

PROGRAM SPOTLIGHT

The University of Texas Medical Branch

EXPERIMENTAL PATHOLOGY: EMERGING AND TROPICAL INFECTIOUS DISEASES

KIM NAGY

In 1967, the Surgeon General of the United States suggested that the war against infectious diseases had been won. In fact, they continued to emerge, reemerge, and spread in human populations around the world—a grim reality soon to be recognized with the shock of the HIV/AIDS pandemic in the early 1980s. In recent years, infectious diseases have once again claimed international attention as the magnitude and scope of natural and manmade microbial threats, along with public perception about their dangers, increase around the world. Researching Lassa Fever virus, and West Nile virus is all in a day's work within the laboratories of the Experimental Pathology Program at the University of Texas Medical Branch (UTMB) in Galveston.

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THE BIRTH OF A PROGRAM

Nearly seventeen years ago, Dr. David Walker accepted the Chair in Pathology at the University of Texas Medical Branch in Galveston with an ambitious plan for the future. One of his immediate goals was to recruit leading researchers and faculty members who would support the establishment of a Ph.D. Program in Experimental Pathology. He also hoped to build a center for the study of tropical diseases, an aim that was realized when the Center for Tropical Dis-

ases was inaugurated in 1994. Ten years later, the Experimental Pathology Graduate Program has grown into one of the most reputable in the nation, with over 30 students enrolled in the Ph.D. program, a prestigious faculty, and diverse research with the most sophisticated research facilities in the world.

Described by faculty members as an “open-minded visionary,” Dr. Walker developed his curiosity about infectious tropical diseases during his third year of medical school at Vanderbilt University. Walker said, “I realized my focus was outside the mainstream.” With his attraction to laboratory research, he also knew that he didn’t want “to be writing prescriptions.”

After graduating from medical school, Dr. Walker interned at the Peter Bent Brigham Hospital at Harvard University and conducted research at the Gorgas Memorial Laboratory in Panama. He also worked as a Research Medical Officer in the U.S. Public Health Service and at the Centers for Disease Control in Atlanta. The author of over 200 scientific papers, 5 books, and 92 book chapters, Walker currently holds 7 patents.

Dr. Walker’s thirty-year research career has focused on tick-related diseases, particularly rickettsias and *Ehrlichia*, and he has made important contributions to the discovery and characterization of emerging infectious diseases, including human granulocytotropic anaplasmosis and flea-borne spotted fever. His pioneering utilization of the application of immunohistochemistry to infectious disease provided diagnostic methods for rickettsioses and the first identification of the target cells of rickettsialpox and scrub-typhus. He has conducted research projects and trained international scientists all over the world, including Slovenia, Mexico, Inner Mongolia, Peru, Cameroon, Brazil, and Japan. Walker is also the founding director of the World Health Organization Collaborating Center for Tropical Diseases and the Center for Biodefense and Emerging Infectious Diseases Research at UTMB.

THE BEST AND BRIGHTEST

Under Dr. Walker’s direction, the educational program at UTMB has grown dramatically since the early 1990s. Not only did he

quickly recruit leading faculty to the program, but he also boosted the funding and research that attracted highly qualified graduate students to Galveston.

Dr. Stanley Lemon, Dean of the School of Medicine, commented, "After successful early recruitment of faculty in the first few years, the program gained momentum like a snowball rolling down a hill. The number of graduate and postdoctoral applications increased and recruiting the 'best and brightest' students became easy." This growth also eventually led to funding from many external sources, including the National Institutes of Health, National Science Foundation, American Heart Association, Environmental Protection Agency, DARPA, DTRA, NASA, and the Centers for Disease Control and Prevention. Dr. Walker facilitated the rapid expansion of the program "by keeping those grants going." "It was very satisfying to watch the program develop," said Dr. Walker, "but it was more a matter of persistence than lightning striking."

Dr. Norbert Herzog, who joined UTMB in 1989 and is Director of the Graduate Program in Experimental Pathology, reflected, "Initially we were a little frustrated. It was tough getting the word out to students." One of their most successful recruiting methods was to use the Summer Undergraduate Research Program (SURP), sponsored by the Graduate School of Biomedical Sciences. SURP offers a course of summer study for undergraduate students to gain "hands-on" experience in the laboratory. Students who attend these programs during the summer take their excitement for the burgeoning graduate program and its research back to their home institutions and many of them later apply.

Perhaps the easiest aspect of establishing the program was getting an already enthusiastic faculty on board. "After that," Dr. Herzog said, "it was just a matter of slogging through the paperwork."

According to Dr. Walker, the students enrolled in the program demonstrate its strength. "At UTMB, our students have a strong idea about what they want to do. They are very excited

about the opportunity to investigate clinically relevant problems with scientific rigor. They want to make a difference and are motivated by the subject matter.”

A COLLABORATIVE ATMOSPHERE

For many of the faculty, the program in pathology at UTMB offers an academic environment where you can easily bounce your ideas off other scientists. “Never have I been at a place that has such a collaborative atmosphere,” said Dr. Herzog. “There isn’t a ‘what’s in it for me?’ attitude. When prospective graduate students interview, they can sense the collegiality here.” He added, “This attitude makes a tremendous difference in research.” Dr. Robert Tesh, Codirector of the World Arbovirus Reference Center, said, “At UTMB, there are no barriers to working with other people in the University.”

Students are also often attracted by the range of research encompassed in the program. As Dr. Scott Weaver, Chair of Graduate Student Admissions and Recruitment, remarked, “Researchers know that UTMB is the place to go as there are only a few places like it around the world. The applicant pool is way up for infectious disease work. One of the nice things about the program that surprises many applicants is that experimental pathology at UTMB covers a huge breadth of research from ecology to pathogenesis. So there are a wide variety of approaches and opportunities, from field work in the tropics to epidemiological studies.”

“Toxicology and infectious diseases may seem to have nothing to do with one another, but students in each branch can contribute a great deal to the overall discussion,” Dr. Walker said. By pursuing both traditional and nontraditional research, researchers find themselves in a far better position from which to pursue every angle of infectious disease, from prevention to therapeutics.

Fields of concentration in UTMB’s pathology program reflect this interdisciplinary approach, including the study of viruses and bacteria and other intracellular pathogenic organisms, mechanisms of chemical injury, environmental toxicology,

chemical carcinogenesis, cellular signal transduction, vector biology, neuropathology, renal pathology, and mycology.

BUILDING CRITICAL MASS

Last September, UTMB was selected as the site of one of two National Biocontainment Laboratories (NBL) in the country by the National Institute of Allergy and Infectious Diseases (NIAID), and it is already the lead institution for one of eight Regional Centers of Excellence (RCE) for Biodefense and Emerging Infectious Diseases Research, for which it received a \$48-million grant. The Biocontainment Laboratory award came with a \$110-million grant to help build a seven-story, state-of-the-art research facility, where pathogens can be studied safely. UTMB is the only institution in the country to receive both the NBL and the RCE designations awards. With more than 374,000 square feet dedicated to research and \$110 million in sponsored research grants, UTMB also hosts three World Health Organization collaborating centers.

“My main resource is my building,” Dr. Walker said, referring to the Center for Biodefense and Emerging Infectious Diseases Research. Located at the academic heart and center of campus, this building has literally changed the physical map of UTMB. Highly specialized resources there include the Robert E. Shope Biosafety Level-4 (BSL-4) Laboratory. This laboratory houses highly infectious agents, including a wide variety of hemorrhagic fever and encephalitis viruses. While the current Center contains 2,000 square feet of BSL-4, the forthcoming Biocontainment Laboratory will house 13,000 square feet of such space.

Dr. Walker has always acknowledged the importance of community relations in his administrative approach, particularly emphasizing faculty and staff efforts to allay concerns about contaminant agents. “We held meetings early on and directly addressed questions about environmental impact, and we gained community support. We haven’t had many problems. Fears always arise, but we faced the hardest questions with the facts,” Dr. Walker

commented. “We work with research quantities in these labs, not the amount you would use to make weapons,” said Dr. C. J. Peters, Director of Biodefense for the UTMB Center for Biodefense and Emerging Infectious Diseases Research and Director of UTMB’s BSL-4 laboratory, who himself has conducted research on Ebola in Africa and hemorrhagic fever in Bolivia.

Peters added, “The lab allows you to work on viruses that are not studied anywhere else. There are some serious opportunities now. Until ten years ago, it wasn’t considered a growth area. This is long overdue. Research efforts on these viruses have all been so under funded in the past. There remains a dearth of scientists trained in BSL-4. It takes a lot more than putting on a space suit.”

Increasing opportunities for research at UTMB signify not only the current “buzz” around infectious diseases but also the faculty’s commitment to their underlying mission: alleviating human suffering through the prevention, diagnosis, and treatment of infectious disease.

A PRACTICAL VISION

Researchers at UTMB work side by side with government public health agencies nationally, such as the Centers for Disease Control and Prevention, and internationally, such as the World Health Organization. By pooling their resources, researchers can more quickly assess biological threats to humans. “Public health is the answer to disease,” Dr. Tesh said. “If you can understand the ecology, you can better understand and control the disease.”

The study of infectious diseases is also tied directly to developing vaccines that prevent them entirely. Dr. Douglas Watts, Associate Director for Scientific Administration for the Regional Center of Excellence, oversees and manages research aimed at the development of products for diagnosing, treating, and preventing infectious diseases that pose biodefense and public health threats. Dr. Watts, who has served in numerous high-ranking positions in the field, including Chief of an

Arboviral Diseases Research Program at the Walter Reed Army Institute of Research in Washington, D.C., and Scientific Director of the Naval Medical Research Center Detachment, stresses that interface with industry is crucial in this pursuit. “Infectious diseases have been with us since the origin of mankind. They will continue to present us with public health challenges. Look at the versatility of these agents and their ability to mutate. . . . It can take decades to produce an effective vaccine. Fifteen years would usually be considered excellent time.” Between receiving approval from the Food and Drug Administration and collaborating with biopharmaceutical companies, creating vaccines can also be a bureaucratic challenge. “It will take the right partners to carry this through,” said Dr. Peters.

PREPARING THE FUTURE

Dr. Walker is most proud of the educational program he has helped build at UTMB. “We are very fortunate that Dr. Walker is a clinical scientist who appreciates the importance of graduate education,” said Dr. Herzog. As a passionate teacher himself and winner of the Bromberg Professorship for Excellence in Teaching in 2001, Dr. Herzog hopes to inspire and support a new generation of biomedical scientists. “Teaching is the best way to influence the next generation. We have a responsibility to teach what we have been taught.”

Over the past ten years, the pathology program at UTMB has grown into one of the most important communities of biomedical research in the nation. As faculty members directly pursue public health efforts against bioterrorism, SARS, and West Nile virus (among other biological threats), their role has become more important than ever before. As Dr. Herzog said, “The world has come to appreciate that we have not won the war on infectious disease.”