kinase D3 (PKD3) contributes to prostate cancer cell growth and survival through a PKCepsilon/PKD3 pathway downstream of Akt and ERK 1/2. Cancer Res. 2008 May 15;68(10):3844-53.

Bai X, Ma D, Liu A, Shen X, Wang QJ, Liu Y, Jiang Y. Rheb activates mTOR by antagonizing its endogenous inhibitor, FKBP38. Science. 2007 Nov 9;318(5852):977-80.

Lu, G., Chen, J., Espinoza, L.A., Garfield, S., Toshiyuki, S., Akiko, H., Huppler, A., and Wang, Q.J. Protein kinase D 3 is localized in vesicular structures and interacts with vesicle-associated membrane protein, Cell Signal, 2007 Apr;19(4):867-79.

Wang, Q.J. PKD at the crossroads of DAG and PKC signaling. Trends Pharmacol. Sci., 27:317-23, 2006.

John Wittschieben, Ph.D.
Research Instructor

Gan GN, Wittschieben JP, Wittschieben BØ, Wood RD. DNA polymerase zeta (pol zeta) in higher eukaryotes. Cell Res. 2008 Jan;18(1):174-83. Review.

Wittschieben J., Reshmi S.C., Gollin S.M., and Wood R.D. Loss of DNA polymerase zeta causes chromosomal instability in mammalian cells. Cancer Res. 2006;66:134-142.

Dong Xiao, M.D.
Research Instructor

Xiao D, Singh SV. Guggulsterone, a constituent of Indian Ayurvedic medicinal plant Commiphora mukul, inhibits angiogenesis in vitro and in vivo. Mol.Cancer Ther. 2008; 7: 171-80.

Singh SV, Choi S, Zeng Y, Hahm ER, Xiao D. Guggulsterone-induced apoptosis in human prostate cancer cells is caused by reactive oxygen intermediate-dependent activation of c-Jun NH2-terminal kinase. Cancer Res. 2007; 67:7439-49.

Kim YA, Xiao D, Xiao H, Powolny AA, Lew KL, Reilly M, Zeng Y, Wang Z, Singh SV. Critical role of Bax/Bak and Reactive oxygen species in mitochondria-mediate apoptosis by dially trisulfide, a highly promising cancer chemopreventive constituent of processed garlic. Mol.Cancer Ther. 2007; 6:1599-609.

Herman-Antosiewicz A, Stan SD, Hahm ER, Xiao D, Singh SV. Activation of a novel ataxia-telangiectasia mutated and Rad3 related/checkpoint kinase 1-depedent prometaphase checkpoint in cance cells bt diallyl trisulfide, a promising cancer chemopreventive constituent of processed garlic. Mol.Cancer Ther. 2007; 6:1249-61.

Hu J, Straub J, Xiao D, et al. Phenethyl isothiocyanate, a cancer chemopreventive constituent of cruciferous vegetables, inhibits Cap-dependent translation by regulating the level and phosphorylation of 4E-BP1. Cancer Res. 2007; 67: 3569-73.

Xiao D, Singh SV. Phenethyl isothiocyanate Inhibits Angiogenesis In Vitro and Ex Vivo. Cancer Res. 2007; 67:2239-46.

Choi S, Lew KL, Xiao H, Herman-Antisiewicz A, Xiao D, Singh SV. D,L-Sulforaphane-induced cell death in human prostate cancer cells is regulated by inhibitor of apoptosis family proteins and Apaf-1. Carcinogenesis. 2007; 28:151-62.

Xiao D, Dhir R, Singh SV. Benzyl isothiocyanate-induced cell death in MDA-MB-231 and MCF-7 human breast cancer cells is initiated by reactive oxygen species and regulated by Bax and Bak. Mol.Cancer Ther. 2006; 5:2931-45.

Xiao D, Lew KL, Kim YA, Zeng Y, Hahm ER, Dhir R, Singh SV. Diallyl Trisulfide Suppresses Growth of PC-3 Human Prostate Cancer Xenograft In Vivo in Association with Induction of Multi-domain Pro-apoptotic Proteins Bax and Bak. Clin Cancer Res. 2006; 12: 6836-43.

Xiao D, Lew KL, Zeng Y, Xiao H, Marynowski SW, Dhir R, Singh SV. Phenethyl isothiocyanate-induced apoptosis in PC-3 human prostate cancer cells is mediated by reactive oxygen species-dependent disruption of the mitochondrial membrane potential. Carcinogenesis. 2006: 27: 2223-34.

Xiao D, Li MF, Herman-Antosiewicz A, Antosiewicz J, Xiao H, Lew KL, Zeng Y, Marynowski SW, Singh SV. Diallyl trisulfide inhibits angiogenic features of human umbilical vein endothelial cells by causing Akt inactivation and down-regulation of VEGF and VEGF-R2. Nutrition and Cancer. 2006; 55:94-107.

Xiao D, Singh S.V. Diallyl trisulfide induced apoptosis in Human Prostate Cancer Cells is mediated by inactivation of Akt. Carcinogenesis. 2006; 27: 533-40.

Jack Yalowich, Ph.D.
Associate Professor

Hasinoff BB, Liang H, Wu X, Guziec LJ, Guziec FS Jr, Marshall K, Yalowich JC.
The structure-based design, synthesis and biological evaluation of DNA-binding bisintercalating bisanthrapyrazole anticancer compounds. Bioorg Med Chem. 2008 Apr 1;16(7):3959-68. Epub 2008 Jan 26.

Wu X, Liang H, O'Hara KA, Yalowich JC, Hasinoff BB. Thiol-modulated mechanisms of the cytotoxicity of thimerosal and inhibition of DNA topoisomerase II alpha.
Chem Res Toxicol. 2008 Feb;21(2):483-93. Epub 2008 Jan 16.

Liang H, Wu X, Yalowich JC, Hasinoff BB. A three-dimensional quantitative structure-activity analysis of a new class of bisphenol topoisomerase IIalpha inhibitors.
Mol Pharmacol. 2008 Mar;73(3):686-96. Epub 2007 Nov 28.

Kamath, R., Jiang, Z., Sun, G., Yalowich, J.C., and Baskaran, R. c-Abl kinase regulates curcumin-induced cell death through activation of JNK. Mol. Pharmacol., 71(1): 61-72, 2007.
Zheng, K-C., Yalowich, J.C., Kagan, V.E., Keohavong, P. Mutagenic activity of succinyl acetone at the HPRT locus of HL-60 cells. Cell Biol Toxicol., 22(5):361-70, 2006.

Fan, Y., Schreiber, E.M., Giorgianni, A., Yalowich, J.C., and Day, B.W. Myeloperoxidase-catalyzed metabolism of etoposide to quinone and glutathione adduct forms in HL60 cells. Chemical Research in Toxicology; 19(7): 937-943, 2006.

Tyurina, Y.Y., Kini, V.,Tyurin, V.A., Vlasova, I.I., Jiang, J., Kapralov, A.A., Belikova, N.A., Yalowich, J.C., Kurnikov, I.V., and Kagan, V.E. Mechanisms of cardiolipin oxidation by cytochrome c: relevance to pro- and anti-apoptotic functions of etoposide. Molecular Pharmacology, 70(2):706-17, 2006.

Hasinoff, B.B., Wu, X., Begleiter, A., Guziec, L.J., Guziec Jr., F., Giorgianni, A., Yang, S., Jiang, Y., and Yalowich, J.C. Structure-activity study of the interaction of bioreductive benzoquinone alkylating agents with DNA topoisomerase II. Cancer Chemother. Pharm., 57(2):221-33, 2006.

Hasinoff, B.B., Wu, X., Yalowich, J.C., Goodfellow, V., Laufer, and Dmitrienko, G.I. Kinamycins A and C, bacterial metabolites that contain an unusual diazo group, as potential new anticancer agents: antiproliferative and cell cycle effects. Anti-Cancer Drugs, 17(7):825-37, 2006.

Liang, H., Wu, X., Guziec, L.J., Guziec Jr., F.S., Larson, K.K., Lang, J., Yalowich, J.C., and Hasinoff, B.B. A Structure-based 3D-QSAR study of anthrapyrazole analogs of the anticancer agents losoxantrone and piroxantrone. J. Chem. Inf. Model., 46(4):1827-35, 2006.

Lin Zhang, Ph.D.
Associate Professor

Qiu, W., Carson-Walter, E.B., Liu, H., Epperly, M., Greenberger, J., Zambetti, G.P., Zhang, L.*, Yu, J.* (2008) PUMA regulates intestinal progenitor cell radiosensitivity and gastrointestinal syndrome. Cell Stem Cell (Accepted) *corresponding authors.

Lee, D.H., Kim, C., Zhang, L., and Lee, Y. J. (2008) Role of p53, PUMA, and Bax in wogonin-induced apoptosis in human cancer cells. Biochemical Pharmacology (In Press).

Luo, W., Liu, J., Li, J., Zhang, D., Liu, M., Addo, J.A., Patil, S., Zhang, L., Yu, J., Buolamwini, J.K., Chen, J. and Huang, C. (2008) Anti-cancer effects of JKA97 are associated with its induction of cell apoptosis via a Bax-dependent, and p53-independent pathway. Journal of Biological Chemistry (Epub ahead of print Jan. 23, 2008).

Chen, K., Tu, Y., Zhang, Y., Blair, H.C., Zhang, L., and Wu, C. (2008) PINCH-1 regulates the ERK-Bim pathway and contributes to apoptosis resistance in cancer cells. Journal of Biological Chemistry 283: 2508-2517.

Bank, A., Wang, P., Du, C.Y., Yu, J., and Zhang, L. SMAC mimetics sensitize NSAID-induced apoptosis by promoting caspase-3-mediated cytochrome c release. Cancer Research 68: 276-284.

Yue, W., Sun, Q.H., Dacic, S., Landreneau, R., Siegfried, J.M., Yu, J. and Zhang, L. (2008) Downregulation of Dkk3 activates □-catenin/TCF-4 signaling in lung cancer. Carcinogenesis 29: 84-92.

Yue, W., Dacic, S., Sun, Q.H., Landreneau, R., Guo, M.Z., Zhou, W., Siegfried, J.M., Yu, J. and Zhang, L. (2007) Frequent inactivation of RAMP2, EFEMP1 and Dutt1 in lung cancer by promoter hypermethylation. Clinical Cancer Research (In Press).

Yu, J., Wang, P., Ming, L.H., Wood, M. and Zhang, L. (2007) SMAC/Diablo mediates the proapoptotic function of PUMA by regulating PUMA-induced mitochondrial events. Oncogene 2007 Jun 21;26(29):4189-98.

Wu, B., Qiu, W., Wang, P., Yue, W., Yu, H., Cheng, T., Zambetti G.P., and Zhang, L.* and Yu, J.* (2006) p53-independent induction of PUMA mediates intestinal apoptosis induced by ischemia reperfusion. Gut May;56(5):645-54 (* corresponding authors).

Yu, J., Yue, W., Wu, B. and Zhang, L. (2006) PUMA enhances the apoptotic responses of lung cancer cells to chemotherapeutic agents and irradiation. Clinical Cancer Research 12: 2928-2936.

Ming, L.H, Wang, P., Bank, A., Yu, J., and Zhang, L. (2006) PUMA dissociates Bax from Bcl-XL to induce apoptosis in colon cancer cells. Journal of Biological Chemistry 281:16034-16042.

Wang, H.J., Qian, H.L., Yu, J., Zhang, XY, Zhang, L., Fu, M, Liang, X, Zhan, Q.M. and Chen, L. (2006) Administration of PUMA adenovirus increases the sensitivity of esophageal cancer cells to anticancer drugs. Cancer Biology & Therapy. 5:380-385.

Jiang, M., Wei, Q., Du, Q., Yu, J., Zhang, L. and Dong, Z. (2006) Regulation of PUMA by p53 in cisplatin-induced renal cell apoptosis. Oncogene 25:4056-4066.

Financial Plan

Executive Summary

I. Mission and Goals

The principal goal of the Department of Pharmacology and Chemical is the creation of an intellectual and physical environment in which teaching and research in Pharmacology are pursued as one common enterprise. The major responsibilities of the Department are to: (1) educate medical students and physicians in the rationale for drug selection; (2) train contemporary pharmacologists; (3) develop new knowledge in the biomedical sciences; and (4) provide information about existing and emerging drugs to members of the University of Pittsburgh Medical Center, the University of Pittsburgh and the general community.

The philosophical approach of the Department is guided by the view that the field of Pharmacology exhibits a unique combination of characteristics that distinguish it from other basic medical sciences. Pharmacology encompasses a broad range of interests extending from the abstract domain of the physical chemistry of ligand-receptor interactions to the therapeutic use of drugs in patients. Thus, Pharmacology has stronger clinical ties than most other basic science disciplines. In the current revised medical curriculum, the faculty inculcates both core pharmacological principles and places them in the context of specific organ systems and bodily functions. Collectively, we provide a key educational experience to both medical and graduate students. Our faculty members also maintain vigorous research programs that are interactive and interdisciplinary. We have bridged with the Department of Chemistry in a unique and constructive manner through our activities in Drug Discovery.

The goals of the Department are:

- To be one of the top five NIH funded Departments of Pharmacology in the USA.
- To define pharmacological research for the 21st century.
- To improve the presence of Structural Pharmacology and Drug Discovery at the University of Pittsburgh.
- To educate premier future basic researchers, physician-scientists and teachers.
- To enhance the quality of graduate students matriculating and graduating from our PhD program at the University of Pittsburgh.

II. Departmental History and Status:

Major growth in the Department of Pharmacology and Chemical Biology occurred within the last 16 years after a new Chair was recruited and new funds were directed to the Department. As evidenced by the tremendous growth in research support funds, faculty publications, numbers of postdoctoral fellows and the number of members on the Graduate Faculty, we have evolved to become one of the top departments in the country based on our extramural research support and our impact on postdoctoral training. Last year we were ranked eighth in the nation for NIH funding among the more than 100 medical school departments and this year we were ranked seventh. Our Department now views its primary peer programs to be the following institutions: Yale University, University of Michigan, University of North Carolina, University of Pennsylvania, University of Virginia, Emory University, University of Texas Southwestern, University of Washington, Washington University, Vanderbilt University and the Johns Hopkins University.

III. Strengths:

In January 2006, Dr. Bruce A. Freeman was appointed Chair of the Department of Pharmacology and Chemical Biology to lead our strong cohort of well-funded and nationally recognized pharmacologists, cell and chemical biologists and geneticists. The department has about 50 primary faculty and 35 secondary faculty that contribute to the missions of the department. The members of the Department of Pharmacology and Chemical Biology are highly interactive with frequent co-authorship and co-funding. In spite of challenging times, our faculty members are well-funded, with departmental primary faculty currently receiving $7.4 million in total direct annual costs and $10.3 million in total annual costs. During the past five years, the Department has emphasized cell signaling as an area of excellence. These interests address primary themes such as cancer, cardiovascular,

renal and neurobiology. We are now extending this research focus to include two new areas of excellence: drug discovery and structural pharmacology. To supplement our training in these areas, the Department of Pharmacology has an NIH Predoctoral Training Grant in Pharmacological Sciences. The faculty also is well recognized for both their Medical School and Graduate School teaching. The prominence of our faculty members is recognized by their important leadership positions with Centers and Institutes, such as the UPCI, the PINDS, the Drug Discovery Institute, the School of Medicine and the University.

IV. Initiatives:

The Department will initiate a search for two or three new faculty members. The Department also intends to continue to replace aging equipment, renovate laboratory space and in this context, relocate faculty within thematic areas. We will also continue developing a strong interdisciplinary Drug Discovery Program, The Department will continue to partner with the emerging programs in Computational and Structural Biology as we emphasize Structural Pharmacology in faculty recruiting processes.

SWOT Analysis

Strengths

Since John S. Lazo assumed the Chair, the Department of Pharmacology and Chemical Biology has grown from three tenure-stream faculty to 49 faculty of which 24 are either tenured or in the tenure stream. This growth reflects department-initiated recruitment as well as "opportunistic" recruitments in collaboration with the UPCI that have benefited both the UPCI and the University. Thus, seven of our current tenure stream faculty members are physically located within the UPCI as well as 9 non tenure stream faculty. One tenure stream faculty member is physically located in the Center for Clinical Pharmacology. One tenured faculty member is located in the University of Pittsburgh Drug Discovery Institute along with three research faculty. Virtually all faculty are well-funded, with the Department currently receiving more than $15.0 million in total direct annual costs, approximately $9.0 million of which is co-credited to the UPCI, UPDDI or the Center for Clinical Pharmacology because the faculty members have appointments and space there. Our research success reflects strong independent investigator-initiated research support, a key factor for the development of future thematic research projects. We have already begun to define areas for interactive intra-institution research teams. During the past five years, the Department has emphasized cellular signaling and communication as an area of excellence. These interests are spread over three existing disease/organ areas: cancer, cardiovascular/renal and neurobiology. We are now intending to complement this research focus on cellular signaling with two new areas of excellence: drug discovery and structural pharmacology.

The members of the Department of Pharmacology and Chemical Biology have extensive interactions with other Basic Science Programs. In particular, strong collaborative relationships exist with School of Medicine faculty studying cellular communication and signaling, including faculty from the Departments of Cell Biology and Physiology, Molecular Genetics and Biochemistry, Pathology, Neurobiology, and Immunology. Topics of interest range from protein phosphorylation and dephosphorylation, cell cycle checkpoints, G proteins, receptor biology, cell death, pain, combinatorial chemistry, neurotransmitters, channels and redox signalling. Forceful relationships with clinical elements of the Medical Center also exist. These include strong collaborative projects with the Departments of Medicine, Surgery, Anesthesiology, Critical Care Medicine, Pediatrics, Neurology, Urology, Psychiatry and Pathology. The laboratories of members of the Department of Pharmacology house advanced fellows from several clinical units: Pulmonary Medicine, Medical Oncology, Surgery, Anesthesiology and Critical Care Medicine. Interactions also exist with the key Centers and Institutes within the Medical Center and Main Campus including the CNUP, UPCI and the newly created Hemostasis and Vascular Biology Research Institute. These activities reflect the strong commitment of the Department of Pharmacology to engage in translational research and to provide a forum for integrative sciences. The Department considers its role in bridging the basic and clinical sciences of UPMC as a core element of its missions related to fundamental investigation and drug discovery.

Active programs reaching out to the Main Campus have also been instituted. Consequently, there are major collaborations between members of the Department of Pharmacology and the Department of Chemistry. Members of the Department also interact with investigators in the Departments of Environmental and Occupational Health, Biological Sciences and Neuroscience, as well as investigators at Carnegie Mellon University, particularly from the National Science Foundation Center for Fluorescence. Because of this multidisciplinary research activity, the Department took a leadership role in the submission of the multimillion dollar Pittsburgh Molecular Target Laboratory application, which is making Pittsburgh an epicenter for academic drug discovery.

The Department of Pharmacology and Chemical Biology was honored that it was selected to receive an NIH Predoctoral Training Grant in Pharmacological Sciences. This was the only new graduate Training Grant for Pharmaceutical Sciences to be awarded by the NIH in 1994. Moreover, our program was one of only a few recently initiated grants to be renewed for a second cycle. The acquisition of this training grant, which supports four students, was a primary goal of the Department for several years and we are proud to have obtained it.

In addition to their splendid research record, the faculty has displayed outstanding teaching records, both in the Medical School and Graduate School courses. We believe this is due primarily to placing special emphasis on quality teaching and limiting the student interactions of those teachers rated less effective by the students. Our faculty members have also assumed important leadership positions with Centers and Institutes, such as the UPCI, the School of Medicine and the University. To summarize, we have created:

- Strong research activities and NIH grant support
- Interactive faculty
- Interdisciplinary program with the Department of Chemistry
- NCI funded Program Project on Drug Discovery
- Funded NIH Predoctoral Training Grant in Pharmacological Sciences
- NCI funded Specialized Program of Research Excellence in Lung Cancer
- Focus on Cell Communication, Drug Discovery and Structural Pharmacology
- Outstanding teachers of medical and graduate students, e.g. Professor de Groat, who is a five-time winner of the School of Medicine “Golden Apple Award”.

Weaknesses

During the past five years tenured and non-tenured faculty left the Department. We expect that one of our prized lecturers, Professor de Groat, will select retirement within the next three years. Thus, the Department must continue to recruit new faculty to ensure quality teaching to medical school students and retain the critical mass required to be among the top five programs nationally. The curriculum for medical students is routinely being reviewed so that we can develop more blueprints for teaching pharmacology to medical students. We are encouraged by the medical students who realized the importance of strong pharmacological training not only for scoring highly on board examinations but also for treating patients. A basic introductory lecture series on classical pharmacology is currently deemed essential to the current organ system-based training of medical students.

The Department was criticized in the most recent review of its Training Grant that it had too few junior faculty members. To allow the Department to function effectively and to achieve critical mass, additional faculty will be needed.

Currently there are only two program project-type research grants (PO1, P50) within the Department of Pharmacology and Chemical Biology; the national emphasis on specific disease areas lends itself to programmatic efforts and the Department should exploit this. The increased awareness of the productive aspects of linking contemporary chemistry with modern biology also should be an area in which Pharmacology plays a key role. Indeed, we organized a response to an NIH Request for Proposals on Molecular Targets Laboratory, because of the close research links between these two programs. The Department has now focused on Cellular

Signaling and Communication as a major theme. We also believe our interest in Drug Discovery and Structural Pharmacology is both timely and institutionally appropriate. In contrast to the Cellular Signaling and Communication, we have not yet reached critical mass in Drug Discovery and Structural Pharmacology. We plan to fortify these areas by recruiting new faculty members in a manner that would complement the academic mission of the University.

There are limited amounts of pharmaceutical research dollars awarded to the Department of Pharmacology and Chemical Biology. The Department has not placed enough emphasis on obtaining funding from pharmaceutical organizations but rather has paid more attention to Federal dollars. We are now placing more focus on the commercial sector to support research, but intellectual property issues and data sharing are still hurdles.

There continues to be a need for capital investment within the Department of Pharmacology and Chemical Biology to replace aging equipment and to advance our depth in new technological capabilities. The rapid advances in new technologies mandate that new investments be made for our faculty and trainees to maintain our national competitive standing. In summary, we need to:

- Maintain critical mass of faculty
- Grow and better integrate space and facilities for research
- Limited financial research support from pharmaceutical and biotechnology firms and budget cuts at the National Institutes of Health

Opportunities

During the past four years there has been a remarkable and unprecedented growth in drug discovery and development in the US. Both large pharmaceutical firms and biotechnology companies have invested heavily to exploit this new knowledge. Consequently, major new therapeutic advances directed against important disease groups are now emerging. The completion of the Human Genome Project has increased the number of potential therapeutic targets by more than one order of magnitude. The future challenge will be to identify the drugs that will interact with these emerging biochemical and molecular targets. Because of the unique attributes at the University of Pittsburgh that place Chemistry physically close to Biology, we posit:

- There is a unique opportunity for a few academic institutions to participate and profit from this changing paradigm in drug discovery. The Bayh-Dole Act now allows resourceful Universities the opportunity to replace the income lost from managed care with income derived from its intellectual property. A strong Department of Pharmacology is a vital component of such an activity.
- There will be a significantly increased industrial and academic need for well-trained graduates from Ph.D. granting programs with a concentration in Pharmacological Sciences and Drug Discovery. A strong Department of Pharmacology and Chemical Biology is a vital component of such an activity.
- Important new knowledge and reagents continue to emerge that are relevant to many biological systems and all aspects of cell communication. A strong Department of Pharmacology and Chemical Biology is a vital component of such an activity.
- Advances in Structural Biology and Bioinformatics should make it possible in the near future to optimize small molecules that are more selective and potent towards their molecular targets. The area of Structural Pharmacology will be grown to be a vital component of the Department of Pharmacology.
- Ph.D., D.M.D. and M.D. students will need to become even more cognizant and thoughtful about the highly selective therapies of the future that may be used based on the genetic profile of each patient. A strong Department of Pharmacology is a vital component of such an activity.

The University of Pittsburgh is uniquely situated to participate in defining future research and graduate education in Pharmacology and in recruiting to its campus some of the best students. The University of Pittsburgh's advantages are:

- A cohort of dedicated faculty members, who are eager to teach graduate students

- The presence of strong existing programs in neuroscience, virology, tumor immunology, cancer biology, developmental biology, structural biology and computational biology
- The presence of strong clinical programs
- A growing drug discovery enterprise

Threats

One of the greatest threats to the Department of Pharmacology and Chemical Biology would be to lose its vigor and enthusiasm during the current downward trend in NIH funding. Currently the program is nationally identified as a model of growth. This has helped in the recruitment of new faculty. Nonetheless, other institutions have become eager to develop programs in drug discovery and to enhance their pharmacology departments. We believe it is likely that they will seek to recruit our valuable faculty.

Initiative and Implementation Strategies

- To achieve the overall goal of becoming one of the top three Departments of Pharmacology in the next three years, the Department will recruit new faculty members during the next few years. The Department of Pharmacology and Chemical Biology intends to focus on the three defined areas of research interest previously identified: Cellular Communication, Structural Pharmacology and Drug Discovery. In particular, the Department will continue to partner with the new Drug Discovery Institute, providing unique instrumentation, archived chemical libraries and specialized research services and teaching for members of the University and UPMC.

3. Financial Statement

University of Pittsburgh School of Medicine
Statement of Revenues and Expenses – June 30, 2008

	Hard Money	Self Supporting (a)	Discretionary and Restricted	Research	Total
Revenue					
School of Medicine - ECU	487,940				487,940
Indirect Cost Recovery	2,132,170				2,132,170
Direct Grants				5,690,140	5,690,140
Endowment Income			74,918		74,918
Other Revenue	-	37,965	242,529		280,494
Total Revenue	2,620,110	37,965	317,447	5,690,140	8,664,662
Expense					
Medical Faculty Salary	1,198,962	-	89,746	1,785,256	3,073,964
Other Faculty Salary		-	84,726	841,337	926,063
Staff Salary	707,901	6,484	180,047	800,431	1,694,863
Medical Faculty Fringes	272,164	-	22,103	373,998	668,265
Other Faculty Fringes		-	29,015	277,460	306,475
Staff Fringes	220,003	-	24,952	185,110	430,066
Subtotal Compensation	2,399,030	6,484	430,589	4,329,398	7,099,696
Other Expense	598,224	26,713	750,888	1,426,548	2,802,372
Transfers (intra-department)	43,871	13,375	(135,035)	-	(77,789)
Transfers (inter-department)	-	-	(1,843,406)	-	(1,843,406)
Subtotal Other Operating	642,095	40,088	(1,227,553)	1,426,548	881,177
Stepdown	2,321,302				2,321,302
Total Expense	5,362,428	46,572	(796,964)	5,690,140	10,302,175
Surplus/(Deficit)	(2,742,318)	(8,787)	1,032,670		(1,637,513)

June 30, 2006 Fund Balance	5,569,765
Restricted Net Activity Year to Date (from above)	1,114,411
Prior Year Settlement Transfer	79,189
Current Month end Restricted Fund Balance	6,763,364
SOM Quasi Endowment Market value – June 2007	2,104,509
Total Available Balances	8,867,873