Finding Cures, Saving Lives

Padmanee Sharma
Professor of Immunology and Genitourinary Medical Oncology
University of Texas MD Anderson Cancer Center

Researchers are turning the immune system into a potent weapon against cancer and other diseases. Here's how to accelerate progress.

Staring down the barrel of a cancer diagnosis usually means enduring the harsh side effects of chemotherapy. But the use of chemotherapy may become less frequent as novel therapies are developed. Researchers have made great strides in developing treatments that use the body's natural defense mechanism, the immune system. Immunotherapy pioneers have figured out how to teach immune cells to recognize and mobilize against cancer cells like snipers, thus moving away from the chemo-bombs that can't distinguish malignant cells from healthy ones.

Padmanee Sharma, a physician-scientist on the frontlines of this groundbreaking research, shares her perspectives on these developments in cancer research.

Q: What is immunotherapy, and how did you get involved?

I have been fascinated by the concept of how the immune system can adapt to, recognize, and fight off an infectious agent that comes its way ever since my first immunology course as an undergraduate at Boston University.

The immune system is like a car, with an ignition, gas, and brakes. Early experiments in immunotherapy focused on engaging the ignition switch or stepping on the gas of the immune system. But then it was discovered that the immune system has brakes. Jim Allison showed in murine experiments that these brakes need to be turned off for the immune system to attack cancer. This realization was the paradigm shift in immunotherapy. For the first time, someone suggested taking off the brakes to drive the anti-tumor response. Also known as "immune checkpoint therapies," these have been applied to skin, blood, lung, and bladder cancers, among others.

Q: Why is this field of research getting a lot of attention?

Immunotherapy gives patients, especially those who have exhausted other treatment options, real hope. It's been successful in clinical trials, with some patients continuing to live a decade on after receiving treatment. Immune-related side effects exist, but can be managed. Now we have to take it to the next step and continue to better understand how the immunotherapy agents change patients' immune responses and how they work with other therapies, which will help us to get them to work for more patients.

Q: Where is the field going?

We are learning more and more about how immunotherapy works. At the same time, we are looking for other treatments rather than just the "one size fits all" approach of chemotherapy and irradiation, and toward drugs that target specific cancer-causing mutations, also known as precision medicine, with genomically targeted agents. Efforts to combine immunotherapy and targeted therapies have already begun, with promising overall response rates, though more time is needed to determine the survival rates of patients. The way forward is to focus funding and research priorities so that these complementary approaches can be combined and we optimize our chances for better results for a greater number of patients.

Q: These developments in cancer research allow us to hope for a time when we can actually win this war against cancer, but the path to a cure is long, costly, and risky. What do we need to accelerate this process?

We need to focus on three things:

1 **Collaboration.** Fighting disease has to be a team effort. We need to get government, academia, clinicians, pharmaceutical companies, and nonprofit foundations involved and working together. We need to identify and address the legal and regulatory barriers that get in the way of progress.

For example, I'm part of the MD Anderson Moon Shots Program's immunotherapy platform that brings together the scientific and clinical capabilities of MD Anderson and the global leaders in pharmaceutical and biotechnology development. Partnerships like these are vital because they allow all parties involved to leverage expertise and resources.

2 **Data.** As we learn more about disease and have access to critical information from large cohorts of patients, we must figure out what to do with data to make it meaningful. We have to expand our team to include experts who can help us build the right database that will allow us to interrogate data to advance understanding of disease.

3 **Funding.** We are at a remarkable time in science and medicine, and yet funding for some of the most transformative efforts remains limited. Traditional sources of funding from federal agencies are drying up. Even more reason to ensure that available funding is directed to support efforts that could make a real impact in improving patients' lives.

Research programs in my lab rely on philanthropic funding to get started. Foundations like the Prostate Cancer Foundation and Melanoma Research Alliance allow us to pursue the most promising scientific discoveries and begin to translate these into viable therapies. This seed funding allows us to get established, particularly during a very risky phase in the research process, and attract additional funding needed to move our work forward.

Q: Does what we know in cancer apply to other diseases as well?

First, it's important to remember that cancer is not one disease. It's hundreds. Second, what we're learning about the body's response to cancer therapies is being extrapolated to find solutions for other diseases—from HIV/AIDS to Alzheimer's. And finally, new approaches to cancer research, from adaptive clinical trials to ways of engaging patients, are paving a faster, more effective path for many other diseases. We need to make sure innovation in one disease is translated to another because patients are waiting.