

VCU Pharmacology & Toxicology

School of Medicine • VCU Medical Center

Summer 2006

www.vcu.edu/pharmtox

Vol. 5 • Issue 1

Chairman's corner



Dr. Billy R. Martin

by Dr. Billy R. Martin

Virginia Commonwealth University is undergoing considerable change that has the potential to affect the university at large, and more specifically our department, for years to come. The dean of the School of Medicine, Dr. Heber H. "Dickie" Newsome, ended a 40-year career at VCU when he retired in June 2005.

We owe a great deal to Dr. Newsome who has been a strong supporter of our department.

With an eye toward the guiding role that academic medical centers should take in improving the nation's health, Dr. Jerome F. Strauss III was appointed as the 23rd dean of the School of Medicine. Dr. Strauss, a third-generation physician with a large, active research program "is the right person at the right time to lead our efforts across the next decade to establish the preeminence of the VCU School of Medicine," said Dr. Sheldon M. Retchin, vice president of VCU health sciences and CEO of VCU Health System.

It has been an extraordinary year. The arrival of the new dean provided us with the opportunity to develop a strategic plan for the department. We are very pleased to have begun the implementation of this plan with the addition of three new faculty members. Dr. Hamid I. Akbarali joined us in October 2005 followed by Drs.

Jill C. Bettinger and Andrew G. Davies in December. We are continuing our aggressive recruitment campaign with the goal of strengthening our strong programs while at the same time identifying new opportunities. These three faculty members fulfill both of these objectives.

Our faculty and alumni continue to be recognized for their accomplishments in areas of leadership, scholarship and teaching as you will see with articles in this issue about Drs. Jonathan B. Perlin, William L. Dewey and Edward J.N. Ishac. Speaking of Dr. Ishac, without his outstanding service contribution, we would not have this newsletter and a revamped Web site. I encourage you to visit our site at www.vcu.edu/pharmtox to view our history as well as learn about recent events, such as the celebration of Dr. Edward R. Bowman's 50th anniversary as a member of our department.

Although it has been a year filled with success and celebration, it also has been a time to reflect on the loss of two dear colleagues: Dr. Robert G. Lamb and Dr. Melinda Lynn "Mel" Cox. Dr. Lamb had proven himself as a distinguished faculty member for his innovative research and masterful teaching. Mel had just completed her doctoral degree requirements and had her career before her. We will miss them both.

I am excited about our future. I am confident that we will continue our tradition of excellence because of our outstanding faculty. Moreover, the strong university commitment to enhancing scholarship provides vital new opportunities for us. Recent newsletters have been devoted to the different areas of our scholarly research and teaching. The emphasis of this edition is the recent recognition bestowed upon several of our faculty members, along with a spotlight on research by some of the younger faculty members.

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Department develops 2005-11 strategic plan

Vision

There are several new initiatives at Virginia Commonwealth University that have a positive impact on the department. VCU is embarking on a new strategic plan that will serve as our road map for the next 15 years. There will be a strong emphasis on enhancing scholarly activity in the university, particularly as it relates to elevation of our national rankings. At the same time, the School of Medicine has developed a bold goal for expanding basic research, enhancing our National Institutes of Health research ranking and expanding doctoral programs. This plan calls for an investment of more than \$300 million between 2005 and 2011 for the recruitment of 102 new faculty members (in addition to replacement of retirees) and construction of new facilities. The focus of this building program will be cancer, neurosciences, translational research and other areas reflecting NIH priorities. The department currently is a major contributor to both neuroscience and cancer research, and therefore will play a key role in achieving the school's mission.

In addition, the School of Medicine has appointed Jerome F. Strauss III, M.D., Ph.D., a physician-scientist as our next dean. The state has committed funds to Virginia's universities for the sole purpose of enhancing existing research programs that represent our greatest strengths. VCU received research funds specifically designated for research in cancer and in the neurosciences, particularly substance abuse and brain trauma — all areas of strength in our department.

Given these unprecedented opportunities, it is imperative that the Department of Pharmacology and Toxicology develop a vision for how it can most effectively contribute to the initiatives of the School of Medicine, VCU and the state in achieving these carefully crafted goals for our future.

Faculty

Our 46 full-time and seven part-time faculty members are scholars renowned nationally and internationally in the fields of neuroscience, cancer, toxicology and other areas of research. They also are outstanding educators who have a strong dedication to the university teaching mission. We have a long and proud tradition of leadership roles in science and education at VCU as well as in national and international arenas. We will strive to strengthen departmental programs that are already strong in order to maintain excellence. At the same time, it is important to develop underserved or new areas of research as we recruit faculty with experience and skills in cutting-edge technology. Our goals are to fill vacant tenure-eligible faculty positions, recruit additional tenure-eligible faculty members in the next six years (in response to the School of Medicine's strategic plan), and recruit collateral faculty and partner with other academic units



Dr. Richard G. Moran

and programs within the university. These combined recruiting efforts will result in an increase of 15 to 20 new tenured or tenure-eligible faculty members, will build on the existing strength of the department and is consistent with the vision of the School of Medicine. In addition, we will add an undetermined number of collateral-track faculty to complement existing and new research strengths.

Research

The department is ranked as one of the country's top 10 pharmacology/toxicology departments in NIH funding and has been ranked first nationally for pharmacology and toxicology publications as a percent of institute publications. This excellence is reflected in high-quality publications in leading journals, leadership roles in scientific societies, journal editorships, membership on grant-review committees and funded research. In fiscal year 2006, the department has more than 50 sponsored programs awards, with total direct costs in excess of \$10 million. In addition, faculty members in our department serve as principal investigators on grants and contracts in institutes and centers at the university, at nearly \$2 million in direct costs, for a total in department support of more than \$12 million. Our goal is to become one of the nation's top five NIH-funded pharmacology/toxicology departments. Based on current funding levels of top departments, a 25 percent increase in NIH funding will allow us to achieve this goal. In addition, we will continue to attract funding for translational research through industrial support.

Teaching

Education represents a major responsibility of the department faculty. Our two major educational missions are teaching in the professional schools and educating and training graduate students.

Currently, we are responsible for full courses in the schools of Allied Health Professions, Dentistry, Medicine and Pharmacy. Our faculty members also advise students and participate in teaching leadership and program development in the professional schools. Additionally, they contribute lectures in many other courses throughout the university, including classes held on the Monroe Park Campus. Our faculty participates in continuing education and in-service training, as well as community education through talks at schools and community events. The number of total classroom lecture hours is approximately 1,200 annually, or about 35 lecture hours per teaching faculty member. This teaching load far exceeds that of most pharmacology/toxicology departments in medical schools. In addition, our faculty devotes approximately 13,000 lab-contact hours each year for training graduate students.

Excellence in teaching students in the health professions is a key mission. Indeed, our faculty members have received many teaching and mentoring excellence awards over the years from national organizations, the university and the school, illustrating our commitment to education. Basic scientific knowledge is an essential background for health professionals to embark on the lifelong learning they will need to keep abreast of the ever-accelerating pace of medical discovery. We also believe that teaching and research complement each other and that excellence in gathering new knowledge has important, positive benefits on knowledge dissemination.

Graduate program

The department continues to emphasize graduate education with 231 doctoral and 48 master's degrees awarded. Our program currently consists of 26 doctoral students and six Master of Science and certificate students (one-year training principally for those seeking admission to medical school). Doctoral students are supported by fellowships from the VCU Graduate School, an NIH training grant,

individual NIH predoctoral fellowships and research grants. In the immediate future, we plan to increase the number of doctoral students to approximately 35, with 45 to 50 by 2011.

Infrastructure

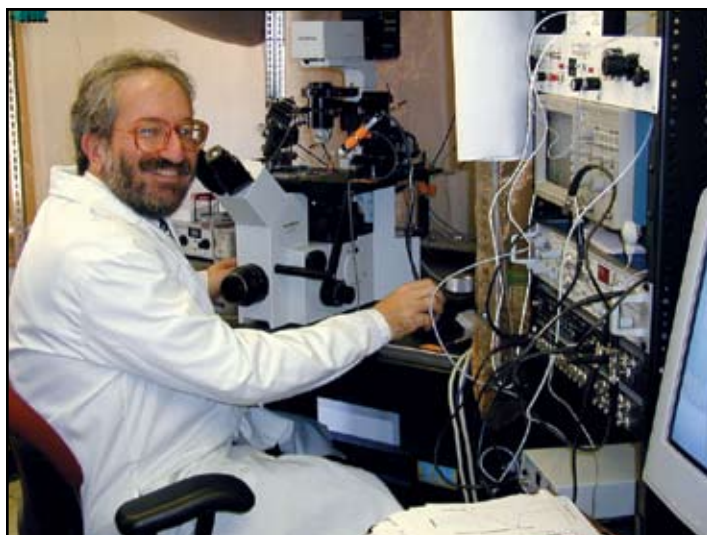
The department is unique among basic science departments in the School of Medicine in that it is dispersed among five buildings at the VCU Medical Center. Moreover, our space within a given building is not always contiguous. Obviously, our faculty members have found ways to work together under these circumstances. Our goal is to consolidate portions of the department, improve the quality of our space and ensure that all faculty members have access to adequate animal facilities. While it is not likely that we will be able to consolidate the entire department into a single location, our goal is to reduce the number of departmental sites as much as possible.

Department snapshot

- The department has 46 full-time and seven part-time faculty members. Of the full-time faculty, there are 20 full professors, nine associate professors, nine assistant professors, seven research associates and one research assistant.
- Our department is currently ranked ninth in NIH-funded pharmacology and toxicology programs.
- Current members of our faculty have published more than 2,200 entries in peer-reviewed journals and trained more than 160 postdoctoral fellows.
- The National Institute on Drug Abuse training grant (1976 – 2011), in its 31st continuous year, is directed by Dr. William L. Dewey.
- The department has awarded the most doctoral degrees (231) in the School of Medicine.

Current endowments

- Ambrose Research Fund
- Butler Memorial Fund Professorship
- Everette May Lectureship
- Graduate Student Endowment
- Haag Professorship
- Harris Professorship
- Lauren and Carol Woods Ph.D. Prize
- Robert G. Lamb Memorial Lectureship
- Schultz/Klingman Graduate Student Fellowship
- Sterling Visiting Professorship
- Wasserman Medical Student Award
- Wazeter Professorship



Dr. Leslie S. Satin

Strauss appointed new dean of medicine

Jerome F. Strauss III, M.D., Ph.D., was appointed dean of Virginia Commonwealth University's School of Medicine in September 2005.

Since 1987, Strauss had been associate chairman of the University of Pennsylvania School of Medicine's Department of Obstetrics and Gynecology, considered to be one of the nation's top programs in women's health.



Dr. Jerome F. Strauss III

"Dr. Strauss' strengths in medical education research and research training rose to the top in a highly competitive field of candidates from across the country," said VCU President Eugene P. Trani, Ph.D.

Strauss has been internationally recognized for his research and research training programs, which have been sponsored

continuously by the National Institutes of Health for more than 20 years. He also has served as an elected officer or member of many national and international medical science organizations.

In recognition of his outstanding achievements and internationally renowned scholarship, Dr. Strauss was elected to the Institute of Medicine in 1994. The institute is the component organization of the National Academies of Sciences that serves as adviser to the nation on matters of health and health policy. Election to the institute is considered one of the highest honors in medicine.

"Dr. Strauss' credentials as a nationally renowned researcher, educator and administrator are a perfect match for VCU's aggressive agenda to dramatically grow the research program at the medical school," said Sheldon M. Retchin, M.D., vice president of VCU health sciences and CEO of the VCU Health System. "Dr. Strauss is the right person at the right time to lead our efforts over the next decade to establish the pre-eminence of the VCU School of Medicine. We are very excited to have someone of Dr. Strauss' caliber as our next dean."

As dean, Dr. Strauss serves as chief administrator of the School of Medicine and also serves as executive vice president for medical affairs for the VCU Health System, overseeing MCV Physicians, the 600 physician-faculty group practice of VCU Medical Center.

"I am thrilled to have the opportunity to work with VCU leadership and faculty to move forward research at the School of Medicine — making the science enterprise relevant to clinical medicine and building upon strong education programs to fashion exciting and relevant activities to promote the highest quality of medical care," Dr. Strauss said.

Dr. Strauss earned a bachelor's degree from Brown University in 1969. He earned a medical degree in 1974 and a doctorate in molecular biology in 1975, both from the University of Pennsylvania.

Dr. Strauss continued his postgraduate training at the University of Pennsylvania and joined the faculty in 1976. He held dozens of hospital and administrative appointments during his 29-year career at the university and received numerous awards and honors. Over the years he has contributed to the international scientific community as an editor and editorial board member for journals in the gynecology and obstetrics discipline as well as general scientific publications such as *Science*.

'Gentleman's dean' retires after 40 years

Heber H. "Dickie" Newsome, retired as dean of Virginia Commonwealth University's School of Medicine in June 2005 after 40 years of service. Newsome held leadership positions in the School of Medicine during most of his tenure at VCU, becoming dean in 2000. Under his guidance, medical school faculty and staff achieved national recognition for their programs in faculty development and women in medicine. The school also saw a 50 percent increase in federal funding for biomedical research.

As dean, Dr. Newsome participated in the restructuring of the VCU Health System, introduced faculty teaching and research awards, emphasized humanism and professionalism and ably dealt with significant funding cuts. He also instituted greater accountability in teaching activities, financial stewardship and faculty development.

Dr. Newsome quarterbacked two state championship teams in high school in North Carolina. He attended Wake Forest University on a football scholarship and was voted class president all four years, graduating with a Bachelor of Science degree. While at Tulane University Medical School, he earned his medical degree as well as a Master of Science in pharmacology, graduating second in his class.



Dr. Heber H. Newsome

Dr. Newsome, 69, continues to live in Richmond with his wife, Jerome. They have three children and five grandsons.

Newsmakers: Perlin, Dewey and Ishac

Dr. Perlin to lead quality initiatives at HCA



Dr. Jonathan B. Perlin

Dr. Jonathan B. Perlin (Ph. D. '91, M.D. '92) was appointed senior vice president, quality, and chief medical officer of Hospital Corporation of America in August. Dr. Perlin will provide senior clinical direction, oversee monitoring and lead the effort to continually improve quality at HCA's approximately 180 hospitals. He also will be responsible for leading and advancing HCA's patient safety initiatives, including the use of an electronic medication administration record and bar coding to reduce medication errors; numerous perinatal safety efforts to help ensure the health of babies and mothers; improved emergency room technology and processes; and clinical improvement in cardiovascular, orthopedics and oncology. In addition, he will oversee HCA's Quality Review System, which measures clinical outcomes, satisfaction and regulatory compliance to improve hospital clinical quality.

Previously, Dr. Perlin served as under secretary for health in the U.S. Department of Veterans Affairs where he directed the provision of care to more than 5.3 million patients annually by more than 200,000 health care professionals at 1,300 sites, including hospitals, clinics, nursing homes, counseling centers and others. Before joining the VHA in 1999, Dr. Perlin served the VCU Health System as assistant professor of internal medicine and as medical director for quality control.

Dr. Dewey receives Friends of NIDA award

At the Feb. 8, 2006, meeting of the National Advisory Council for the National Institute on Drug Abuse, Dr. Nora D. Volkow, NIDA director, presented the institute's Public Service Award to Dr. William L. Dewey, professor in the Department of Pharmacology and Toxicology. The plaque's inscription reads, "In recognition of his pioneering vision in creating Friends of The National Institute on Drug Abuse, and for outstanding leadership in raising public awareness about drug abuse and addiction research." The Friends of NIDA is a coalition of 150 scholarly organizations collectively representing more than 2 million people, professional societies, patient groups and others committed to the elimination of drug abuse and addiction through education, advocacy and the promotion of broad public and private support for NIDA's research agenda. Activities

of the two-year-old coalition include the presentation of many briefings on drug abuse and addictive diseases for congressional members and staff, continual interactions with congressional offices, including visits to appropriate members of Congress, and constant input to all federal policy makers on issues related to drug abuse and addiction. The coalition is now launching a campaign to educate the public about the benefits of the research advances and the future research efforts needed to solve the diseases of addiction.



NIDA Director Dr. Nora D. Volkow presents the Friends of NIDA award to Dr. William L. Dewey.

Dr. Ishac appointed to national medical board

Dr. Edward J.N. Ishac, associate professor in the Department of Pharmacology and Toxicology, has been appointed to the National Board of Medical Examiners' Pharmacology test committee for preparation of the U.S. Medical Licensing Examination's Step 1 examination. NBME is an independent, nonprofit organization that prepares and administers the USMLE Step exams to medical school students nationwide. The tests determine if an applicant is competent to practice medicine and assesses the important concepts of the sciences basic to the practice of medicine, with special emphasis on principles and mechanisms underlying health, disease and modes of therapy. The Step 1 exam ensures mastery of not only the sciences that provide a foundation for the safe and competent practice of medicine in the present, but also the scientific principles required for maintenance of competence through lifelong learning.



Dr. Edward J.N. Ishac

Focus on research: Bettinger and Davies

Studying the neurobiology of alcohol intoxication and tolerance

What can a 1-mm long worm with fewer than 1,000 somatic cells and only 302 neurons tell us about interactions of the nervous system with drugs of abuse? Two recently arrived assistant professors, Drs. Jill C. Bettinger and Andrew G. Davies, believe that the nematode, *Caenorhabditis elegans*, has much to offer on this subject by providing researchers with a combination of a relatively simple nervous system that has been painstakingly described, and powerful genetics and genomics. Although its nervous system is small, there are at least 118 distinct neuronal cell types, and nearly all human neurotransmitters and signaling systems are conserved in *C. elegans*. For these reasons, findings in worms are likely to have direct relevance to humans. The two neurogeneticists bring to the Department of Pharmacology and Toxicology an established program of alcohol research that focuses on using the behavioral effects of alcohol on *C. elegans* to identify and characterize mutant worms that respond differently to the drug.

Dr. Bettinger, a native of Shreveport, La., received her doctorate from the University of Minnesota in St. Paul in 1998. It was there that she began her love affair with *C. elegans*. Her graduate work focused on the genetics of developmental timing and how different tissues in the animal coordinate morphological changes through regulated gene expression, a process that must occur during the embryonic and four larval stages of *C. elegans*' development. In 1999, Dr. Bettinger began studying the effects of alcohol on the *C. elegans* nervous system as an associate research scientist at the Gallo Center, a nonprofit research institute within the University of California, San Francisco.

Dr. Davies, an Australian, received his doctorate from the University of Melbourne in Australia, where he studied the genetics of insecticide (dieldrin and Diazinon) resistance in field populations

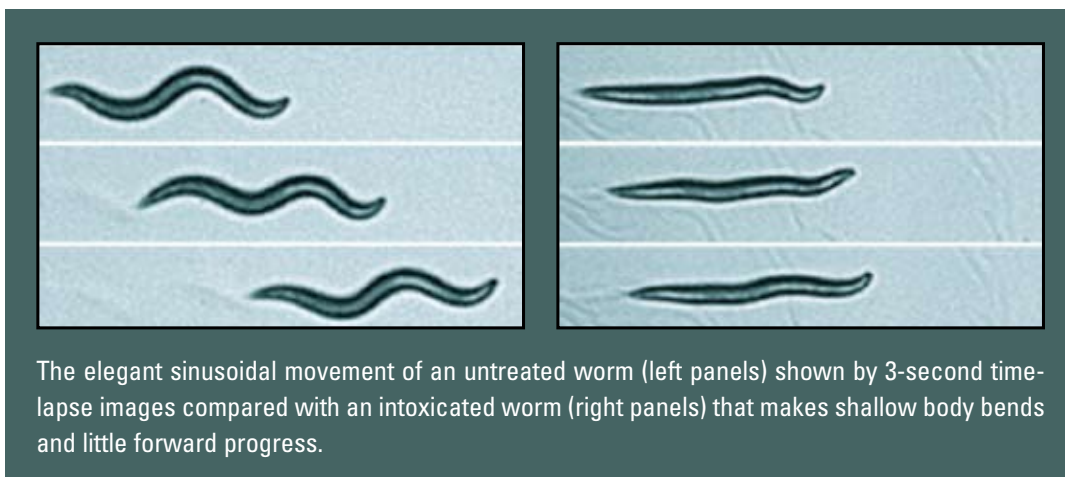
of the Australian sheep blowfly, *Lucilia cuprina*, an agricultural pest. Moving to the U.S. in 1993, Dr. Davies carried out postdoctoral research at the University of Minnesota, working on questions of developmental biology and cell fate determination in *C. elegans*. Then, working as a senior research scientist at the Gallo Center, beginning in 1999, Dr. Davies focused his studies on the genetics of acute alcohol sensitivity.



Dr. Jill C. Bettinger

The pair of researchers has made a number of independent and collaborative findings. Dr. Bettinger found that, as is true in humans, *C. elegans* can associate the state of alcohol intoxication with a learning event, a phenomenon known as state-dependent learning. In this learning paradigm, an animal that learns while intoxicated cannot recall the learning when sober but can do so when intoxicated. Dr. Bettinger showed that the neurotransmitter dopamine is required for state-dependent learning in *C. elegans* and continues to screen for mutants that cannot learn state-dependently. Learning behaviors have been implicated in the addiction process, so pursuit of the molecular mechanism of state-dependent learning is likely to provide insights into alcoholism and other addictions.

Dr. Davies carried out a large-scale genetic screen for mutants that have altered sensitivity to alcohol as measured by the effect of the drug on the ability of the animals to make coordinated movement. Alcohol exposure causes *C. elegans* to lose coordination of their normally elegant sinusoidal movement pattern; the amplitude of their body bends is decreased and there is a dose-dependent decrease in speed (see photos). Among the mutants that displayed decreased sensitivity to the effect of alcohol were animals that carried loss of function mutations in the SLO-1 gene, which encodes the *C. elegans*' voltage and calcium-dependent, large-conductance potassium



The elegant sinusoidal movement of an untreated worm (left panels) shown by 3-second time-lapse images compared with an intoxicated worm (right panels) that makes shallow body bends and little forward progress.

channel, also known as a BK channel. The name SLO-1 is derived from the homologous *Drosophila melanogaster* gene slowpoke. The strength of the resistance displayed by these SLO-1 mutants suggested the possibility that the SLO-1 channel may mediate a significant portion of the behavioral effects of alcohol in *C. elegans*. Electrophysiological analysis of SLO-1-dependent currents in *C. elegans* neurons carried out by Jon Pierce-Shimomura at the Gallo Center showed that alcohol could activate SLO-1-dependent currents and that such an effect was absent in the neurons of SLO-1 mutant animals (where no SLO-1 channels are present). In vitro experiments by other researchers in the field have shown that the mammalian homologues of SLO-1 also can be activated by alcohol, including situations where the channel is present in artificial lipid bilayers, which suggests a direct effect of alcohol on the channel. Activation of these BK channels would lead to a decrease in the activity of the excitable cells expressing the channel, an effect that may well contribute to the behavioral changes associated with intoxication in both worms and humans.

Together, Drs. Bettinger and Davies have examined the response of the *C. elegans* nervous system to alcohol. It is clear that the nervous system is not a passive target of alcohol and that it actively adapts to the effects of the drug during exposure. Such an adaptation within a single prolonged alcohol dose is termed acute tolerance. *C. elegans* display acute alcohol tolerance, such that animals exposed to a steady concentration of alcohol will appear less affected after one hour than they do after 10 minutes of exposure, despite there being no change in internal alcohol concentration. The pair found that a G protein-coupled receptor named NPR-1, which is closely related to the vertebrate neuropeptide Y (NPY) receptors, regulated the rate at which acute tolerance develops in *C. elegans*. They showed that allelic differences in this receptor could account for much of the natural variation in acute tolerance in wild strains of *C. elegans*. NPY and its receptors have been implicated in alcohol responses in mouse knockout studies and with inbred rat studies. This overlap in phenotype suggests the possibility that there is a conserved mechanism for how the nervous system responds to prolonged exposure to alcohol. Dr. Bettinger is now carrying out genetic screens to look for genes that regulate the development of acute alcohol tolerance by searching for mutants that fail to develop acute tolerance. These mutants will identify

genes that interact with NPR-1 or act in parallel pathways to regulate acute tolerance. The identification of genes that play a role in regulating an acute response to alcohol is likely to be valuable for the study of human alcoholism. There is a strong correlation between individuals who have a high level of naive tolerance to the effects of alcohol and the likelihood of abusing alcohol later in life.



Dr. Andrew G. Davies

Dr. Davies is examining the response of the nervous system to alcohol using an alternative approach. *C. elegans* that have been withdrawn from a prolonged exposure to the drug demonstrate behavior that is distinct from their untreated and intoxicated behaviors. It is likely that the removal of alcohol from their system has uncovered the compensatory physiological changes that have occurred in the nervous system to cope with the presence of the alcohol. One of those changes appears to involve the NPR-1 gene or the pathway in which the gene acts, suggesting that regulation of that pathway is occurring during prolonged alcohol exposure. The identification of other pathways that are regulated during alcohol exposure may provide key insights into the mechanism of tolerance, including a better understanding of the chronic alcohol tolerance that develops during the development of alcoholism in humans.

Finally, the approach of using *C. elegans* to better understand the targets of alcohol that mediate the behavioral effects of the drug can be applied to other drugs and compounds. Dr. Davies will take advantage of one of the strengths of the Department of Pharmacology and Toxicology and will be initiating a study using *C. elegans* genetics that seeks to identify novel targets of cannabinoids.

And, in case you haven't guessed, Drs. Davies and Bettinger are a husband-and-wife team, the third within the department.

Request for news items

Have you changed employment, been promoted or received an award or honor recently? Share your good news. Please forward your information to eishac@vcu.edu. Remember, this is your newsletter and your contributions or suggestions are appreciated.

Focus on research: Hamid I. Akbarali, Ph.D.

Investigating ion channels in gastrointestinal function



Dr. Hamid I. Akbarali

Dr. Hamid I. Akbarali completed his Bachelor of Science with honors in pharmacology from Chelsea College, University of London, in 1982 and earned his doctorate from Memorial University of Newfoundland in St. John's, Canada. He subsequently did his postdoctoral fellowship at the Oregon Health Sciences University and at the University of Calgary with Dr. Wayne Giles, where he learned the technique of

patch-clamp in smooth muscle cells. In 1992, Dr. Akbarali joined the Department of Gastroenterology at Harvard Medical School in Boston as an instructor and was promoted to assistant professor of medicine in 1994. In 2000 he moved to the Department of Physiology at the University of Oklahoma Health Sciences Center as an associate professor and was promoted to professor in 2005. In October 2005, Dr. Akbarali joined the Department of Pharmacology and Toxicology at Virginia Commonwealth University's School of Medicine as professor.

Dr. Akbarali has spent the past 15 years characterizing and defining the physiological role of various ion channels in gastrointestinal smooth muscle and sensory neurons. His research combines molecular and cellular techniques with electrophysiology to study the ionic basis of gastrointestinal function. The area of "channelopathies" is now recognized as a major clinical entity resulting from genetic defects of ion channels, such as in cystic fibrosis as well as in "transcriptional channelopathies" that results from abnormal transcription of normal genes under stress, for example during inflammation. Dr. Akbarali's laboratory has focused on altered

channel function in gastrointestinal disorders, in particular during active colonic inflammation. Gastrointestinal motility is severely compromised in inflammatory bowel disease. In mouse models of colitis, Dr. Akbarali's research demonstrated that the calcium entry through voltage-dependent calcium channels was markedly suppressed. Calcium currents measured in single smooth muscle cells by patch-clamp techniques showed that during active colitis in mice, calcium currents were reduced by almost 60 percent. Further studies using real-time PCR techniques to measure gene expression showed that the calcium channel mRNA was not altered by inflammation and neither was protein expression; rather the decrease may occur as a result of altered regulation by the tyrosine kinase, c-src kinase. Present studies are directed toward defining the cellular mechanisms by which c-src kinase may regulate calcium channels, including identifying the site(s) on the calcium channel protein.

Inflammation of the colon affects smooth muscle motility and also results in pelvic pain. The pain may not only emanate from the colon (the site of active inflammation) but also from other visceral and somatic regions — a process referred to as cross-organ sensitization. The cell bodies of the sensory afferents from these organs lie within the dorsal root ganglia. Dr. Akbarali's group identified a population of cells in the DRG that appears to receive innervation from both the colon and bladder. These convergent neurons may form the basis for pelvic pain transmission across organs. The electrophysiological properties of these "convergent" neurons and the ion channels associated with regulating the excitability of DRG neurons are currently being studied.

Dr. Akbarali has been continuously funded by the National Institutes of Health since 1993 and presently holds two NIH grants. He has served as an ad hoc member on NIH study sections, and is on the editorial boards for *Cell Physiology* and the *American Journal of Physiology: Gastrointestinal and Liver Physiology*. He also is a reviewer for several national and international journals. His research combines molecular, systems and integrative pharmacology, and he has trained several postdoctoral fellows who now hold academic positions nationally and internationally.

Department launches enhanced Web site

As you may have noticed, we have launched a newly redesigned department Web site at www.vcu.edu/pharmtox, developed by Virginia Commonwealth University's Creative Services. The graphic interface has been enhanced with streamlined navigation and improved use of color. We hope that you find the navigation more intuitive and the overall experience more

enjoyable. Some sections have changed names and new features have been added. In particular we have added a username/password-protected alumni section focused on your needs. To gain access to this section, e-mail Dr. Edward "Eddy" Ishac at eishac@vcu.edu. We would appreciate your comments on items you would like to access online.

Focus on research: Charles Cook, Ph.D.

Examining sex differences in pain sensitivity and drug-induced effects

Dr. Charles D. Cook, a native of Baltimore, earned his undergraduate psychology degree in 1994 from Randolph-Macon College in Ashland, Va. During his senior year, he participated in an internship in Virginia Commonwealth University's Department of Pharmacology and Toxicology under the direction of Dr. Patrick Beardsley. After graduating from Randolph-Macon, Dr. Cook entered the biological psychology program at the University of North Carolina at Chapel Hill under the mentorship of Dr. Mitchell Picker. His initial research efforts at UNC focused on examining the discriminative stimulus properties of mu and kappa opioid drugs and, in particular, the interaction between the dopamine and opioid systems. Later studies showed that sex differences in opioid-induced antinociception are evident when a pharmacogenetic analysis was employed.

In the summer of 2000, Dr. Cook returned to VCU's Department of Pharmacology and Toxicology for a postdoctoral fellowship with Dr. Beardsley. He continued to explore the interaction between the opioid and dopamine receptor systems using drug discrimination and locomotor activity procedures.

In 2002, Dr. Cook attained faculty status as an assistant professor and later was a scholar in VCU's Building Interdisciplinary Research Careers in Women's Health program from 2002 to 2005. The BIRCWH scholars program was an institutional career development award funded through the National Institutes of Health that was designed to increase the number of junior faculty researchers at VCU conducting science that will directly affect the health of women. As part of that program, Dr. Cook was afforded 75 percent protected time to initiate his research on studying sex differences in chronic pain and opioid-induced effects. Upon completion of the BIRCWH program, Dr. Cook continued to develop his research.

There is ample evidence in the literature that indicates that female humans experience more chronic pain that is of greater intensity than male humans. Findings such as this imply that sex hormones may be important factors in mediating the sex differences in chronic pain states in humans. Interestingly, little preclinical work has been done investigating the role of sex hormones using animal models of chronic pain. As such, Dr. Cook is interested in expanding on his previous work to include exploration of sex differences in animal models of chronic pain. This current work is supported by VCU's Institute for Drug and Alcohol Studies. Administration of Complete Freund's Adjuvant (*Mycobacterium butyricum*) into the hind paw of rats produces a chronic inflammatory pain state that closely resembles

human rheumatoid arthritis. Initial studies demonstrated that the chronic pain state develops at a faster rate in female rats and the severity of the hyperalgesic response that develops is greater in female than male rats. Moreover, the potency of morphine to produce analgesia in response to the hyperalgesic state is greater in male than female rats, further demonstrating that sex hormones are involved in mediating the pain system in male and female rats.

Ongoing studies are addressing the role of sex hormones through the testing of castrated male and ovariectomized female rats as well as studying the ability of low-to-intermediate efficacy opioids to produce pain relief. The goal of this research is to develop a more complete understanding of the role that sex hormones play in mediating pain sensitivity and responsiveness to opioid analgesics using a clinically relevant animal model of chronic pain. Additional studies, funded by a Jeffress Memorial Trust award, are designed to investigate the role of the serotonin system in mediating sex differences in chronic pain. Dr. Cook also has established collaborative efforts with several members of the department, including Drs. William Dewey, Dana Selley and Laura Sim-Selley, to further explore the relationship between opioid-induced behavioral effects and opioid-induced cellular changes.

In addition, Dr. Cook is working with Drs. Louis S. Harris and Mario D. Aceto on a contract funded by the National Institute on Drug Abuse. They are using various animal models of reward, including drug self-administration and intracranial self-stimulation procedures, to evaluate potential pharmacotherapies as substance abuse medications. Dr. Cook also has taught several classes to graduate and undergraduate students at VCU. He is a member of the graduate student recruitment committee for the Department of Pharmacology and Toxicology, a councilor for the Central Virginia Chapter of the Society for Neuroscience and an active member of the College on the Problems of Drug Dependence and the American Pain Society.



Dr. Charles D. Cook

Remembering our colleagues, our friends

It is with great sadness that we report the untimely passing of a long-time faculty member, Robert G. Lamb, Ph.D., and senior graduate student, Melinda "Mel" Cox in 2005. If you would like to post a reminiscent note about Drs. Lamb or Cox to the department's Web site, or would like to send a note to their families, please e-mail Dr. Edward Ishac at eishac@vcu.edu. Bob and Mel, you were loved by many, touched our lives deeply and will be very much missed.

... a loved one is not gone, they live in the hearts of those who loved them and their memory will live forever!

Melinda L. Cox, Ph.D.

Melinda Lynn "Mel" Cox, born Dec. 25, 1977, passed away Sept. 16, 2005. As a child, Mel attended Luther Memorial School, was valedictorian of the class of 1995 at St. Gertrude High School and graduated with honors from the University of Virginia in 1999. In the fall of 1999, Mel entered the graduate program within our department. Under the guidance of Dr. Sandra Welch, her thesis



Dr. Melinda Lynn "Mel" Cox

project examined the role of endogenous opioids in cannabinoid-induced antinociception. In December 2005, Dr. F. Douglas Boudinot, dean of the Graduate School presented posthumously to the Cox family Mel's diploma and copies of her thesis. Although it was quite emotional for the family, they were pleased to receive Mel's diploma that would have meant so much to her. Mel is survived by her parents, Phyllis and Wayne Cox, and her fiancée, Nicholaus Hudert, as well as her two beloved cats, Zack and Miss Priss. Her love of animals, her attention to details and her strong work ethic shall always be remembered.

Robert G. Lamb, Ph.D.

Dr. Robert G. Lamb, professor of pharmacology and toxicology, passed away April 17, 2005. He was 60 years old. Dr. Lamb came to Virginia Commonwealth University as an assistant professor in 1974. He was promoted to associate professor in 1980 and became a full professor in 1990.

"Dr. Lamb taught a heavy load of courses and won several teaching awards," said Dr. Billy Martin, department chair.

Lamb taught classes for medical, dental and pharmacy students, as



Dr. Robert G. Lamb with one of his four grandchildren

well as graduate students and undergraduate honors students.

"Just about every doctor, nurse, dentist and physical therapist at MCV had my dad for a class," said Dr. Lamb's daughter, Julie Marsh, who lives in New York City.

A native of Portland, Ore., Dr. Lamb attended the University of North Carolina at Chapel Hill. He earned a bachelor's degree in chemistry in 1967 and a doctorate in biochemistry in 1970. He served as a postdoctoral fellow and taught at UNC before coming to Richmond, Va. In addition to teaching, Dr. Lamb spent years researching how different chemicals and drugs affected liver function. His goal was to find ways to prevent and treat that damage.

"Recently, he discovered that vitamin E phosphate, an antioxidant, could protect the liver from damage," said Dr. Martin. Dr. Lamb had recently received a patent on the idea of adding the vitamin to beverages to reap the benefits of that protection.

Dr. Lamb was an active member of the VCU community, serving two terms on the Faculty Senate and serving on a number of committees within the department and the School of Medicine.

"While VCU lost a faculty member, most importantly, it lost a good friend," Dr. Martin said.

Dr. Lamb considered teaching to be one of the most important parts of his job as a VCU faculty member. He was passionate and very principled about what he thought students should learn. He taught a very complex topic. He was willing to take on the tough topics and make sure that the students learned the material.

In addition to his daughter, Dr. Lamb is survived by his wife, Debby Hougland Lamb; two sons, Robert Gregory Lamb of Fairfax County, Va., and C. Scott Lamb of Doylestown, Pa.; one brother, Richard Lamb of Newport, Pa.; and four grandchildren.

Bowman marks 50 years of service at VCU

After earning his bachelor's degree in biology and chemistry at Concord College, Dr. Edward R. Bowman completed a master's degree in physiology at West Virginia University. Arriving in Richmond, Va., in 1954, he began work as a bacteriologist for the Virginia State Health Department, where he remained until he attended graduate school at Duke University for one year.

In the spring of 1956, Dr. Bowman came to the Medical College of Virginia as a research assistant to the Department of Pharmacology and Toxicology and completed his doctoral degree in pharmacology. Since then, he has served on the department's faculty roster as a research associate. In his career, Dr. Bowman has dedicated a quarter-century to the study of the metabolism of nicotine in several mammalian species, including man. As pioneers in this field, he and his co-workers were the first to identify at least 10 metabolites of nicotine without the aid of some of the more modern instrumentation.

Earlier in his career at VCU, Dr. Bowman taught in the schools of Pharmacy, Dentistry and Medicine. Currently, his research

focuses on the evaluation of drugs associated with dependence liability. As his research has progressed, Dr. Bowman has authored or co-authored 160 articles on his findings in some of the scientific field's leading publications. He belongs to several professional societies, including the American Chemical Society, the Society of Pharmacology and Experimental Therapeutics and the Society for Experimental Biology and Medicine.



Dr. Bowman with his wife, Wilma, and daughter, Gay, in 1955, just months before coming to Richmond

Graduate corner: student and alumni news

Student awards

At the 2006 annual meeting of the Virginia Academy of Sciences, Alex Putman won first place in the Best Student Paper Award for "The Genetic Analysis of Ethanol-induced Anxiolysis in BXD Recombinant Inbred Mice." He also was the Pharmacology and Toxicology Department's nominee for the Phi Kappa Phi Scholarship in 2006.

Phil Yeager was the Virginia Commonwealth University representative at the University of Messina (Center for Integrative Mediterranean Studies for Health and Peace) as part of a VCU international partnership with the University of Messina in Italy and the University of Cordoba in Spain. He also was a nominee for the American Association for the Advancement of Science/Program for Excellence in Science in 2006.

In 2006, Putman and Yeager received National Institutes of Health F31 Predoctoral Fellowships. Congratulations to them both.

Students receiving awards in the department include: Laxmikant "LD" Deshpande (first) and Gerald DeMasters (second), recipients of the 2005 Lauren A. Woods Award; Chris Sheth and Phil Yeager, co-recipients of the 2006 Anthony Ambrose Award; Denise Hernandez, recipient of the 2005 Anthony Ambrose Award; and Scott Lawrence, recipient of the 2005 Charles C. Clayton Fellowship. Chris Sheth also received the Phi Kappa Phi Nomination Award.

Latest graduates

Congratulations to the recent graduates: Randy Abutin (Ph.D., adviser Dr. Stephen Sawyer), George Dalton (Ph.D., adviser Dr. William L. Dewey), Erin McCarthy (Ph.D., adviser Dr. Richard Moran), Kristini Miles (Ph.D., adviser Dr. Joseph Ritter), Laxmikant Deshpande (Ph.D., adviser Dr. Robert DeLorenzo), Gerald DeMasters (Ph.D., adviser Dr. David Gewirtz), Katie Falenski (Ph.D., adviser Dr. Robert DeLorenzo), Molly Cage (Ph.D., adviser Dr. Michael Miles), William Holbert II (M.S., adviser Dr. Severn Churn), Anne Johnston (M.S., adviser Dr. Robert DeLorenzo), Lauren Collier (M.S., adviser Dr. Laura Sim-Selley), Elizabeth Hendrick (M.S., adviser Dr. Keith Shelton) and Haritha Tatavarthi (M.S., adviser Dr. Larry Povirk).

PTSO

Current officers in the Pharmacology and Toxicology Student Organization are Alex Putman, president; Denise Hernandez, vice president; Lynn Hull, secretary; Scott Lawrence, treasurer; Phil Yeager and John Harloe, SGA representatives; Anne Johnston and Dena Kota, honor council representatives; and Teneille Walker, library representative.

If you have any questions regarding PTSO, please contact Lynn Hull at hulllc@vcu.edu.

Summer 2006 • Vol. 5, Issue 1

Contributions

We welcome your contributions. Please send any news and information to:

Dr. Edward J.N. Ishac, editor
VCU Pharmacology & Toxicology
 410 North 12th Street, Room 742
 P.O. Box 980613
 Richmond, Virginia 23298-0613

Phone: (804) 828 2127

E-mail: eishac@vcu.edu

Web site: www.vcu.edu/pharmtox

Acknowledgments

Thank you to the following individuals for their contributions to this issue of the *VCU Pharmacology & Toxicology* newsletter: Brenda Caine, Sheryol Cox, April Filips and Drs. Billy Martin, William Dewey and Susan Robinson.

VCU Pharmacology & Toxicology
 is a newsletter providing news and
 information from the Department
 of Pharmacology and Toxicology at
 Virginia Commonwealth University.



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