When Olugbeminiyi “Niyi” Fadeyi first started working in drug discovery, he was struck by a statistic he heard tossed around: that there was maybe a 1% chance that a drug he worked on would ever make it to patients. “I really wanted to figure out why,” he says.

Being able to impact patients’ lives is what drew Fadeyi to science in the first place. When he was growing up in Nigeria, his best friend died from sickle cell disease. This loss catalyzed his journey to study chemistry and later chemical biology so he could one day invent treatments for such diseases. In fact, his first project in industry was on a sickle cell drug candidate which is currently advancing in clinical trials.

After almost a decade in drug development, Fadeyi says he now knows why so many drugs fail. “The reason is not because we don’t have good small molecules,” he says. “It’s usually because the biology we’re chasing is wrong.” Tien Nguyen spoke with Fadeyi, who co-leads an interdisciplinary team at Merck Exploratory Science Center in Cambridge, Massachusetts, that is working to solve that problem by developing new technology to better understand the underlying biology. This interview has been edited for length and clarity.

Tell us about your team at Merck

It’s a unique group; it’s very different from traditional drug discovery efforts. I work in a team with folks of all different backgrounds—chemists, biologists, microbiologists, etc. One of the key things that we’re doing is to merge the fields of chemistry and biology. We’re using synthetic chemistry to not only ask really unique biological questions but also develop technologies that enable us to ask those questions.

What is MicroMapping?

MicroMapping technology is a way to identify with high resolution where proteins are in relation to each other.

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We use light-activated photocatalysts to generate reactive species that label proteins immediately proximal to a particular protein.

With this approach, we are now labeling just a very tiny cellular microenvironment—only a few proteins near our protein of interest. In contrast, with existing technology, you end up labeling the entire cellular compartment. As an analogy, sitting here in Massachusetts, if I want to map who is right next to me with our MicroMapping technology, I could say, “Oh, Connecticut is next to me; Maine is next to me.” But with the previous technology, it could erroneously send me off comparing Los Angeles and Boston, when I really want to be comparing Boston to Portland, Maine.

Your team, along with collaborators at Princeton University, used this technique to map the environment of the programmed-death ligand 1 (PD-L1) protein earlier this year. Why did you choose that protein? PD-L1 is a surface protein that’s expressed on tumor cells. It’s a target that’s attracting a lot of attention from those who are interested in treating cancer using immune system targets. Once researchers realized that this protein binds a protein on T cells, a type of immune cell, to block the T cells from killing the tumor cells, several drugs were created to block that interaction. By blocking that interaction, your T cell can still recognize and kill the tumor cell.

But the drugs that block this interaction work in only about 20% of people that have cancer. We don’t know why they don’t work in the rest. So, by MicroMapping near PD-L1, we can identify other proteins that we didn’t previously know either affect or interact in some way with PD-L1. This information could help us figure out what we’re missing with the 80% who don’t respond to these drugs.

How would mapping the microenvironment help scientists design better drugs to block that interaction? The proximal environment of any protein is valuable information. If you understand the microenvironment of that protein, maybe you learn that you need to not just target that protein; maybe you need to target another protein that’s in that microenvironment. On the other hand, what is proximal is not always what is useful. After we learn what’s nearby, we need to go and do knockout studies. If I knock out this protein, do I get a functional response? So knowing the proteins that are proximal gives you leads to find something that’s more functional.

That’s the kind of information that we get from MicroMapping. And that’s not just for oncology or immunology. You can imagine you can go into any area of biology where you want to understand the microenvironment of a particular protein.

What excites you about the work that you’re doing? Thirty or 40 years ago, the way we did medicinal chemistry and the way we did science were completely different. The technologies that we have now to apply to the problem of solving disease have gotten a lot better. I feel excited in the morning just for the fact that I’m in this generation. I really do feel that we can make important discoveries that can benefit patients.

I also love what I’m doing because of the people that I work with. I get excited about working with people from completely different backgrounds. We all bring our experiences, our backgrounds, and what makes us who we are to solve a problem.

Tien Nguyen is a freelance contributor to Chemical & Engineering News, the weekly newsmagazine of the American Chemical Society.