



A Prescription for Involvement

Research, discovery, outreach, and practice all play a role

BY RANDOLPH FILLMORE

As the second decade of the 21st century approaches, the University of Maryland School of Pharmacy is assuming a greater role in improving the health and welfare of the citizens of Maryland through continuing research and discovery. Extending efforts to translate those advancements into clinical practices and outreach programs that improve health care will be the focus of the next several years, says Natalie D. Eddington, PhD, new dean of the School of Pharmacy.

“We are making great and significant strides in our research programs from new nanomedicine therapeutics that image and treat cancer tumors simultaneously, to the emerging area of evidence-based assessment of pharmaceuticals to determine preventable mortality and morbidity,” Eddington says.

The Fight Against Microbes

According to Angela Wilks, PhD, vice chair of research in the Department of Pharmaceutical Sciences, basic science carried out at the School identifies promising new compounds that may become the next generation of antibiotics. Current research efforts are focused on moving discoveries aimed at serious health problems from the bench to the bedside.

“The high level of antibiotic drug resistance in the hospital and community setting is a huge problem,” Wilks says. “Making new versions of older drugs is not going to solve the problem because they become obsolete very quickly. Instead, we are developing new compounds with new pathways and protein targets that will lead to novel drugs with broad spectrum effectiveness.”

Much of this work is being carried out in the School’s Computer-Aided Drug Design (CADD) Center. Here, computational and theoretical studies on the three-dimensional structure of molecules and proteins provide better understanding of how compounds bind to targets and how proteins function and inter-

act with each other. This knowledge can lead to the development of novel therapeutics.

Under Director Alexander MacKerell, PhD, and the School’s first Grollman-Glick Professor, the CADD Center is working on many projects, including studies related to cancer, rheumatoid arthritis, antibiotics, and the treatment of pain.

“The CADD Center can build on research discoveries in the basic sciences by School of Pharmacy faculty,” explains MacKerell, “leading to the identification of chemical compounds with the potential to be developed into novel therapeutic agents. The use of computers greatly speeds up the discovery process and lowers costs significantly.”

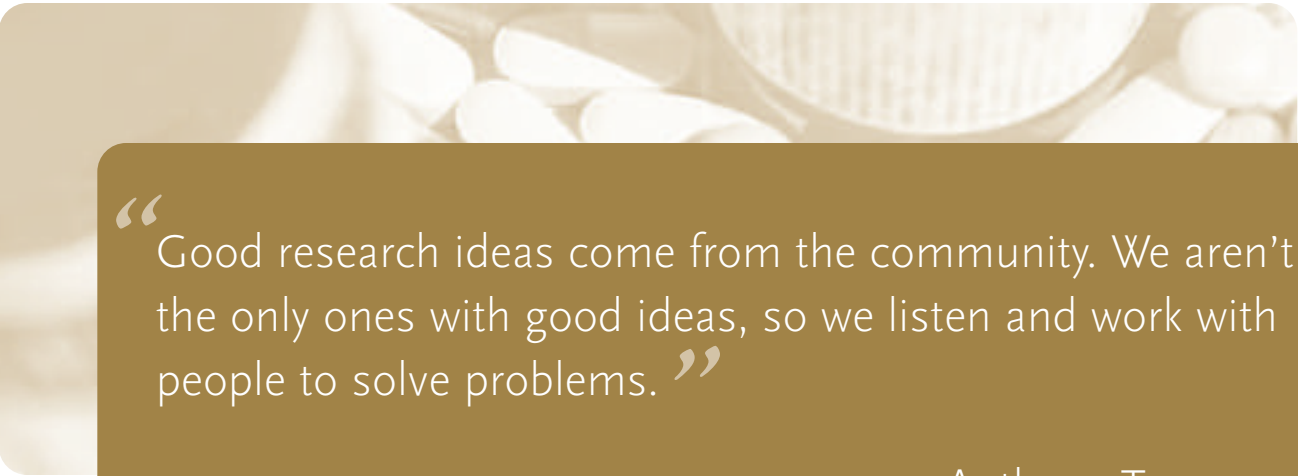
Researchers are especially interested in developing a new anti-microbial to use in the fight against hospital-acquired infections, called “nosocomial infections.” Individuals with compromised immune systems, especially people with cystic fibrosis, are especially susceptible to nosocomial infections. Researchers also are looking at developing compounds to create new antibiotics to battle meningitis, cholera, and dysentery.

“By using CADD to look at the 3-D crystal structure of a bacterial protein involved in iron metabolism, we can develop compounds that will cross the bacterial cell membrane and target proteins required for the utilization of heme [the iron-containing co-factor found in hemoglobin] as an iron source,” Wilks says.

This research already has been patented and will soon be available for licensing, a step that will facilitate clinical trials. Wilks and MacKerell published their research results in the July 2007 issue of the *Journal of Medicinal Chemistry*.

Substance Abuse Outreach Critical

For more than 30 years, Anthony Tommasello, PhD, MS ’82, BSP ’73, associate professor in the Department of Pharmaceutical



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Health Services Research, has been involved in building community outreach programs designed to help curb substance abuse. One program, the Student Committee On Drug Abuse Education (SCODAE), trains pharmacy students to go into the community to talk to schoolchildren about the consequences of substance abuse.

“This program is a clear way to use science for community education,” says Tommasello, who also directs the School’s Office of Substance Abuse Studies. “Young people need to know why to say no to drugs and we present scientific evidence on the consequences of substance abuse.”

SCODAE has just published the 2007 version of its booklet “Know WHY to Say No” that School of Pharmacy students are taking into the community. Based on research, the booklet covers the physiological principles and medical consequences of drug addiction as it breaks down the dangers of cocaine, stimulants, alcohol, depressants, marijuana, and psychedelic drugs.

Research in other areas that overlap with substance abuse—such as HIV infection and homelessness—also is translating into programs to benefit the community. For example, research has led Tommasello and his colleagues to focus on efforts to improve the lives of homeless substance abusers.

“Alcohol abuse is very high among homeless persons,” Tommasello says. “And homeless persons also often have co-existing mental health disorders.”

Another issue on the research agenda has been community involvement in the effort to have buprenorphine, a new drug for treating opiate addiction, made available by physician’s prescription and for home use by recovering addicts. Methadone,

available only at clinics, was formerly the only pathway for treatment. Now, select patients can get buprenorphine by prescription for home use.

“This effort took a lot of work,” admits Tommasello, noting that buprenorphine is now available from certified physicians.

“Methadone clinics are limited by size and it can take months of waiting to get into clinics,” he points out. “Now, pharmacists can dispense buprenorphine.”

Tommasello says that research into substance abuse and its co-existing problems of homelessness and mental illness can only become “translational” through relationship building in the community.

“Good research ideas come from the community,” Tommasello says. “We aren’t the only ones with good ideas, so we listen and work with people to solve problems.”

Community Involvement

Fadia Shaya, PhD, MPH, associate professor in the Department of Pharmaceutical Health Services Research and associate director of the School’s Center on Drugs and Public Policy, agrees with Tommasello. Community inclusion, she says, assures that research will be translational with the potential to make a difference in real health problems and outcomes.

“We have a mandate to improve the health of people in the state of Maryland,” Shaya says. “No one knows more about medications than pharmacists and, at the end of the day, we know that people who are compliant with their medications fare better. So, we can have a great impact on health and quality of life by using our expertise when reaching out into the community.”

For Shaya, the success of collaborative research depends on developing “networks,” not only researchers from across the University of Maryland, Baltimore (UMB) campus, but networks built with community and health system leaders as well.

“We aim to bring all the parties to the table,” Shaya emphasizes. “That includes faith-based organizations, community hospitals, clinics, educators, insurers, and social service organizations. These entities have their own infrastructure, resources, manpower, and intellectual engines.”

For Shaya, part of the School of Pharmacy’s responsibility in the research/outreach continuum is the evaluation of a program’s effectiveness. Currently, she is working on designing the network component for a campuswide grant that will increase the opportunities for translational research.

“Too often there is a gap between what we know scientifically and what we don’t know about how people fare after clinical interventions,” she points out. “For that reason, we are greatly concerned with building the right evaluation components into research, ones that involve community participation.”

A future, campuswide Center for Clinical Translation, the focus of a grant in-progress for UMB’s schools of dentistry, law, medicine, nursing, pharmacy and social work, will have 20 percent of its budget devoted to evaluation of what impact translational research has had in the community, says Shaya.

“Through these efforts, we will raise health awareness and improve health prospects for people in Baltimore and beyond,” she concludes.

Poison Center Steps Up Research

Not only does the Maryland Poison Center (MPC) serve the community by being there 24/7 for physicians, nurses, first responders, and anyone else who has a potential poisoning emergency in the home or workplace, but researchers in the center also turn data into life-saving information that poison center-certified specialists have at their fingertips when handling emergency calls.

“Our research is focused on how we can take better care of people in the community,” says Bruce Anderson, PharmD, MPC director and associate professor at the School of Pharmacy. “Based on research, we may change our management of any one of the almost 70,000 calls we get annually. Research may determine whether a patient can be managed at home or should go to an emergency room. The difference in knowing how we can do our job better can spell the difference between life and death or save health care dollars when treatment needs are clearer.”

The MPC’s coordinator of research and education, Wendy Klein-Schwartz, PharmD, MPH, emphasizes the real-world utility of their research.

“We can examine existing MPC call center data, request data

from other centers or get data from the national network of poison centers,” Klein-Schwartz says. “Analysis of that data often allows us to better serve the community as we may change response and treatment guidelines or generate new guidelines.”

A case in point is recent research carried out on buprenorphine, approved by the Food and Drug Administration in 2002 for home use as a treatment for opioid dependence. Having the drug available in home medicine cabinets increases the likelihood that children will accidentally ingest it. Research was needed about dose and toxicity in children.

“As reported to poison centers from November 2002 to December 2005, we examined data on unintentional buprenorphine overdoses in children age 6 and under who had been followed to a known medical outcome,” Klein-Schwartz says.

The study showed that drowsiness and lethargy were frequent, with serious toxicity with respiratory depression and coma less frequent. Data also showed that potentially serious respiratory depression could occur up to three hours after ingestion.

“With this finding, we were able to recommend that children ingesting 2 milligrams or more, and children under age 2 who ingest less, should go to an emergency department to be monitored for at least six hours,” Klein-Schwartz says. This new information quickly went to the MPC call staff.

Other MPC research projects currently under way include developing more palatable forms of activated charcoal, which is used after poison is ingested, and monitoring patients who have taken an overdose of the anti-depressant Wellbutrin.

Found In Translation

According to Wilks, the School of Pharmacy is in an advantageous position to engage in more translational research.

“We have made great strides working at the interfaces of basic science in pharmacology, pharmacokinetics, and computational and medicinal chemistry,” Wilks says. “We now have a critical mass of faculty and the potential to take research to the next step, which will put us in an excellent position to translate research into clinical practice.”

Among the goals of Eddington are to foster collaboration among disciplines and to commit resources and imagination to research that will ultimately provide innovative pharmaceutical treatments.

“It is clear that our research enterprise is focused on new discoveries, as well as the development and assessment of pharmaceuticals and biotechnology products,” Eddington says. “Our innovation, imagination, and talents will not only boost our research standing among pharmacy schools, but more importantly will transform our research to enhance health care in the state of Maryland and the nation.”