PATHWAYS

WINTER 2009

Presidential Award for Faculty Excellence

William E. Pelham Jr., PhD, inaugural recipient

William E. Pelham Jr, PhD, UB Distinguished Professor in the departments of Psychology, Pediatrics and Psychiatry, and one of the leading experts in attention deficit hyperactivity disorder (ADHD), has been named the inaugural recipient of the Presidential Award for Faculty Excellence.

The award was established last spring by President John B. Simpson to recognize a UB faculty member who has achieved the highest degree of excellence as a scholar, community citizen and educator.

Pelham, who also directs UB's Center for Children and Families, will receive the award at a public event held in the spring, during which he will deliver a lecture on his research.

In explaining his choice of Pelham to be the first recipient of this award, Simpson noted that it came as no surprise, given UB's extraordinary faculty, that the call for nominations attracted a large pool of distinguished, eminently qualified nominees from across campus.

"Bill Pelham stood out as a truly exemplary candidate, even among this august group," Simpson says. "As one of the world's principal authorities on ADHD, as a generous and effective mentor to graduate students and young researchers, and as an educator of the first order, he is the epitome of the well-rounded faculty member—equally accomplished, dedicated and influential in the areas of research, teaching and service.

"He fully embodies the qualities the provost and I intended this award to honor, combining outstanding interdisciplinary scholarship with a commitment to using his research and talents to serve the public while educating and mentoring a new generation of scholars and clinicians," he adds. "As the inaugural recipient of this well-earned award, he sets the bar very high indeed."

Pelham

Pelham joined the UB faculty in 1996 after serving for 10 years on the faculty of the University of Pittsburgh, where he directed the Attention Deficit Disorder Program at the University of Pittsburgh School of Medicine.

In addition to directing UB's ADHD program, he conducts a highly successful behavior-modification summer program at the university for children with ADHD, which has been named by the American Psychological Association (APA) as a Model Program in Service Delivery in Child and Family in Mental Health.

Over the years, Pelham has studied many aspects of ADHD, including the nature of cognitive deficit; peer relationships; diagnosis; pharmacological, psychosocial and combined treatments; motivation and persistence; family factors, such as parental alcohol problems; service delivery; and outcome.

He has been a principal or co-principal investigator on multiple clinical trials and research grants from federal agencies, such as the National Institute of Mental Health, National Institute on Drug Abuse, the Substance Abuse and Mental Health Services Administration, National Institute on Alcohol Abuse and Alcoholism, National Institute of Neurological Disorders and Stroke, and from numerous foundations and pharmaceutical companies.

He received a bachelor's degree from Dartmouth College and a doctorate in clinical psychology from Stony Brook University. BP

—Sue Wuetcher

Home-Based Therapy for IBS

Jeffrey M. Lackner, PsyD, leads $8.8 million, seven-year clinical trial

By Lois Baker

Irritable bowel syndrome (IBS) is a chronic, debilitating disorder affecting 25 million people in the U.S.—14 to 24 percent of women and 5 to 19 percent of men.

No reliable and satisfactory medical or dietary treatment exists for the full range of IBS symptoms, which can cause severe physical and psychological distress and deprive sufferers of their quality of life.

Jeffrey M. Lackner, PsyD, assistant professor in the department of medicine, who recently led a successful pilot study of a primarily at-home, self-administered cognitive-behavior therapy program he developed, has received $8.8 million from the National Institute of Diabetes, Digestive and Kidney Diseases (NIDDK) to lead a seven-year multisite clinical trial of the program.

The trial, which is the largest IBS clinical trial conducted to date and one of the largest behavioral trials without a drug arm funded by the NIH, will be conducted at three sites: UB, University at Alabama-Birmingham, and Northwestern University. Following a 12-month planning period, 480 patients between the ages of 18 and 70 with moderate to severe IBS will be recruited over the following four years.

Participants will be assigned randomly to one of three treatment groups: standard cognitive-behavior therapy (CBT), in which patients will receive 10 weekly one-hour sessions with a therapist; home-based CBT plus four one-hour therapist sessions over 10 weeks; or education and support.

Participants will be reassessed at five points during the 12 months following the intervention to determine the long-term effectiveness of each treatment.

Jeffrey Lackner, PsyD

"In the short term, we hope to show that a self-administered version of cognitive behavior therapy for IBS is as effective as standard in-office treatment but is more efficient, more accessible and less costly to deliver," says Lackner, who also serves as director of the UB Behavioral Medicine Clinic.

"In the long term, we hope to show that a self-administered behavioral treatment program maintains its effectiveness over time, can enhance the quality of patient care, improve clinical outcomes and decrease the economic costs of one of the most prevalent and intractable GI disorders."

Lackner notes that the trial addresses a major priority of the NIDDK of improving the quality of care for IBS and the U. S. Surgeon General's call to develop relatively simple behavioral approaches for enhancing the long-term health of chronically ill Americans.

UB co-investigators are Leonard Katz, MD, Michael Sitrin, MD, Susan Krasner, PhD, Changxing Ma, PhD, and Ann Marie Carosella, PhD. Rebecca Firth is project coordinator. BP

Harris Named Distinguished Fellow

Linda M. Harris, MD, associate professor of surgery, was elected a Distinguished Fellow of the Society for Vascular Surgery at the society's 62nd Vascular Annual Meeting.

Her election to the society was based on her scholarly research activities, creative professional activities and teaching excellence. The Society for Vascular Surgery is a not-for-profit medical society that seeks to advance excellence and innovation in vascular health.


Harris

Harris is director of the Vascular Laboratory of Kaleida Health and Erie County Medical Center and has served as interim director of vascular surgery at UB since 1999. She also is program director for the university's vascular surgery residency and has been involved with teaching medical students and residents since joining the full-time faculty in 1996.

Harris has published 39 articles in peer-reviewed journals, authored two book chapters and served as a reviewer for several journals, including the *European Journal of Vascular Surgery, Annals of Vascular Surgery* and the *Journal of Vascular Surgery,* where she serves as a distinguished reviewer. She has given numerous local, regional and national presentations.

Harris is active in the American College of Surgeons, American Venous Forum, Association of Program Directors in Vascular Surgery, Association of Women Surgeons, Eastern Vascular Society and the Society for Clinical Vascular Surgery.

She also is a member of the Accreditation Council for Graduate Medical Education's Residency Review Committee for Surgery, and is involved in a variety of community service activities related to vascular disease.

A graduate of the honors college of Kent State University, Harris earned her medical degree from Northeastern Ohio University College of Medicine and completed general surgery residencies at the University of Michigan Medical Center and at UB.

She completed a two-year vascular fellowship at UB before joined the full-time faculty as an assistant professor of surgery. In 2005, she was promoted to associate professor. BP

—Lois Baker

Wagle Leads American Urological Association

Datta G. Wagle, MD, clinical assistant professor of urology in the School of Medicine and Biomedical Sciences, has been elected president-elect of the American Urological Association (AUA).


Wagle

The nomination means he will serve for three years, starting in May 2009, and become president of the association in May 2010. It is the first time in the AUA's 110-year history that a Western New York physician has been named as its president.

Wagle is a senior partner at Main Urology Associates in Williamsville, New York, and chief of urology at St. Joseph and Sisters of Charity hospitals, part of the Catholic Health System.

A board certified urologist and fellow of the American College of Surgeons, Wagle has had a distinguished career in professional service. He is a member of 21 national and international organizations and has served on 15 different medical boards and 79 organizational committees locally, regionally, statewide and nationally.

In 2003, he was appointed by former Governor George Pataki to serve on the state's Administrative Review Board for Professional Medical Conduct.

The Administrative Review Board for Professional Medical Conduct is the highest decision making body for public safety and physician discipline in the state. It was the first time a representative had been appointed to the board from Buffalo. BP

—Dennis J. McCarthy

Buffalo Physician Online

You can now read *Buffalo Physician* online.
Just go to **www.smbs.buffalo.edu/bp.**
Back issues, starting with autumn 2004, also are available.

By Tara A. Ellis

Characterizing Protein Linked to Blindness

Federico Gonzalez-Fernandez, MD, PhD

FEDERICO GONZALEZ-FERNANDEZ, MD, PHD, who holds the Olmstead Ross Chair of Ophthalmology, and Debashis Ghosh, PhD, senior research scientist at Hauptman-Woodward Medical Research Institute, have been awarded a $1.6 million grant from the National Institutes of Health to support their research into a human eye protein found to be essential to vision.

Gonzalez-Fernandez, an ocular pathologist at the Buffalo VA Medical Center and the Ross Eye Institute at UB, and Ghosh, who also holds a joint appointment at Roswell Park Cancer Institute, have collaborated to uncover the role of the interphotoreceptor retinoid-binding protein (IRBP). IRBP, which is secreted by the rods and cones, is an abundant protein in the retina. It appears to protect vitamin A from oxidation damage and chemical isomerization. The protein does this while somehow targeting the exchange of different chemical forms of vitamin A between the photoreceptors, pigmented epithelium and Muller cell glia in the complex biochemical pathway known as the "visual cycle."

The importance of IRBP in the visual cycle is underlined by the finding that mutation of a highly conserved residue within the vitamin A binding pocket causes a form of automosal recessive retinitis pigmentosa, a degeneration of the photoreceptors that leads to blindness. To uncover the role of IRBP in the visual cycle, Gonzalez-Fernandez and Ghosh plan to combine X-ray crystallographic and biochemical methods with cellular and transgenic approaches. The latter utilize the African clawed toad, *Xenopus laevis,* whose large rods and cones are particularly suited for functional studies.

"Our research combines structural and cellular studies to address the structure and function of this interesting protein in health and disease," says Gonzalez-Fernandez. "Our recent success with the NIH, I think, is due to the potential to really break open this field through a synergy of diverse approaches." BP

Debashis Ghosh, PhD

Newly Unified Health System Named

On October 17, 2008, the governing board that was established to unify Kaleida Health and the Erie County Medical Center Corporation (ECMCC) announced its new name: the Great Lakes Health System of Western New York. The new not-for-profit corporation comprises board membership from Kaleida Health, ECMCC, the University at Buffalo and members of the community.

"Today, we take another step forward in building a new era for health care," said Robert Gioia, chair of the Great Lakes board of directors, at the time of the announcement. "Great Lakes Health conveys a strong geographical presence that is consistent with our mission. We are no longer limiting ourselves to serving a part of the city or any particular suburb. As a single entity, we have the resources to serve the entire region and beyond."

Unified governance creates a process that will create an integrated health system with a vibrant ECMCC campus, along with the five Kaleida Health campuses. It also optimizes and integrates physicians through private practices and the University at Buffalo partnership.

"Through the Great Lakes Health name and brand, we are confirming our mission of creating the preeminent health-care delivery system for Western New York and beyond," said James R. Kaskie, president and CEO of Great Lakes Health and Kaleida Health.

"We have taken competitive energy and turned it into collaboration with a shared common goal of taking what we have today and making it better for the patients we serve."

Kaskie said the work since the signing of the binding agreement between Kaleida Health and ECMCC in June 2008 has been ongoing and positive. The Professional Steering Committee is now staffed and is focusing on four areas: intensive care, transplant, psychiatry and orthopaedics.

Great Lakes Health will develop a clinical services and tactical plan for integration and growth. Key to this will be solving issues with ECMCC labor, resolving its complicated financial relationship with Erie County and ensuring the long-term financial stability of the hospital.

"Both organizations are working very well together and have begun to build a very productive relationship," said Jody Lomeo, interim CEO of ECMCC and the vice chair of the Great Lakes Health Board of Directors. "This is about building, not taking away. We all have one goal in mind—that all of our patients receive the very best care possible. If we keep that in mind, the other issues will work themselves out."

While not a full-asset merger, unified governance is the first step of a commitment to get Erie County taxpayers out of the health-care business. State legislation is still necessary to accomplish County Executive Chris Collins' goal of "protecting county taxpayers."

This would include modifying the public benefit corporation law to allow ECMCC to be subordinate to Great Lakes Health. As these necessary steps are undertaken, Kaleida Health and ECMCC will continue to operate as separate organizations with no immediate changes relative to their respective employees, services or programs. This includes each organization retaining its respective name. BP

Office of Communications Established; Leadership Change for Development and Alumni Affairs


Wiater


Alcott

KATHLEEN WIATER, formerly the head of the Office of Advancement, now leads the newly established Office of Communications in the School of Medicine and Biomedical Sciences. As senior associate dean for communications, she is responsible for all internal and external communications that position the school strategically with its constituencies and increase its visibility, ensuring that school messages are consistent and integrated with the university's strategic plan, UB 2020.

Staff members include Stephanie Unger, editor of *Buffalo Physician* magazine, and Joyce Kosinski, communications associate.

ERIC ALCOTT has been named senior associate dean for development and alumni relations and will lead the reorganized Office of Medical Development and Alumni Relations, formerly the Office of Advancement. The office is responsible for fundraising for the school, design and implementation of the upcoming campaign and ongoing constituent relations activities. Staff members include David Draper, director of development; Kim Venti, director of annual leadership gifts and program planning; Jennifer Lobaugh, director of special events and constituent relations; and staff support, Jeffrey Miller.

The Office of Communications can be reached at (716) 829-3375, and the Office of Development and Alumni Affairs at (716) 829-2773. BP
—S. A. Unger

Gronostajski Selected for Leadership Program

Richard M. Gronostajski, PhD, professor of biochemistry in the School of Medicine and Biomedical Sciences, is one of two faculty members selected to join the 2008–09 UB Faculty in Leadership Program. The program, which was established in 2005, gives interested faculty an opportunity to explore ways to augment research and scholarly activities with administrative responsibilities. Throughout the course of this academic year, participants are paired with a senior administrative officer from UB's Office of the Provost and engage in projects and university-level discussions introducing them to important and timely issues in higher-education administration.


Gronostajski

The other faculty member selected for this year's program is Robert Knopf, PhD, chair and professor of the Department of Theatre and Dance.

"The program provides our UB faculty with a unique opportunity to learn about university administration and enables them to determine whether they have an interest in pursuing university administration in addition to their traditional faculty responsibilities," says Satish K. Tripathi, PhD, provost and executive vice president for academic affairs. "As the Faculty in Leadership Program enters its third year, it is already becoming a University at Buffalo tradition launching many successful careers in higher education administration." BP
—S. A. Unger

Dosluoglu Named to Editorial Board of *Journal of Vascular Surgery*

Hasan Dosluoglu, MD, assistant professor of surgery in the School of Medicine and Biomedical Sciences, and acting chief of surgery at the VA Western New York Healthcare System, has been named to the board of editors of the *Journal of Vascular Surgery.*


Dosluoglu

Dosluoglu—an enthusiastic and popular teacher of UB medical students, residents and fellows—also is chief of vascular surgery at the VA. In this capacity, he has adopted what he calls an "endovascular-first approach" to treating the high-risk population he sees. In 2001 he began collecting data on the patients with claudication, or critical-limb ischemia, who underwent revascularizations at the VA.

"Although the database is primarily maintained for follow-up purposes for improving outcomes," he explains, "it also enables us to analyze our results retrospectively and has provided us with data that we have presented at national meetings and published in various journals, including the *Journal of Vascular Surgery.*"

Dosluoglu also has published papers on the technical aspect of endovascular and hybrid interventions and collaborates with university and community surgeons on a variety of topics.

"The most attractive aspect of being elected to the editorial board of the journal," he says, "is the knowledge that its members are responsible for selecting the articles that are published in it and, therefore, ultimately determining the knowledge base for our discipline." BP
—S. A. Unger

Munschauer Receives National Award

Frederick E. Munschauer III, MD, the Irvin and Rosemary Smith Professor and Chair in the Department of Neurology, and chief of the Jacobs Neurological Institute, received the 2008 Stephen H. Kelly Award from the National Multiple Sclerosis (MS) Society at its annual dinner on October 7, 2008. The award is given each year to an individual who has dedicated his or her time and effort to improving the lives of people with MS.


Munschauer

Munschauer participated in the development of interferon beta as a treatment for MS and has worked within the Baird MS Center of the Jacobs Neurological Institute on developing diagnostic and therapeutic interventions for the disease.

He is a member of the National Board of Directors of the National MS Society and also serves on its National Medical Advisory Board. BP
—Jana Mertz

PHOTO BY DOUGLAS LEVERE

Georgirene D. Vladutiu, PhD

Statin-Induced Muscle Disorders

The focus of $2.5 million in grants from the NIH

By Lois Baker

Approximately 200,000 of the 38 million people in the U.S. who take statins to treat high cholesterol may develop life-threatening muscle disease.

Currently there is no comprehensive way to identify those who may be at risk for this debilitating condition, but new research by UB scientists may correct that situation.

GEORGIRENE D. VLADUTIU, PHD, professor of pediatrics, neurology, and pathology and anatomical sciences, heads a research group that has received three grants totaling $2.5 million to investigate the genetics behind these myopathies.

"The combined NIH-funded research projects will contribute to developing a better understanding of the risk factors associated with statin myopathy and its prevalence in the general population, will develop tools used in comprehensive genetic testing for muscle disease and contribute to the characterization of new genes associated with neurodegenerative disease and aging," explains Vladutiu.

The lead grant is a $2 million, five-year award to Vladutiu from the National Heart Lung and Blood Institute (NHLBI) to study the relationship between certain rare mutations, more common genetic variants and the development of myopathy triggered by statin therapy.

In addition, Paul J. Isackson, PhD, research associate professor of pediatrics in Vladutiu's laboratory, received $383,000 from the National Institute of Arthritis and Musculoskeletal and Skin Disorders to characterize the structure, function and expression of a novel gene associated with statin myopathy.

The third grant, for $110,000 from the NHLBI, funds a Phase I Small Business Technology Transfer project that will explore the technological feasibility of commercializing customized genotype technology (chip development) for variants implicated in muscle disease. Vladutiu expects the results of this project to lead to launching a business that will use the chip technology to screen for individuals at high risk of developing metabolic muscle disease if exposed to one or more triggers.

These triggers include environmental stressors, such as extreme exertion, extreme temperatures, anesthesia, viral infection, fasting, sleep deprivation and taking statins and other medications. Groups who could benefit from such screening include armed services personnel, patients undergoing anesthesia, those prescribed statins and people in strenuous professions, such as firefighters, police officers and professional athletes. The chip also could identify individuals who carry risks for as-yet-unidentified muscle myopathies.

Vladutiu's five-year statin myopathy project has dual aims.

The first is to determine the prevalence of mutations known to cause metabolic muscle diseases in patients taking statins who developed serious muscle symptoms triggered by environmental stressors, such as those described.

The second aim is to identify clinically relevant associations between statin myopathies and common genetic variations in the human genome known as single nucleotide polymorphisms or SNPs.

For the first aim, the investigators will use a customized genotyping technology that will allow them to expand their genetic screening studies from seven common mutations causing three disorders, to more than 380 mutations causing at least 10 disorders.

The genome-wide association studies, which involve scanning more than one million SNPs across the entire human genome, will be performed on DNA samples from individuals with severe statin myopathy. The results will be compared with those of age- and gender-matched individuals who have no muscle side effects from statin therapy.

"Identifying underlying hereditary risk factors will lead to cost-effective screening of individuals who take statins, reduce illnesses and deaths caused by taking statins, and lower health-care costs," says Vladutiu.

Project collaborators include investigators at Johns Hopkins University School of Medicine in Baltimore, Maryland; McMaster University Health Sciences Center in Ontario, Canada; Cedars-Sinai Medical Center in Los Angeles, California; the Medical College of Wisconsin in Milwaukee, Wisconsin; Henry Ford Hospital in Detroit, Michigan; Scripps Mercy Hospital in La Jolla, California; and William Beaumont Hospital in Ann Arbor, Michigan.

ISACKSON, Vladutiu's collaborator at UB, is working with a novel gene he has named narexin for its similarities to two molecules known as notch and agrin. "Both of these molecules play critical roles in skeletal muscle formation, maintenance of integrity and regenerative potential," he explains.

"The predicted functions and specific expression of the narexin gene in the spinal cord suggests it will have novel diagnostic and therapeutic applications to neuromuscular disease and skeletal muscle degeneration during aging."

The Small Business Technology Transfer grant requires partnering between an academic research laboratory and a small business with common interests—in this case, JK Autoimmunity, Inc, in Oklahoma City, Oklahoma. Kenneth Kaufman, PhD, who heads the firm, is principal investigator.

"The goal of this project," says Vladutiu, who applied for the grant and serves as the local principal investigator, "is to develop comprehensive genetic-based testing for metabolic muscle diseases triggered by environmental exposures that are increasingly prevalent in the U.S. and Canada.

"We have identified at least seven high-risk groups that will benefit from genetic-risk assessment. The proposed technology also will be very useful for the diagnosis of muscle disease in individuals referred to our clinical laboratory."

The Robert Guthrie Biochemical Genetics Laboratory, which Vladutiu directs, receives more than 700 muscle biopsies annually from across the United States and Canada for diagnostic studies. Located in Buffalo General Hospital, it performs more than 5,000 biochemical and molecular tests per year on various blood and tissue specimens to diagnose inborn errors of metabolism.

The NIH grants to Vladutiu and Isackson were made possible through the support of an Interdisciplinary Research and Creative Activities Award from the UB Office of the Vice President for Research, and by a grant from the John R. Oishei Foundation. BP

> "Identifying underlying hereditary risk factors will lead to cost-effective screening of individuals who take statins, reduce illnesses and deaths caused by taking statins, and lower health-care costs."
>
> *—Georgirene D. Vladutiu, PhD*

PHOTO BY DOUGLAS LEVERE

Paul J. Isackson, PhD

The Right Combination

UB pharmacists receive $7.6 million grant for global HIV/AIDS program

By Lois Baker

A seven-year, $7.6 million contract has been awarded to the UB School of Pharmacy and Pharmaceutical Sciences to train laboratory specialists in countries around the world where HIV/AIDS infection rates are highest, to test their proficiency and to conduct quality-control analysis of HIV/AIDS clinical trials.

Funded by the National Institute of Allergy and Infectious Diseases, the award establishes a Clinical Pharmacology Quality Assurance (PQA) program and laboratory in the UB Pharmacotherapy Research Center on UB's North Campus and at the Translational Pharmacology Research Core in the New York State Center of Excellence in Bioinformatics and Life Sciences in downtown Buffalo.

The UB PQA program and laboratory, the only one of its type in the world, will assure that AIDS researchers in developing countries conduct the highest quality clinical trials. An estimated 33 million adults and children are living with HIV worldwide, according to the World Health Organization. The UB program and lab will be integrated with global research networks to target some of the regions where the infection rate is highest.

Gene D. Morse, PharmD, professor and associate dean for clinical and translational research, is principal investigator on the award.

"We are excited about this opportunity to use our expertise and facilities to help fight the global AIDS epidemic," says Morse. "This award highlights our expertise in this critical area."

Conducting research in developing countries can be challenging because of a lack of clinical scientists, insufficient laboratory facilities to conduct HIV research and the lack of clinics to provide care to HIV-infected patients, notes Morse.

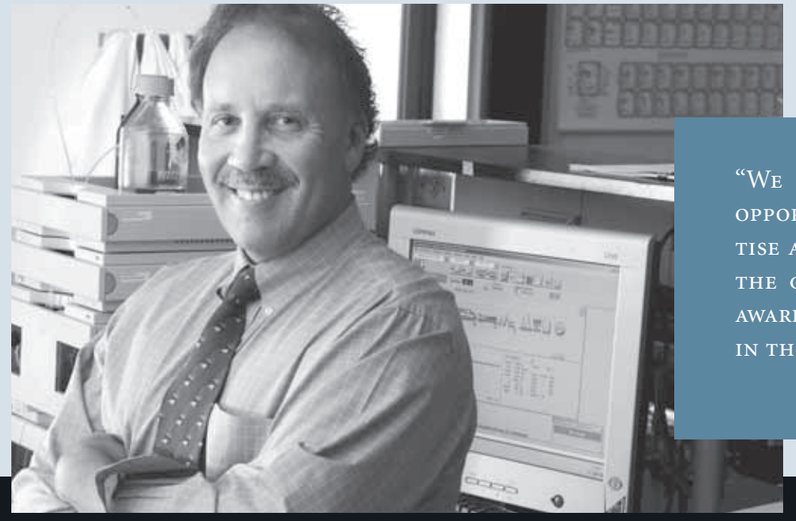
"These difficulties are often compounded by problems such as HIV co-infection with TB and malaria, variable nutritional status among patients, extensive use of traditional and herbal medicines producing unknown drug interactions and counterfeit drugs," he says.

"Building on our extensive experience, our group has been selected to provide a broad-based PQA that will consider each of these factors and guide the growth of HIV/AIDS treatment by facilitating the ability of the pharmacology research laboratories to conduct high-quality research."

The funding represents a significant "next step" in the growth of the UB School of Pharmacy and Pharmaceutical Sciences' clinical research program, says Wayne K. Anderson, PhD, dean of the school. "It is consistent with the UB 2020 vision for the growth of biomedical research collaborations at the Center of Excellence (CoE). Professor Morse and other faculty and staff have made a significant commitment to ensure success at the CoE."

Bruce A. Holm, PhD, UB senior vice provost and executive director of the CoE, says of the award: "This international contract initiative with National Institutes of Health is another positive outcome of the close collaboration between the CoE and the School of Pharmacy. Dr. Morse's program offers great opportunity for further expansion of our viral disease efforts at UB."

HIV/AIDS global efforts currently are focused on increasing antiretroviral access to countries with few resources and conducting clinical trials of new antiretrovirals and combination treatments within their borders. Antiretroviral drugs inhibit the replication of HIV. When antiretroviral drugs are given in combination, HIV replication and immune deterioration can be delayed, and survival and quality of life improved.



Clinical trials of approved and potential new therapies to fight the global AIDS epidemic need to be conducted where the infection rate is highest, but most of those regions are in countries where clinical pharmacology facilities and trained specialists are scarce.

The UB PQA will establish a reference laboratory for antiretroviral bioanalysis that will coordinate key aspects of clinical pharmacology research, including assay development and transfer, global proficiency testing for antiretroviral assays, testing method validation reporting, analytical powder procurement and interlaboratory quality control.

PQA program personnel will provide clinical pharmacology training for clinical research site personnel who conduct clinical and translational studies to assess a drug's effectiveness and its interactions with other HIV medications.

In addition, PQA personnel will conduct on-site audits, disseminate data across HIV/AIDS research networks and establish a centralized website that will integrate the components of the PQA program and provide global information access.

Many of the new drugs developed for HIV have complex pharmacology.

"When patients take the FDA-approved antiretrovirals in fixed doses, they often have variation in individual characteristics such as age, body size, genetic makeup and diet, as well as the occurrence of many drug interactions," explains Morse. "When patients take similar doses of these antivirals, we see great variation in drug exposure from patient to patient. Consequently, clinical pharmacokinetics is a common component of early clinical drug development and later in comparative clinical trials."

Clinical pharmacokinetics involves measuring drug concentrations in patients' blood samples (and other body fluids) to determine the extent of drug exposure and then correlating drug exposure with drug effects (pharmacodynamics) and genetic variation (pharmacogenomics).

"Because measuring clinical drug concentrations in patients who participate in clinical trials is an important aspect of HIV/AIDS drug development and translational research, having pharmacology laboratories that conduct high-quality analysis is essential," says Morse.

"Establishing these laboratories requires extensive training. Personnel need to develop research skills, learn how to conduct critical review of drug assays, do external auditing of laboratory activities, conduct proficiency testing, do quality assessments of the reagents used in the assays and disseminate appropriate information to ensure that the best quality research will be conducted."

Specialists will train through an online tutorial. Two hundred clinical researchers are expected to complete the tutorial annually, notes Morse. UB personnel will conduct antiretroviral proficiency testing twice a year at 10 laboratories the first year, and have options to add one new site each year for the duration of the contract.

Buffalo-based Frontier Science Technology Research Foundation will be responsible for data management and statistical analysis.

Morse says he sees the potential for long-term growth in this area. "In the future, the PQA lab may conduct pharmacology quality assurance for cancer, diabetes and other trials, and could attract companies involved in IT and analytical technology." BP

> "We are excited about this opportunity to use our expertise and facilities to help fight the global AIDS epidemic. This award highlights our expertise in this critical area."
>
> —Gene D. Morse, PharmD

By Lois Baker

Human Exposure to Pesticides

$1.5 million grant to assess these exposures and their adverse effects

PESTICIDE EXPOSURE, particularly in children, is a serious health problem in many parts of the world, including the U.S.

James Olson, PhD, professor of pharmacology and toxicology, is leading research studies on exposure to pesticides, the potential for adverse effects associated with exposures in certain populations and genetic susceptibility to the pesticides.

James Olson, PhD

THE STUDIES ARE FUNDED by $1.5 million in new grants from the National Institute of Environmental Health Sciences (NIEHS) and the Environmental Protection Agency (EPA).

The three-year EPA grant focuses on the activation and detoxification of organophosphate pesticides (OPs), the most commonly used pesticides in the U.S. and worldwide. OPs can stop the action of acetylcholinesterase, an enzyme essential to nerve function in humans and in other animals and insects.

"One objective of this study is to use experimental data on the rates of activation and detoxification by specific human enzymes, and assess the potential for genetic variability in these processes," says Olson. "Levels of pesticide metabolites reported in human urine will be used along with these data to better estimate exposures and the resulting effects of OPs."

The researchers will use an approach called "back-modeling" to better estimate what type of daily human exposure would result in the levels reported in the urine.

"Our mathematical models will help us to estimate doses of the pesticide in specific tissues and the resulting inhibition of acetylcholinesterase, a key enzyme that inactivates neurotransmitters," explains Olson.

"Together, these results will provide better estimates of what levels of exposure to a pesticide may be 'safe' and what would be harmful."

UB is collaborating with Oregon Health and Sciences University, the University of Washington and Egypt's Menoufia University on the four-year NIEHS grant. The researchers will assess exposures to OP pesticides in 255 Egyptian cotton field workers and determine if there are neurotoxic effects.

They hypothesize that neurobehavioral deficits induced by OP exposure are dose related, and that oxidative stress and inflammation are better measures of deficits than inhibition of acetylcholinesterase.

Olson says it has been difficult to predict the risks of exposure to OPs in humans because the relationship of OP doses to neurobehavioral deficits hasn't been well established in humans. In addition, there are no reliable biomarkers to predict deficits, he says, and the potential for genetic variation to modify sensitivity to exposure hasn't been investigated thoroughly.

UB will lead studies assessing human exposure to these pesticides in the study population, carry out pharmacokinetic and pharmacodynamic modeling of pesticide exposure and effect, and investigate the potential of genetic variability of drug-metabolizing enzymes to modify biomarkers of exposure and effect.

"These studies will provide data necessary to develop biomarkers of OP exposure, biologic response and genetic susceptibility," says Olson. "Having markers will help identify people at risk and make it easier to test the usefulness of interventions and treatments.

"This information is important because OPs are used widely throughout the world, and they are potential chemical agents of terrorism."

Matthew Bonner, PhD, from the UB School of Public Health and Health Professions' Department of Social and Preventive Medicine, and James Knaak, PhD, from the UB Department of Pharmacology and Toxicology, are coinvestigators on the UB portion of both grants.

UB co-investigators on the EPA grant are Aiming Yu, PhD, from the School of Pharmacy and Pharmaceutical Sciences; Richard Browne, PhD, from the Department of Biotechnology and Clinical Laboratory Sciences; and Paul Kostyniak, PhD, from the Department of Pharmacology and Toxicology, both in the School of Medicine and Biomedical Sciences. BP

In Memoriam

Allan Oseroff, MD, PhD

Professor and Chair of Dermatology

Allan Oseroff, MD, PhD, professor and chair of the Department of Dermatology in the School of Medicine and Biomedical Sciences and at Roswell Park Cancer Institute (RPCI), died October 16, 2008, from cancer. He was 65.

Oseroff joined the staff at RPCI and the faculty of the School of Medicine and Biomedical Sciences in 1989. He was appointed interim chair of dermatology in 2000 and chair in 2001. At the time of his death, he also held joint appointments in molecular and cellular biophysics and pharmacology and therapeutics at RPCI, and was the Lawrence and Joan Castellani Family Chair in Dermatology, which was created in his honor. In addition, he served as coleader for RPCI's Cell Stress and Biophysical Therapy Program.

A native of Jersey City, New Jersey, Oseroff completed his undergraduate studies at Princeton University. He earned a doctoral degree in applied physics from Harvard University in 1971 and a medical degree from Yale University Medical School in 1977. He completed residency training in medicine and dermatology at the University of Chicago in 1980, and fellowship training in immunology, oncology and dermatology at Stanford Medical Center in 1982. Before coming to Buffalo, he held faculty appointments at Tufts University and at Harvard University.

Oseroff was an internationally recognized expert in the use of lasers and light-activated molecules—known as photodynamic therapy—for the treatment of various forms of cancer. He specialized in the treatment of skin and other cancers that were unresponsive to standard therapy. The protocols he developed have been adopted by practitioners throughout the world. He played an instrumental role in obtaining FDA approval for photodynamic therapy as a treatment for skin cancer and was a leader in setting the national standards for non-melanoma skin cancer as a participant on the National Comprehensive Cancer Network Guidelines Panel for skin cancer.

Oseroff was widely respected as a compassionate physician and brilliant scientist who was a supportive mentor, colleague and friend. He authored or coauthored over 200 publications and held over 20 major research grants, including the highly coveted nanotechnology platform grant from the National Cancer Institute. His name routinely appeared on lists of the nation's top doctors, and he was the "go-to" expert for the national media on all topics relating to skin cancer.

Survivors include his wife, Stephanie Pincus, MD; a son, Benjamin; and two stepchildren, Matthew and Tamara Pincus. BP

—Deborah Pettibone

James F. Mohn, MD '44

Longtime professor of microbiology

James F. Mohn, MD '44, a longtime professor of microbiology in the School of Medicine and Biomedical Sciences, died on November 9, 2008, at his home in Orchard Park, New York, after a lengthy illness. He was 86.

A native of Buffalo, Mohn was a gifted student who received his medical degree from UB at age 22. A year later, he joined the faculty of the medical school as an instructor of bacteriology and immunology under the chairmanship of Ernest Witebsky. In 1949 he initiated the master's and PhD graduate studies program of the Department of Bacteriology and Immunology and became its first director. His career was interrupted to serve as a captain in the U.S. Army at Walter Reed Medical Center during the Korean War.

Mohn, who retired in 1991, was employed by the university for more than 45 years, believed to be one of the longest tenures of any faculty member in the history of the School of Medicine and Biomedical Sciences. During the course of his career, he founded and was director for 35 years of the Blood Group Research Unit and concurrently served for 20 years as director of the Ernest Witebsky Center for Immunology. Mohn also was a director of blood transfusion services at the Buffalo General Hospital and chair of the New York State Council on Human Blood and Transfusion Services.

His research publications during his tenure included important work in the field of blood group antigens and antibodies and acquired hemolytic anemia.

As an expert in blood group research, Mohn was a cofounder of the International Society of Hematology and received several prestigious awards for his work in hematology and blood transfusion. He helped develop the first cell-washing centrifuge and was appointed by the governor of New York State as an adviser on AIDS education. A 47-year volunteer director in the American Red Cross, he was a recipient of the Greater Buffalo Chapter's Clara Barton Volunteer of the Year Award, and in 1995 received the Charles R. Drew Award from the national American Red Cross.

Mohn is survived by his wife of 63 years, Marjorie Jane, of Orchard Park; four children: Barbara Photopoulos, Susan Goodman, Deborah Burzynsk, and Philip Mohn; and by his brother, Wallace Mohn, and his sister, Norma Brason. BP