PhD Programs Adopt Bench-to-Bedside Model to Speed Translational Research

Bridget M. Kuehn

WITH THE HELP OF A TOTAL OF $10 million in training grants from the Howard Hughes Medical Institute (HHMI), 13 graduate schools across the country are reworking their curricula to give PhD students a solid background in clinical medicine.

The revamped programs aim to speed translational research by boosting the number of clinically savvy basic research scientists. They are Baylor College of Medicine (Houston, Tex); the Cleveland Clinic Lerner College of Medicine at Case Western Reserve University (Cleveland, Ohio); Harvard University (Cambridge, Mass); Massachusetts Institute of Technology (Cambridge); Rice University (Houston, Tex); Stanford University (Stanford, Calif); the University of Alabama, Birmingham; the University of California, Davis; the University of California, San Diego; the University of North Carolina, Chapel Hill; the University of Pennsylvania, Philadelphia; the University of Washington, Seattle; and Yale University (New Haven, Conn). Each of the graduate schools has designed a unique program that mixes elements such as medical course work, seminars, clinical rotations, and 2 mentors—one physician, one scientist.

While research in areas such as genomics, proteomics, and molecular biology have led to huge advances in basic science, these advances have been slow to yield clinical advances. A shortage of qualified investigators conducting clinical research is one reason that has been cited (Sung NS et al. *JAMA*. 2003;289:1278-1287 and Pober JS et al. *FASEB*. 2001;15:2303-2313). The length of time required to complete MD-PhD programs has reduced the pool of physician scientists, while funding and promotion structures that favor basic research have kept many scientists from pursuing translational research, according to the articles. Additionally, the structure and culture of many research institutions discourage the kind of collaborative, multidisciplinary teams necessary for successful translational research.

To help overcome some of these obstacles, HHMI has developed a training grant program specifically designed to foster translational research. Peter J. Bruns, PhD, HHMI vice president for grants and special programs, said the institute has two goals for the training grants. One is to produce basic scientists who will have a strong clinical background and be able to bring discoveries from bench to bedside. The other is to unite the faculties of graduate and medical programs to foster interdisciplinary research and collaboration.

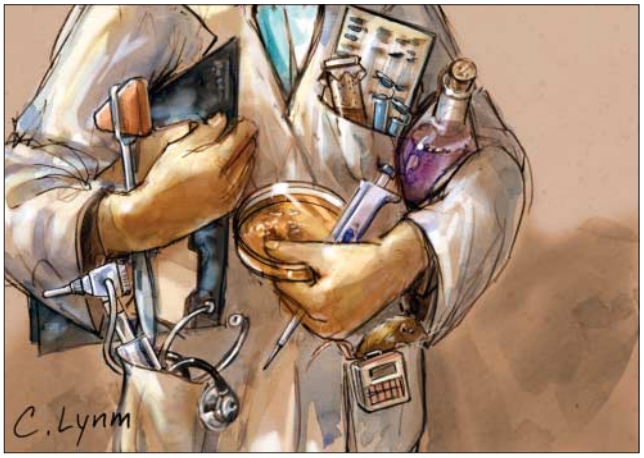
"We are really trying to bring PhD scientists into a partnership with the medical research community," Bruns said.

In addition to funding the training grants, HHMI will bring together the programs' directors each year to allow them to share successful strategies. Officials from the National Institutes of Health also will be invited to attend these meetings, and Bruns said he hopes that the agency will decide to provide financial support for such programs in the future.

NEW DEGREES

To familiarize laboratory scientists with the basics of medicine, many of the programs receiving HHMI grants will require students to take courses from their institution's medical school's curriculum. Some will provide these students with specialized degrees.

Stanford University's Master of Science in Medicine program is offering students a dual degree track, in which students can simultaneously earn a master of science degree in medicine and a doctorate in a basic science discipline.



A new effort is under way to enhance the training of biomedical scientists by giving them a strong clinical background that will prepare them for a career in translational research.

Ben A. Barres, MD, PhD, a professor of neurobiology at Stanford and director of the new master's degree program, explained that while medical students who are interested in research have the option of pursuing a joint MD-PhD degree, until now there had not been a similar option for scientists with an interest in medical or translational research.

The program will start next fall with 6 students who will spend their first year and a half taking courses in the medical school along with courses in their basic science discipline. They will also attend a series of seminars on issues in translational research. During the second year, the students will select a laboratory in which to conduct their PhD research, as well as a physician co-mentor. For example, explained Barres, a student choosing to work in Barres' laboratory studying failure of the central nervous system to regenerate might select as a clinical mentor a neurologist for discussions of the clinical implications of the research. Completing the joint degree program will add about 12 to 18 months to the time students normally take to complete their PhD.

Barres anticipates many of the students who complete the program will go on to conduct translational research. There is an increasing realization that as things become more specialized in medicine, there is a greater need for a dialog between physicians and scientists, Barres said. He added that translational researchers must understand clinical needs to fill the gaps.

Case Western Reserve University is using its training grant to help fund a new PhD program in molecular medicine that will be offered through the Cleveland Clinic Lerner College of Medicine. The program will complement the college's innovative medical degree program, which incorporates problem-based learning, small groups, and a requirement that medical students conduct research for 1 year and complete a thesis. Martha K. Cathcart, PhD, a professor of molecular medicine at Case Western Reserve University and a researcher at the Cleveland Clinic, will lead the new PhD program.

"Our goal is to train students who can be comfortable and know the limits and regulations involved in taking laboratory findings and applying them to a clinic situation," Cathcart said. She explained that students who graduate from the program would ideally go to work at academic institutions affiliated with medical centers.

The students will begin the program with course work in physiology and go on to take more traditional basic science courses in such areas as cellular and molecular biology. Basic science course work will be paired with demonstrations from clinicians about how the subject relates to clinical situations. For example, students learning about mitochondria and electron transport also will see a presentation from a clinician who will describe a condition caused by a defect in an enzyme that is important for mitochondrial function.

The program's instructors will come from a variety of medical and academic institutions affiliated with Case Western Reserve University and the Cleveland Clinic, which have recently merged. Cathcart said she hopes the effort will help familiarize students with the various vocabularies used by different disciplines and prepare them to successfully collaborate during their career with scientists with different backgrounds.

"It's been very hard to train scientists with adequate clinical and scientific knowledge to have a career where they integrate both," she said.

After they complete their course work students will choose an advisor and begin their thesis work, which must have a translational bent. They will also select a clinical mentor.

ENGINEERING AND CANCER

Applying bioengineering to real-world problems in diagnosing and treating cancer will be the emphasis of the training program at Rice University, which is teaming up with the University of Texas MD Anderson Cancer Center.

The program, which will begin this summer with 7 students from Rice's bioengineering program, requires each student to complete two clinical internships. During the first internship, students will do rotations through the various clinical specialties at the MD Anderson Cancer Center, such as diagnostic cancer imaging, surgery, radiotherapy, internal medicine, laboratory medicine, pathology, cancer prevention, and bone marrow transplantation. The goal of this internship is to help students understand the current clinical challenges physicians face and to see firsthand the capabilities and limitations of biomedical technology, said Rebecca Rae Richards-Kortum, PhD, professor of bioengineering at Rice and director of the program.

The second internship, which takes place the following summer, will be in a specialty related to the student's thesis project. For instance, a student conducting research in Richards-Kortum's laboratory researching improved early detection methods for cervical cancer would complete an internship in gynecologic oncology.

In addition to traditional bioengineering courses, the students will take five courses in cancer-related medical and translational research topics taught by medical center faculty or by bioengineering faculty. Students will also select a physician co-mentor. They also must participate in a series of seminars that will bring together a basic scientist, a clinician, and an engineer to discuss a common problem. Second-year students in the program will be responsible for organizing each year's seminar series. Richards-Kortum said she hopes organizing the seminars will help students learn to identify leaders in various specialties and teach them the organizational skills they will need to bring together multidisciplinary teams for their future research.

"We're hoping it will bridge some of the gulfs that have existed between the basic science side, the applied technology development side and the clinical side," Richards-Kortum said. "We'll have students who can speak the language of all three disciplines."