SPARK plugs gap in drug-development process

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Daria Mochly-Rosen is the engine behind the SPARK program, which helps Stanford researchers navigate the process of turning their lab findings into potential drug therapies.

Daria Mochly-Rosen, PhD, was about as hardcore a basic science researcher as you can be. For more than 20 years, she lived and breathed basic research, reveling in the microscopic world where molecules formed, changed shape and danced with one another. The professor of chemical and systems biology was even known to sketch cartoons of them wearing fanciful hats.

That was until 13 years ago when she made a discovery she thought could save people's lives. Her research on a group of enzymes offered clues to designing better heart disease drugs, and she wanted to take her discoveries to the next level.

When Stanford's Office of Technology Licensing had no success getting the idea picked up by industry, she decided to take it into her own hands. "I thought, obviously the problem is with the OTL. I'll pitch it myself," said Mochly-Rosen, now the School of Medicine's senior associate dean for research. She soon learned how wrong she had been.

One fruit of her crash course in turning biomedical discoveries into medical tools is SPARK, Stanford's bioscience incubator, founded five years ago. And what started as a program to put Stanford researchers' discoveries to work for society has grown as an educational venture as well. From the beginning, the program's weekly seminars were open to graduate students. But since 2009, students in the med school's drug discovery class became active participants, presenting development plans to the program's experts and getting their feedback.

SPARK provides Stanford students and researchers expertise in everything from drug formulation and biochemical assays, to trial design and consent forms, to intellectual property law and regulatory agency requirements. At their weekly seminars, held Wednesday evenings, SPARK participants get advice from angel investors such as Sand Hill Angels' Ted McCluskey, MD, PhD; clinical trial hands such as Stanford's Bill Robinson, MD; and biotech scientists such as Telik's VP for R&D Steve Schow, PhD, and industry veteran Lyn Frumkin, MD, PhD, who trained at Stanford and flies down from Seattle to participate.

Such lessons on how to demonstrate the clinical utility of the initial scientific findings and how to interest companies in using these discoveries are rarely taught at medical schools. But that's starting to change. In addition to SPARK, Stanford has a few other programs with similar goals, such as Biodesign, for medical devices, and the NIH-supported C-IDEA, which supports Stanford medical innovations addressing health problems in the developing world. Like SPARK, both programs also offer some seed funding.

SPARK typically grants about $50,000 per project to cover the necessary studies to show the invention's utility, and offers guidance from those with know-how from industry and academia. The money is paid in increments upon reaching milestones pre-specified by the inventor together with the SPARK consulting team. Applications for this year's SPARK grants will be accepted through September 30.

The U.S. Food and Drug Administration continues to approve about 20 new drugs a year — a number that has not changed since at least 2000. The need for better drugs is a big part of SPARK participants' motivation.

SPARK's track record is substantially better than the pharma industry's, where 19 out of 20 or so discovery projects fail to move forward after a year or two of work and about $1 million investment per project, said Mochly-Rosen. Of the 19 projects completing SPARK training, approximately half have entered clinical trials, been licensed or both.

But back in 2000, Mochly-Rosen wasn't looking to start a new program as she blithely sallied forth with her idea for a drug to develop, speaking to dozens of CEOs and research program leaders at biotech and pharmaceutical companies. "They all told me, nicely: 'Go away.' Everybody told me how cool the idea was — 'and absolutely no way.'"

For one thing, her drug would target an enzyme not on the outer surface of a cell (the usual pharma approach) but in the cell's interior. To make matters worse, it wouldn't bind to the enzyme's active site but to a domain that anchors the enzyme to another protein. On top of it all, it was a peptide, a very unstable type of molecule, and one that the pharma industry has little experience using.

"All these features that made the discovery exciting for academic scientists were a headache for drug development," she said.

So in 2001 she started the company KAI Pharmaceuticals to develop drugs based on her ideas. “There was no transition in my life that was more dramatic, except maybe the birth of our first child,” she said. “I knew nothing about drug development, about the rigor and intellectual challenge that drug development entails; I did not realize the size of the team and expertise that need to be assembled and the totally intoxicating feeling of actually getting something that was invented at our bench into the first patient. Nothing is quite like that.”

Mochly-Rosen had initially been reluctant to start a company. Among academic scientists, there’s a feeling that you should focus purely on basic research, where the goal is to generate knowledge and to teach, she said. “It didn’t help to have heard from Roy Vagelos, the retired CEO of Merck, that the public ranks pharma at the bottom with the oil industry,” she said.

She took a leave of absence for a year to get the company rolling. “There’s something extremely rewarding about this process, knowing that it could impact human health,” said Mochly-Rosen. “And it’s humbling that so many people are working on what started as your dream.” KAI successfully completed clinical trials showing the safety of its lead product candidate, and is moving on to test its effectiveness for reducing injuries in heart attack patients and possibly in stroke.

When she returned from her leave she started SPARK to fill the gap she had nearly fallen into. She was soon joined by Kevin Grimes, MD, who left his position as senior director of clinical research at KAI to co-direct the program and co-teach the drug discovery class with Mochly-Rosen.

Unlike most pharmaceutical companies, SPARK is open to “crazy” ideas. “We are not burdened by thinking, ‘It can’t be done,’ because we don’t know any better,” laughs Mochly-Rosen. “By nature, academicians are rewarded for taking the unproven path, whereas the industry is risk

averse due to the high cost of failure. Perhaps academia can step into this gap and improve on the drug development process using new paths — and help generate more treatments for unmet clinical needs."

But Mochly-Rosen has learned developing drugs is not only the right thing to do — it's a joy.

"Pass by the dean's conference room 5:30 to 8 on Wednesday night and you will see what fun is," she said. "We're all there to learn and teach, we're all on an equal level. There's an enormous amount of excitement. And things move. Something happens."

On the first Wednesday evening in June, that was evident. Four groups of students in the drug discovery class pitched their ideas to 25 medical researchers, clinicians, industry experts and venture capitalists. The assembled experts didn't just listen. They enthused: ("I love that test. That's what I use.") They troubleshot: ("You'll have to train people on the ground to monitor if they've taken the medicine. That will take a lot of effort.") They advised: (Investor McCluskey told one group to go ahead with a clinical trial for a nutritional supplement for a digestive disease when he learned that one of its members had already used it — successfully — to treat herself. "Do the placebo-controlled clinical trial. Full speed ahead. Then you'll have the goose that laid the golden egg," he said.)

Sometimes the experts even learned things themselves. Several biotech scientists warned a group pursuing a botanical drug that the toxicity tests required by the Food and Drug Administration would be tricky. So they were surprised when the students told them it really shouldn't be a problem: They learned from the FDA consultants that toxicity testing requirements for botanicals are different from those for drugs. Many eyebrows shot up upon that statement.

Because many of the students who pitched proposals that Wednesday are still working in stealth mode, no further details will be revealed for now. But since SPARK's reviewers recommended that they all receive funding to continue development, you might hear more about them someday, or even use the resulting product a few years down the road.

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