Q&A: Tom Curran on Translational Research

For basic scientists, seeing discoveries change lives can be a profound experience

When the pharmaceutical company he worked for cut his job in basic research, Tom Curran, PhD, changed direction. He landed a job as chairman of developmental neurobiology at St. Jude Children's Research Hospital and co-leader of its brain tumor program.

"Our goal was to develop new treatments for brain tumors, but I knew very little about brain tumors," Curran recalls. "So I spent a week in the clinic. I visited with patients and their families. I was very profoundly affected."

He launched translational research on medulloblastoma and began to help other scientists move into translational work. Now deputy scientific director of The Children's Hospital of Philadelphia Research Institute and associate director of Translational Genomics at the Penn Genome Frontiers Institute at the University of Pennsylvania, Curran is developing programs that introduce basic science researchers to translational science. He shared his perspectives on translational research with *Cancer Discovery's* Suzanne Rose.

What exactly is translational research?

Over the years, there have been multiple, changing definitions, some of which have been pretty strict. I take the broad view that modern translational research embodies the entire continuum from a basic research discovery to the implementation of a new treatment in the clinic.

Is there a bedside-to-bench aspect?

Yes, it's really a 2-way street. Quite frequently, clinical studies affect research in the lab. For example, in recent clinical trials of BRAF inhibitors, some patients developed subcutaneous sarcomas. Research was carried out in the lab to try to understand why that happened, which led to insights into how the RAF and RAS signaling pathways work.

What most surprises basic science researchers about translational research?

As a scientist you have a pretty clear idea of how to design an experiment and interpret data. But when you encounter humans as the experimental subjects, your study design may not be feasible. What's your negative control for the experiment? When you put a face on the negative control, it gets very difficult to imagine treating some patients with a drug that you think works while treating others with standard care. That's when you start to understand the difficulties physicians encounter in developing new treatments.

Regulatory issues are also a surprise. Until people sit in on an IRB (institutional review board) meeting and see that the discussion can become very detailed about what's proposed, they often have no idea about the level of regulation or understanding of the ethical dimensions.

For basic science researchers who want to shift into translational science, what advice can you offer about education or other preparation? Do you need MD and PhD degrees?

The Children's Hospital of Philadelphia

Learning to hand off laboratory discoveries to physicians who will test them in the clinic and to take personal pride in the team's clinical accomplishments are critical for translational scientists, says Tom Curran, PhD.

Having patient encounters in a research setting is very important. Until that happens, it can be difficult to see how the skills you have could be applied in the translational setting. So, visit with clinical researchers. Understand a little bit of their world and understand the patient perspective. Workshops and classes can help with this. You also can approach your colleagues and ask if they can set up an opportunity for you to shadow them in the clinic.

If you look at the successful programs, you will see MDs, PhDs, master's-level scientists, and nurses working together. In this way, diverse educational paths converge to make a truly effective translational team.

Some people have expressed concern that we put MD–PhD candidates through a very long training regimen. They may not need to have all of the clinical training if most of their work will be designing and utilizing clinical trials rather than seeing patients on a daily basis. Maybe we can ground people firmly in basic science and in medical science without spending 7, 8, or 9 years doing it.

Does translational research help to bridge the gap that seems to exist between some MDs and PhDs?

We need to work on breaking down that barrier. One of the first lessons in translational research is that you need to have respect for your peers. If you meet on an equal basis, you will develop synergies that will be more powerful than what either individual is able to achieve alone.

What else should translational scientists expect?

Because I'm not qualified to be treating patients, I can only bring the science so far. I need to partner with physicians who will continue the work in the clinic. So another lesson in translational research is learning to "hand off." A physician who has worked with patients for years should take the lead on the clinical trials. Another aspect to this, which I've heard quoted, is "There's no telling what you can accomplish if you don't care who gets the credit." You need to develop a personal sense of achievement rather than wait for recognition. That might seem hard, but when a bench scientist sees a discovery change someone's life, it's a profound experience. ■