The Pinnacle of Achievement:

N I H

Written by Karen Carlson • Photography by James Hawker

Ed Moticka, Ph.D., associate dean for research and faculty affairs at SIU School of Medicine, has one piece of advice for researchers looking for funding from the National Institutes of Health: "Get to know the program directors. It's their job to help you get funded. It can make or break a grant." He cites one example from his own career in research, where he telephoned a program director about a project he submitted. The director was from the Midwest and was familiar with SIU. "My grant got funded," Dr. Moticka says.

Success stories like that are becoming common at SIU School of Medicine, where in the last five years funding from the celebrated National Institutes of Health (NIH) has grown 50 percent to $6 million. Not a bad improvement for a modestly-sized medical school in the Midwest. "The central part of the country doesn't get as much national funding as the coasts," Dr. Moticka explains.

NIH is renowned worldwide for funding the highest-quality science. Since its beginnings as a one-room laboratory of hygiene in 1887, the NIH has grown to be the leading funding source for the health sciences in the United States, consisting of 27 institutes and centers, including the National Cancer Institute, National Institute of Deafness and Other Communication Disorders, National Institute on Aging, National Heart Lung and Blood Institute and many more.

Receiving an NIH grant, "is the pinnacle of achievement for researchers," Dr. Moticka says. But it's hard work reaching that apex. From the time a researcher submits a grant, the process of review can take nine months before funds are approved or denied.

Among the criteria NIH considers are the project's significance, approach of the design, its innovation, the skill of the investigator and the scientific environment of the institution. After their long and exhaustive review, NIH may bestow contracts anywhere from two to seven years. Funding can range from a few thousand dollars into the millions.

Besides submitting accurate and innovative projects, ambitious scientists face other obstacles to the prized NIH award.

For example, it's rare that a first-time applicant is approved. "You almost always have to submit a revised grant application," Dr. Moticka says. "Persistence is vital." And although there are awards geared toward younger researchers, "It's rare that a researcher under 35 will be funded," Dr. Moticka says. The peak age of researchers receiving NIH funding is 46-50.

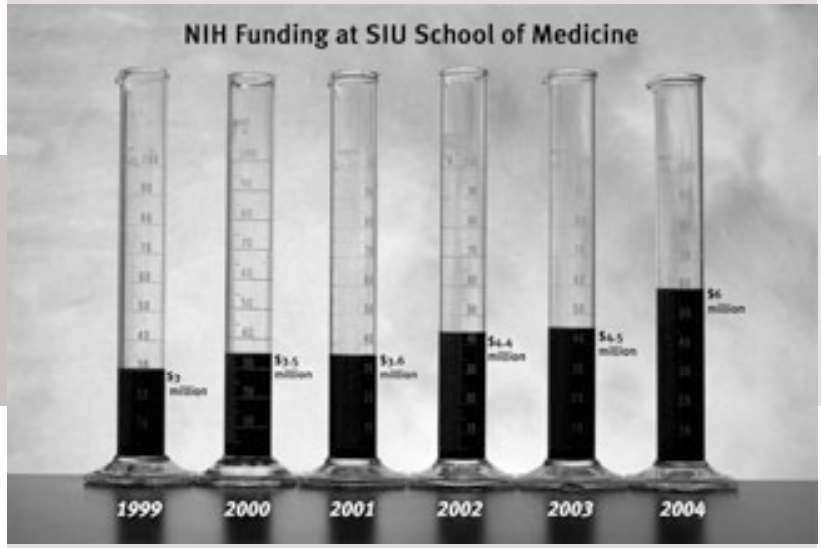
Those with M.D. after their name also have a difficult climb to NIH. The agency requires that scientists log a high percentage of time in the lab. It can be difficult for physicians — committed to seeing patients as their primary function — to squeeze in enough time in the lab to be attractive to the reviewe panels at NIH.

For nearly 30 years, SIU School of Medicine has consistently built a strong reputation at NIH as a quality research institution, initially in the fields of auditory research and more recently in cancer and geriatric research. The School of Medicine's first three NIH grants were given back in 1975, the same year the School held its first commencement.

Enhancing research is a central objective of SIU. In these days of budget cuts, external funding is becoming all the more important for research projects.

The $6 million in NIH grants is funding 29 projects at SIU School of Medicine in both Springfield and Carbondale. That's a healthy part of the $24.1 million the School has earned this fiscal year in total research awards for 177 projects in more than 100 laboratories in Carbondale and Springfield. "In the basic science departments at Springfield, most faculty members do have an NIH grant," Dr. Moticka says.

The NIH will continue to be important for SIU's promising future in research. "Since NIH is such an



In the last five years, the School of Medicine has doubled its NIH funding.

important source of funding for research universities, it is essential that the School continue to increase our success in gaining NIH support," Dr. Moticka explains.

Don Caspary, Ph.D., professor of pharmacology, has the distinction of having the longest record of NIH-funded research at SIU School of Medicine. He is in his 25th year of NIH funding for his auditory work in a project called "Coding in Auditory Neurons: Effects of Amino Acids," funded by the National Institute of Deafness and Other Communication Disorders. The study is examining the neurochemical changes in the central auditory brain processor. The continuing funding has allowed Dr. Caspary to evolve his project over the years. It started as a hunt for auditory transmitters and gradually evolved into an investigation of age-related hearing loss in the late 1980s.

"It's a very personal thing to write grants," Dr. Caspary says. He knows it is disheartening to be turned down, but he urges researchers to be humble. "NIH wants to bet on the winners, so do the best you can with the preliminary data."

He and other researchers hold grant-writing workshops to help their colleagues write and perfect their proposals. "SIU really tries to promote an atmosphere of peer support in reviewing projects," says Pam Helfert, grant administrator in the Office of the Associate Dean for Research & Faculty Affairs.

Though Dr. Caspary's NIH-funded research has totaled more than $4 million over the past two decades, he says that funding is never a sure thing. "I always have doubts when I apply for a grant," he says. His advice: "Work hard and have good people around you. Do the best job you can, and be ready to reapply." His team includes Robert Helfert, Ph.D., Larry Hughes, Ph.D., Lynne Ling, and Jeremy Turner, Ph.D.

The School of Medicine's goal is to be among the top four of the 17 community-based medical schools in NIH funding in the United States within five years. To do that, Dr. Moticka estimates that the School will need to more than double its current awards.

That goal follows SIU Carbondale's plan to become a top 75 public research university in total and federal research and development awards, according to the "Southern at 150" project, a blueprint for the future of the university. The report notes: "Building a culture where research becomes an integral part of all undergraduate and graduate programs is essential." It further acknowledges that national recognition of research and scholarly activities like that gained through NIH funding will best serve the students, so the university will be "considered on par with any public research university in the nation."

While most NIH-funded scientists traditionally have been male, SIU School of Medicine's female researchers are acquiring numerous NIH grants. The SIU Office of Research and Faculty Affairs reports that since 1986, 14 female researchers from SIU School of Medicine have brought in more than $11.4 million in grants from the National Institutes of Health. And most of those faculty members are still at work here. In the past year alone, nine female researchers have received NIH grants for 12 projects, totaling more than $2.2 million.

On the next few pages we'll take a look at three female researchers at SIU who have received funding from the pinnacle of achievement, NIH. ■

CAROL BAUER, M.D.

Translational Tinnitus

The best part of being an academic surgeon, says Carol Bauer, M.D., is getting to do it all: teach, treat patients and do basic and clinical research. "Working with the patients, I can listen to their problems, and that helps me formulate better research questions. Other researchers don't have that opportunity."

Dr. Bauer has used all those skills in her studies of the cause and treatments for tinnitus, chronic ringing in the ears, that afflicts 17 million U.S. citizens.

Dr. Bauer dissects cochleas as part of her tinnitus study.

In the past 12 years, she has acquired numerous grants, including two from NIH's National Institute on Deafness and Other Communication Disorders (NIDCD). Her tinnitus research has received more than $350,000 in funding since 1996. Her research partner is her husband, SIU researcher Thomas J. Brozoski, Ph.D.

Each tinnitus project has built on the results of the previous one, Dr. Bauer says. From developing an animal model in 1992, she was able to create a behavioral model of chronic tinnitus with her first NIH grant, a key development for a disease that has no objective markers. "We developed a chronic model of tinnitus. Before, no one else in the world had a way to study tinnitus in animals over a long period of time." That was an R21 grant, funds aimed to support the early, conceptual stages of research project development.

The model involved training rats to press a lever for a food reward under conditions of background noise and to stop lever pressing when the sound is off. Then, one group of rats was exposed to acoustic trauma to develop tinnitus. "With the constant ringing of tinnitus, we could monitor changed behavior and measure the effects of treatments," Dr. Bauer says. The logic behind the model is that tinnitus can sound like just about anything, except silence.

Her current NIDCD grant totals more than $1 million, and the tinnitus research team will use the same animal model to continue to dig for answers about tinnitus development. "We are looking at neurosignals, the ways that neurons code for sound, to see what the tinnitus signal is in the brain," she notes. The project is an RO1 award, NIH's chief mechanism for funding established research protocols.

Among her achievements is the discovery that an existing drug, Neurontin®, can relieve tinnitus in some patients, a treatment that was revealed by the animal model. Collaborating with Dr. Caspary, SIU Dept. of Pharmacology, she is still investigating the potential of this and other drugs. "This is real translational research," Dr. Bauer says. "The knowledge from the earlier NIH study allowed us to discover the potential of Neurontin®." ■

LINDA TOTH, PH.D.

The Genetics of Sleep

"People often don't get as much sleep as they'd like to," says Linda Toth, Ph.D., DVM, professor of pharmacology and director of laboratory animal medicine. She is studying the mechanisms and functions of sleep.

With millions awarded in NIH funding, Dr. Toth's RO1 grants — one from the National Heart, Lung, and Blood Institute and one the National Institute of Neurological Disorders and Stroke — allow her to characterize how genes influence the pattern of sleep during health and disease, specifically focusing on how infections alter normal sleep patterns, and how sleep loss impacts the mechanisms of infectious disease and recuperation. "Facets of the immune response are likely to mediate the effects of infection on sleep, and sleep may in turn influence facets of the immune response," Dr. Toth says.

As better therapies are developed for some chronic diseases, issues such as fatigue become more important to patients' recovery and overall quality of life. Dr. Toth explains, "Inadequate or poor-quality sleep may increase susceptibility to disease, exacerbate symptoms of disease, or delay recuperation."

Dr. Toth and her staff record the EEGs of mice, comparing the sleep patterns of one genetic strain of mice to another. "We are studying how the sleep patterns change during different infections," she says. "Every mouse of each particular strains we use is genetically identical to all other mice of that strain. We can compare strains to one another and associate the specific types of genes they have with their sleep patterns, and also with factors such as the immune response and temperature response."

She has found that a subset of genes could account for consistent differences among the sleep patterns of mice with influenza. "If we can identify genes that influence responses to disease, then we have a potential target for better therapies."

As a veterinarian and a scientist, Dr. Toth understands both the need to investigate human health problems and the responsibility to treat the animals humanely. Her third NIH grant is funding research to identify additional or improve existing analgesic treatments to keep the mice comfortable during research use.

Dr. Toth measures the EEG signal of her animal subjects .

Her fourth grant, a K26 career development award, allows her to expand her expertise and train others in the behavioral and physiological pathology of mice. "This award gives me time to mentor others and to develop my career as a scientist," she says.

Dr. Toth enjoys looking at both the basic and clinical sides of research. Though she intended to be a veterinarian, not a scientist, research became a kind of addiction, she says, and as she earned her degrees she became "hooked on data." "While on the course of becoming a veterinarian, I learned how to be a scientist. Eventually I realized I wanted to do both." ■

Dr. Pauza works with graduate student Brandon Rakowski.

MARY PAUZA, PH.D.

Chemokine Synergism

For Dr. Mary Pauza, the pleasure of research is asking why — trying to understand something new and novel about how something works.

Her two-year, NIH Academic Research Enhancement Award (AREA) Grant — (R15) from the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health is looking at the function of two molecules called chemokines — small, soluble proteins secreted by cells. Chemokines attract white blood cells to sites of inflammation. Dr. Pauza is studying the impact of these chemokines on the composition, magnitude and kinetics of inflammatory responses, specifically in type 1 diabetes.

Looking at two chemokines, CXCL 9 and CXCL 10, which were believed to be redundant, Dr. Pauza and her team are finding instead that they are potentially synergistic — that is, they are complementary, working together to recruit white blood cells.

These two chemokines bind to the same receptor. If researchers can identify and control the receptors, the chemokines could not call other cells to the sites. That could reduce inflammation, thereby slowing or preventing disease.

Using osmotic infusion pumps full of chemokines, Dr. Pauza can precisely measure the proteins' behavior in the peritoneum of mice (*in vivo*), identifying the specificity, magnitude and kinetics of the chemokines' cellular recruitment, measuring different concentrations of the chemokines and distinguishing different cell types.

"The more we can understand about how cells are attracted to sites of inflammation, the more likely we will be able to design ways to control it," Dr. Pauza says. That has relevance to any kind of inflammatory situation — anything from a cut on a hand (where inflammation may be a beneficial part of the healing process) to type 1 diabetes and other diseases most people don't associate with inflammation such as transplant rejection and atherosclerosis.

"Basic science research can be just as rewarding as clinical research," she says. "The majority of clinical research has its basis in basic research. I love the quest in basic research; I love to ask why something works and how it works." ■