Zooming in. Catherine Wu at Dana-Farber Cancer Institute forged her own path in translational research, but new training programs are making that career path easier.

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Carving a Career in Translational Research

An influx of public and private funding is invigorating a field that challenges some traditional notions of science

As a first-year hematology-oncology fellow at Dana-Farber/Partners CancerCare 10 years ago, Catherine Wu recognized that if she wanted to bridge research and clinical practice, she needed to understand her options. Every day for 2 months, she questioned senior and junior faculty members on the basic and clinical ends of the research spectrum—no small task for someone working 13-hour days, typically without a break.

She ultimately chose to study leukemia patients' immune responses to bone marrow transplants, an area conducive to translational research in part because the work involves treating patients with human cells, which can be prepared at academic health centers. Now a medical oncologist at the Dana-Farber Cancer Institute in Boston, Wu is professionally fulfilled by work that involves a steady interplay between clinic and lab. "There is something truly incredible about seeing whether your patients benefit from the therapy that you've devised," she says. "It inspires you to do better, to think more broadly, to generate the tools that you need to understand what's going on in your patients."

Bridging the divide that separates laboratory biomedical research from improvements at the clinic has always been difficult. Now, translational research has emerged as a field in its own right, aided in large part by the National Institutes of Health (NIH) Roadmap for Medical Research, a collection of initiatives that prioritize efforts to shepherd biomedical discoveries into clinical application. As translational research has gained momentum, training opportunities in the field have expanded rapidly.

Still, embarking on a career in translational research is hazardous, says Anthony Hayward, clinical research director for NIH's National Center for Research Resources. "It's a tremendous leap of faith for young investigators to commit themselves to translational research. It takes a special sort of person; you have to be willing to take risks."

Follow the money

Part of that risk is in funding: Budgets for biomedical research are tight and may remain so for several years. However, funding for translational research appears to be growing. Perhaps the most visible evidence of growth is NIH's new Clinical and Translational Science Awards (CTSA) program. The first 12 CTSAs were bestowed last October, and more will be announced in September. NIH plans to fund 60 awards altogether, worth about $500 million annually by 2012. CTSAs are required to include training and career-development components, and the initial dozen devote about 13% of their budgets to these areas.

"This is what American medicine has tried to do for many, many years," says Robert Rizza, who directs the recently awarded CTSA program at the Mayo Clinic in Rochester, Minnesota.

Training opportunities abound

M.D.-Ph.D. programs are one obvious approach to training young investigators who want to do translational research. An M.D. degree followed by a research fellowship or a postdoc is another.

But institutions all over the United States are developing shorter, more integrated programs that cater to both physicians and Ph.D. scientists. The Mayo Clinic, for example, offers a master's program and a 1-year certificate program in clinical and translational science, both aimed mostly at M.D.'s. Demand for these programs, both now integrated into Mayo's CTSA, has mushroomed, says Sherine Gabriel, director of education resources at the Mayo Clinic's CTSA. "There is such a hunger to do this," Gabriel says. "My biggest challenge is dealing with the queue outside my door." The master's program in clinical and translational science, she says, enrolls more students than all other master's programs at Mayo together.

Other research-oriented programs, many funded by private foundations, try to capture the interest of M.D.'s earlier. The Howard Hughes Medical Institute (HHMI) in Chevy Chase, Maryland, operates two programs that allow medical students to take a year out of medical school to conduct basic laboratory research. The Doris Duke Charitable Foundation in New York City runs a similar program focused on clinical research. Some schools also independently offer such "1 year out" programs.

Translational research training for Ph.D. scientists has been getting more attention, too. Gary Koretzky, associate director of the University of Pennsylvania's M.D.-Ph.D. program, says institutions have started to recognize that "if you give [basic scientists] the vocabulary of medicine and a sense of how physicians think about problems that they encounter with patients, they'll find it easier to do research that is both scientifically

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rigorous and relevant to disease processes and patient care."

M.D.-Ph.D. neurobiologist Ben Barres, who directs a new master's of medicine program for science Ph.D. students at Stanford University in Palo Alto, California, welcomes the shift. Students do the math, Barres says, and "realize that if they did all the traditional training for both degrees, they'd be almost 40 before they finished. It's just too much."

Stanford's program is one of 13 new "Med Into Grad" programs that HHMI launched last year. Students complete the same 1½-year course sequence that all medical students complete, taking classes alongside med students while also working on Ph.D. requirements. Other Med Into Grad programs offer more targeted pieces of the medical school curriculum to science students—for example, steering neuroscience students toward neuroanatomy courses.

These programs are still in their early years, but it's evident that they will be popular. Barres says Stanford's program has been flooded with applications. "There's been a sea change of interest from the Ph.D. students compared with 5 or 10 years ago," he says. Twenty percent of incoming Ph.D. students from Stanford's biosciences programs applied for the program in its first year, Barres says.

Other options are proliferating. This year the Mayo Clinic, like many other CTSA recipients, enrolled its first students in a new Ph.D. program in clinical and translational science. Students work with a multidisciplinary mentoring team to develop research projects and take on a core curriculum that includes rotations in bench science, patient-based clinical research, and population-based research. Coursework is designed to build skills in designing clinical trials, responsible conduct of research, and grant writing. "We want students to explore questions that cross disciplinary boundaries, then develop research projects that are every bit as deep and rigorous as any traditional research project," says Gabriel.

Funding independent research

The transition from trainee to independent investigator is a particularly vulnerable point in a translational researcher's career. William Crowley, director of clinical research for Massachusetts General Hospital in Boston, observes that, although NIH's many programs to support training in clinical and translational research have been "spectacular," the academy is now filled with well-trained translational researchers, all trying to land independent research grants just as the NIH pay line is plummeting. "We're about to lose a generation of young translational investigators," he says.

To avert that outcome, "we need long, steady investments in translational research, not dramatic ups and downs," says Queta Bond, president of the Burroughs Wellcome Fund (BWF) in Research Triangle Park, North Carolina. Her organization and others have stepped in to help. BWF's Career Awards for Medical Scientists provide $700,000 over 5 years to bridge postdoctoral or fellowship training and the early years of independent research. BWF Clinical Scientist Awards in Translational Research provide $750,000 over 5 years to faculty members in the late-assistant-professor or early-associate-professor stages of their careers. The intention of the translational awards, says Bond, is to buy time for junior faculty members "to keep them in research and keep them training younger investigators." Last year, HHMI gave out its first early-career awards—initially to 13 investigators, a group that soon expanded to 20. Awardees receive $375,000 over 5 years.

Translational training. Ben Barres of Stanford directs a new master's of medicine program for science Ph.D. students.

CREDIT: COURTESY OF BEN BARRES

The pharmaceutical industry is another potential player in providing career support for young investigators, but so far it's untapped. The Clinical Research Forum, a consortium of leading academic health centers headed by Crowley, has asked pharmaceutical companies for a combined $10 million per year for 3 years (the minimum length of time the group expects NIH budget problems to persist), to create "bridging awards" for young investigators who have completed an NIH clinical research training grant, have narrowly missed receiving funding for an independent grant, and are employed at institutions that will match the funding and allow recipients to spend at least 75% of their time on research.

It's a creative strategy, but Crowley won't place odds on the initiative's success. "I just don't know how pharma views its collective social responsibility," he says. Some companies have indicated interest, he says, but "no checks are in the mail."

Translating success into tenure

Scarce funding isn't the only barrier that young translational researchers encounter. Other factors challenge traditional measures of scientific success. For example, grant and tenure success depends on researchers' ability to publish in top journals, but as Wu observes, "translational research deals with patients, and patients aren't a model system. Establishing causality is always a challenge. It's not a slam-dunk that you're going to get into *Science* or *Nature*."

Some translational researchers worry that their individual efforts on multidisciplinary teams will go unrecognized, hindering chances for promotion and grant success. In 2006, NIH began accepting grant applications that identify more than one principal investigator, a measure that may partially address this concern.

Physician-scientists—an important part of the translational-research work force—face mounting pressure to generate income through patient care. That makes it tougher than ever to carve out time for research, says William Galey, HHMI's director of graduate and medical education. Crowley adds that complex and conflicting requirements from multiple regulatory bodies "make translational research look as daunting to a young investigator as a steeplechase racecourse looks to a horse."

These obstacles and others add up to the conclusion, Crowley says, that "there's a lot of easier ways to make a living." Nevertheless, he says, "there has never been a better time or opportunity to do good and alleviate human suffering by research than now. If I have one regret about my career in translational research, it's that I'm not 30 years younger."

Time will tell whether institutions and funding agencies will sustain support for translational research and continue to plumb the storehouse of basic biomedical advances to help sick people. Meanwhile, researchers entering the fray should do so with optimism and caution. And, Wu advises, "go with what you passionately care about, because it's a long row, no matter how you hoe it."

–SIRI CARPENTER

Siri Carpenter is a freelance science writer in Madison, Wisconsin.