Translational Research Going Mainstream

By Joel B. Finkelstein

For the past decade, a small division of the National Cancer Institute has been quietly brokering alliances between laboratory scientists and clinical researchers to streamline the process of translating new discoveries into medical practice.

In some ways, the goals of NCI’s Division of Cancer Control and Population Sciences (DCCPS) run against the grain of an institution that has evolved to answer critical, but often isolated, research questions. In contrast, the DCCPS was established to cut across ideological and scientific boundaries to, in effect, break researchers out of their individual silos and force them to consider the larger implications of their work. “We heavily rely on all the basic and clinical research that NCI supports. But we see ourselves as the connector between discovery and implementation,” said division director Robert Croyle, Ph.D.

As such, the division has its feet in two (or more) worlds and navigates a terrain that spans from molecular biology to epidemiology. Despite that wide reach, the division maintains a central focus. “The principle of designing for dissemination is something we try to integrate into everything that we do,” Croyle said.

By funding research on the dissemination and implementation process itself, such as how evidence is used or why it goes unused in clinical and public health settings, the division aims to speed the translation of research into practice, Croyle said. The division also fills in some gaps in research funding that give it a seemingly eclectic portfolio. For example, the DCCPS funds projects ranging from studies on the links between physical activity and cancer risk to the development of methods for monitoring cancer trends, such as refining statistical models for surveillance, creating measurements for exposure, and collecting data on behavioral risk factors in surveys.

The DCCPS’s portfolio has grown slowly over the past decade, from 570 grants in 1998 to just over 900 last year. The division’s budget remains a fraction of NCI’s overall funding, which has been subject to its own rise and fall over that period. Last year, the division funded a little over $381 million in grants, which is about $20 million less than a few years earlier. In part as a result of those funding realities, under Croyle’s leadership the division has strengthened partnerships with other institutes and agencies, including the Agency for Healthcare Research and Quality.

“A lot of the early detection and lifestyle factors are addressed in primary care. AHRQ is a key player in that, but it’s a small agency, with not a lot of funding. What we have done is complement what they do by supporting health services research specifically relevant to cancer,” he said, adding that the division brings NCI’s 63 research centers to the table as well.

Efficacy and Effectiveness

The division is also focused on building the capability to study how scientific discoveries disseminate into clinical practice. “We have a good system now for tracking cancer incidence and mortality. And we have a good surveillance system for behavioral risk factors, tobacco use, and things like that. But what we don’t have in the U.S. is a national system for monitoring health care delivery and the quality of health care delivery,” Croyle said.

One of the first projects the division funded is the HMO Cancer Research Network, which offers a repository of information on patients with cancer or those at risk of developing cancer and the care that they receive. The data reveal the type of cancer prevention and cancer care being provided to people within the U.S. health care system. Previously that type of data was available only from the Medicare program.

Over the past decade, the Cancer Research Network has published more than 100 peer-reviewed articles, including a JNCI monograph. Studies have looked at whether people are getting cancer screening and if not, why not; what health plans are doing to help their populations stop smoking; and whether prophylactic mastectomy reduces recurrence.

“Until it was studied in well over 1,000 women in our network, it wasn’t clear that removing the healthy breast in a woman with breast cancer conveyed any particular advantage. That kind of study was unlikely to be done as a prospective randomized trial,” said Edward Wagner, M.D., director of the MacColl Institute for Healthcare Innovation and Cancer Research Network principal investigator.

In another study, Wagner and colleagues found that older women with breast cancer are not receiving standard care, negatively affecting recurrence and survival in that population. “That’s the kind of question that you need to have large numbers of women, accurate information about the type of care they’re getting, long follow-up on them—and fortunately we have all of those features,” he said.

With the availability of more data on the effectiveness of new treatments, diagnostic tools, or screening within the community setting, a picture began to

Edward Wagner, M.D.
emerge that looked substantially different, and less optimistic, than would have been expected based on the original research conducted within the academic setting. “A lot of the current interest has come from some disappointments in moving certain interventions out into the community and seeing that they were not nearly as promising as they were in the academic setting,” he said.

Wagner said that through translational research it is becoming clearer why there is a difference between the efficacy of an intervention, that is, how it performs in a narrowly defined population under ideal conditions, and its effectiveness, how the intervention performs in the general population often under less than ideal circumstances.

“Translational research can help us understand what makes an efficacious intervention less useful in the community setting, and then we can take steps to remedy that,” he said.

Research Pyramid
In a sense, translational research is a back-to-basics approach, said Robert Schneider, Ph.D., associate director of the New York University Cancer Institute and a co-director of the institute’s translational research program.

“Years ago, translational research mostly meant applied research, and for a lot of people that’s still what it means. But it’s a concept that is continuously being reinvented. The best explanation is that it’s patient-guided and patient-oriented research,” he said.

All biomedical research was once focused on the prevention or treatment of human disease, but that idea has become foreign to many investigators over the past 20 years as the research itself has become self-perpetuating.

“Molecular biology in its own right is just so fascinating and so important and so exciting that it has largely taken over so much of what we do. Research moved from a focus on animal biology to individual cells,” he said.

However, bench scientists are increasingly beginning to probe questions of a translational nature in part driven by the wider availability of human tissue. Whereas in the past, a researcher may have gone as far as to conjecture about the implications of a new discovery, now he or she can take the next step and test those ideas on cellular material. “Now that we have learned so much about molecular pathways and the functioning of the cell, there is an attempt to bring some of that back toward clinical relevance,” Schneider said.

It’s like a pyramid, where a relatively small amount of translation research is built on a large foundation of excellent basic science. Although far more basic research is needed than translational research, there is currently a need to both improve the quality and increase the quantity of translational research, he said.

The translational research movement is still in its fledgling days, with a few institutions plotting their own courses.

“As translational research has become much more mainstream, this would be a good time for [the division] to project themselves much more and become much more involved and apparent and important in the lives of investigators,” said Schneider, whose own work is currently funded by the Department of Defense and private foundations.