ACCP MODEL PRACTICE

Model Practice in Clinical Pharmacy Research: Clinical and Experimental Therapeutics

American College of Clinical Pharmacy

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Background

Individuals are needed to perform both clinical and translational research to make the best use of the results of decades of basic science research.[1] In stroke research, the inability to translate preclinical research into effective treatments has made acute stroke the most "undertreated" of the leading causes of death in the United States.[2] Only tissue plasminogen activator, which is administered to less than 5% of patients with ischemic stroke nationwide, has been incorporated into widespread use.

The Stroke Laboratory of the Program in Clinical and Experimental Therapeutics (CET) at the University of Georgia has a simple mission: "to develop a new treatment for stroke patients." Using animal and cellular models of experimental ischemia and reperfusion, the laboratory is focused on identifying new tactics for intervention, based on known pathophysiologic processes, and translating them into safe, effective, and feasible treatments for human victims of stroke. The laboratory's knowledge of, and capacity for, both clinical and experimental stroke research adds to its competitiveness for extramural research funds and consultantships.

Description

The Stroke Laboratory at the Charlie Norwood VA Medical Center in Augusta, Georgia, was established in 2000. Initially funded by a start-up package (including personnel) from the

Stroke Laboratory Staff: From L to R: H. Elewa, Ph.D. candidate; S. Fagan, Pharm.D.; A. Kozak, M.S., Asst. Research Scientist; L. Machado, Ph.D. candidate; and A. El-Remessy, Ph.D., Assistant Professor and Collaborator

University of Georgia College of Pharmacy, the Stroke Laboratory is adjacent to the Cerebrovascular Research Labs of the Department of Neurology. The laboratory is furnished with a state-of-the-art small animal surgical setup with anesthesia, microscope and equipment for image analysis, wet-lab supplies for protein quantification, and computer stations for students and staff. The Stroke Laboratory was founded with the following core values: ingenuity, collaboration, positive attitude, dedication, responsiveness, independence, and commitment to learning, and all laboratory members were asked to incorporate these values into their daily activities. Members of the laboratory have included research scientists, laboratory technicians, research assistants, graduate students in the CET program, and rotating undergraduate and professional students from various disciplines. Laboratory meetings are held regularly (usually weekly) to present and interpret data, perform regular training required by regulating bodies, and plan upcoming work. A key quality characteristic of the Stroke Laboratory is its extensive collaboration with experts in clinical neurology, cell biology and anatomy, vascular biology, medical physics, and physiology. Graduate students in the Stroke Laboratory are encouraged to learn new techniques from other laboratories to incorporate into their own stroke research projects.

Outcomes Assessments/Impacts

Since its founding in 2000, the Stroke Laboratory has successfully attracted extramural funding (20 grants totaling more than $2.1 million with Fagan as primary investigator) from various sources, including the National Institute of Neurological Disorders and Stroke (NIH); the American Heart Association; the VA Merit Review;

Pfizer, Inc.; Bristol-Myers Squibb; and the Amyotrophic Lateral Sclerosis Association. In the same time frame, the laboratory has published 43 peer-reviewed publications and has presented research papers at 23 national or international scientific meetings. In addition, five students have received scholarships or fellowships from the American Heart Association for their research projects in the Stroke Laboratory. The laboratory currently has two graduate students in the final stages of preparation for graduation with a Ph.D. in CET. Their graduation is anticipated in late 2008.

Perhaps the most notable accomplishment of the laboratory to date, however, is the preclinical work in the Stroke Laboratory[3,4] investigating the use of minocycline as a neuroprotective strategy in the treatment of acute ischemic stroke, which has resulted in the initiation of an NIH-funded Phase I dose-finding trial of minocycline in human patients with stroke (scheduled to recruit the first patient in April 2008). The laboratory is currently investigating two other strategies for neurovascular protection after ischemic stroke that are promising: candesartan[5] and atorvastatin.[6] In particular, acutely administered atorvastatin to diabetic animals undergoing stroke was profoundly neurovascular protective, which was honored by an oral presentation at the AHA Scientific Sessions in 2007.

Applicability and Sustainability

New treatments for acute ischemic stroke are greatly needed; yet, despite repeated failure, optimism remains that agents that are acutely protective or that enhance recovery can be developed. The Stroke Laboratory of the CET program is likely to continue to be successful in attracting funding and creating new knowledge that will be directly

beneficial to patients with stroke. The traditional approach has been to identify targets for intervention and then choose safe drugs that could be used for those targets. Many pharmacological strategies have already been shown to be safe in humans; such strategies have known pleiotropic effects that can be exploited for vascular therapeutics.[7,8] It is anticipated that a great many questions will continue to be asked and answered through therapeutics research in the coming decades.

Maintaining an effective laboratory-based translational research program requires a constant stream of funding. Regular preparation and submission of grant applications (up to one per month) to a variety of funding sources is necessary to ensure that lapses in funding do not result in the loss of extremely valuable and difficult-to-replace staff members. The animal and tissue models used require years of practice to perfect; therefore, consistent, senior research staff is an essential component of sustainability. In addition, a constant infusion of "new blood" through professional and graduate students is necessary to maintain the scholarly, academic environment and contribute to their steadily increasing presence in the literature and at national meetings.

Potential Problems and Possible Solutions

One of the potential problems for a research endeavor of this type is a lack of institutional commitment. Colleges of Pharmacy have increasing pressures to provide additional, labor-intensive experiences for pharmacy students, causing many such colleges to divert human and financial resources toward the support of clinical and educational endeavors and prioritize these endeavors above research. A long-range vision and a commitment to training pharmacy educators of the future,[9] as with the leadership of

the University of Georgia College of Pharmacy, make investment in research sustainable. Institutional commitment is imperative for a promising research program to flourish. Up-front investment in space and start-up is a prerequisite for the future success of any researcher.

Another potential problem is faculty recruitment. Any translational researcher needs collaborators who can assist in bringing projects to a successful end point. A lack of competitively trained pharmacy scientists makes it difficult to get a "critical mass" of faculty to maintain a graduate program. A creative approach and the casting of a wide net (perhaps an advertisement in *Science*?) are required to recruit researchers who are likely to be successful in a highly competitive field. Colleges cannot afford to invest in a junior faculty member with a large start-up package unless there is a high likelihood of return on investment. For example, potential faculty members MUST have already published research papers, submitted grants, and obtained funding for their research to be considered a reasonable risk.

Future Perspectives

Clinical pharmacy scientists who are competent in both clinical and experimental therapeutics are in demand. As a profession, we must ensure that colleges of pharmacy continue to produce individuals who can fill future faculty ranks and improve human health in their unique way.[9]

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