Interview

MUSC Welcomes New Director of the Center for Drug Discovery

Karen Lackey

Karen Lackey, who has led drug discovery efforts in the pharmaceutical industry for more than 25 years, joined MUSC in February 2014 as the Director of the Center for Drug Discovery. Most recently, she served as Vice President, Head of Discovery Chemistry, and Chair of the Global Chemical Biology Initiative at Hoffman La Roche. Prior to Roche, Karen was Vice President of Discovery Medicine Chemistry at GlaxoSmithKline and a key member of the GSK Molecular Discovery Executive Team, where she played an active role in early-stage research that spanned more than 30 therapeutic areas. She also is founder and Chief Scientific Officer of JanAush, LLC, which promotes personalized medicine by developing targeted therapies. She is a co-editor of the recently published *Medicinal Chemistry Approaches to Personalized Medicine*.

PN: What was your most rewarding experience in your years in the pharmaceutical industry?

KL: Undoubtedly, it was the discovery of lapatinib (marketed by GSK as Tykerb®), a dual erbB2/EGFR tyrosine kinase inhibitor for the treatment of breast cancer. I have a picture of lapatinib in my office that reminds me every day to focus on what matters most in drug discovery—the difference the drug can make in a patient's life. Lapatinib was discovered at a time when cancer therapeutics were transitioning from "kill more cancer cells than normal cells" to targeted medicine. It was really tough when we were working on the project to convince management that modulating a signaling protein would actually produce an effective drug. Everybody on the team was driven by the biological data proving at each step that it was going to work. I was very fortunate to be leading that effort and took it all the way

to the market. That experience—especially the opportunity to meet patients who were taking the drug—brought me a lot of learning and a lot of joy. It was rewarding to see someone benefit from a drug I worked on, and it still makes me emotional to remember it.

PN: How important a role do you think targeted therapies/personalized medicine will play in drug discovery in the future?

KL: Why would you ever do anything but personalized medicine? Right now, what the industry is trying to do is make a drug that works for everybody and, let's face it, we are not all the same size and shape, and we don't all have the same metabolism. Imagine if you had a SmartPhone app that could tell you how much of a drug to take and it was exactly as biologically effective as it needed to be for your system—not more, not less. That's the way medicine is going, and not just for drug delivery.

Currently, cancers and clinical trials of anticancer therapeutics are divided by organs and not by mechanisms. Someday it will be different. Genomics has taught us that there are multiple genetic drivers of tumor. One day, genomics centers will stratify patients based on the mechanism driving their particular disease, not on the affected organ, and therapies will be prescribed that target that driver.

So how totally cool would it be to take a biopsy, look at the drivers relevant for that patient's tumor, and then have off-the-shelf agents for those drivers? These could come in pills that could be snapped together to create the exact regimen the patient needed. That's doable; that's completely doable, as long as we can get all of the experts together to make that work.

PN: Can you discuss your plans for drug discovery at MUSC? What are your immediate goals? Your five-year plan?

KL: Since I started in February, my mission has been to take a look at the science going on at MUSC in an unbiased way, without considering the rank of the researcher or the level of grant funding, to pull together a portfolio of opportunities that can be shared with the pharmaceutical industry. For me, an opportunity means that, with the right partnership, you could discover a therapeutic agent that would have an impact on disease. What you want to do is make an impact on health care—that's really what your aim is—so you have to take the talent that's here and align the drug discovery with the talent.

Once we have a validated clinical candidate, we would want to partner with a pharmaceutical company that can provide the Good Laboratory Practice toxicity studies and the multiple animal studies needed for investigational new drug filings. A partnership means that it is a co-ownership or co-invention or co-creation of a novel therapeutic agent.

The five-year vision would be that we would have some drugs emerging from these partnerships and that there would be MUSC-owned agents at every stage of the drug development process. The partnerships would get us in the game and provide us all the parts it takes to discover a drug and do meaningful work in important diseases.

PN: How could these partnerships between MUSC and pharmaceutical companies be mutually beneficial?

KL: What is needed for drug discovery today is deep, deep expertise in biology coupled with experience in the clinical sciences, and that's what MUSC brings to the table. Almost all the researchers here are linking their animal models to the human condition. Many of the researchers are still seeing patients—that is how connected they are to clinical practice and to patients. What we would offer pharmaceutical companies is deep biological understanding and expertise with phenotypic assays.

What's missing at MUSC is the drug development piece, and that is what a partnership with the pharmaceutical industry could provide. Once the agent has been identified, a product has to be created that is stable, potent, and scalable. There is a whole science around selecting the optimized agent, and that is where a partnership with industry could help us.

PN: How have you found the transition from the pharmaceutical industry to an academic institution such as MUSC?

KL: My experience of being able to follow lapatinib throughout the drug development process was a wonderful one, but such experiences are rare in the pharmaceutical industry. Although the industry offers expertise across every platform you can imagine, the drug development environment it creates is a sterile one without connection to the clinic and the patient. I would have expected the environment at a medical university to be just as sterile, but I am learning every day how different academia is. At MUSC, clinical and basic science researchers can sit in the same room and discuss the best profile for a therapeutic agent or the best targets for a patient population. It's a very integrated environment and more connected to the potential patient benefit. Learning to integrate with the world a little better is something industry could learn from academia.