



# BUSINESS DECISIONS

What does it take for an academic scientist to become an entrepreneur? Here are some of their stories

*By Jeffrey Mervis*

**F**or academics, the journey from a discovery to a product can be arduous. But as a culture of entrepreneurship has spread to universities across the country and around the world, aid stations have popped up to ease the way. They come in various forms, including campus competitions to solicit commercially viable ideas, universities establishing their own venture capital funds and “incubators” to nurture startup companies, and programs such as the Innovation Corps (I-Corps) at the National Science Foundation.

“We all know that entrepreneurship is the big buzzword today on campus,” says Laura Ray, an engineer at Dartmouth College, who has founded two firms based on her work in acoustics and signal detection and runs a graduate fellowship program in innovation.

Ray’s own entrepreneurial learning curve has been steep. Her first company, begun in 2005, was the result of a knock on the door from a university tech transfer official who asked if she had anything that could be taken to market. “We thought he was crazy,” Ray recalls—but she was willing to take a shot. Eight years later, a second company grew out of her participation in I-Corps’ 10-week boot camp for would-be academic entrepreneurs. “I-Corps opened my eyes,” Ray says. “It taught me that you need to know the customer, and your value proposition—that is, how you plan to make money.”

Despite those commercial ventures, Ray has remained an academic. And although some scientists leave campus to follow their commercial dreams, most do not. They like research and teaching, for one thing, and may not think they have what it takes to run a

Chemical engineer Jackie Ying has had to modify MIT's entrepreneurial ethos in building up her Singapore research institute.

company. "If I had quit my [academic] job, I don't know that I would have succeeded," Ray admits. Frances Arnold, a biochemist at the California Institute of Technology in Pasadena, who has founded two biofuel companies, advised several others, and is a member of the National Inventors Hall of Fame, echoes that attitude. "I never chose to do the hard work of being a CEO or a chief technical officer," she says.

Research on entrepreneurship—who does it best, what policies promote it, and how it contributes to economies, for example—is flourishing, as an Insight on page 1200 describes. In one story in our special News section, two venture capitalists describe how they vet scientists' pleas for money; a second Feature gives an inside look at the incubator phenomenon. But first, we offer several stories that illustrate some of the many possible paths from campus to commercialization.



Todd Zion

#### THE CATALYST AND THE PROTÉGÉ

Todd Zion came to the Massachusetts Institute of Technology (MIT) in Cambridge in 1999 to earn a Ph.D. in chemical engineering. When he went shopping for advisers, Jackie Ying stood out, in part because of a fanatical work ethic that helped her become a full professor at the age of 35. "Some people would never want to work for Jackie, but I was attracted to the idea of working twice as hard as any other lab," says Zion, who spent 2 years after college as a corporate research scientist at Kodak, before deciding he needed a Ph.D. to make his mark.

Ying's business-minded approach—she says that "every grad student should tackle a project not only of tremendous scientific interest, but also of great commercial potential"—also appealed to Zion's nascent interest in becoming an entrepreneur. "I saw people in her lab go off and start a company," he says, "and I'd think, 'Hey, that's something I'd like to do, too.'"

So Zion signed on. Eager to push her already productive lab into the life sciences, Ying asked Zion to see if the same technology her lab had used to make a nano-emulsion to coat the turbines in jet engines could create a platform for delivering insulin to treat diabetes. The idea was to create an insulin-containing polymer that would break down after interacting with

glucose in the patient's blood, releasing the insulin as it was needed.

Zion spent 2 years trying to find a material that prevented the insulin from leaking out before he realized that the secret lay in chemically modifying the insulin itself. That discovery led to SmartCells, a company he and Ying co-founded in 2003. Zion and a small team spent another 7 years improving the technology before selling the company for an undisclosed upfront sum to Merck, which is betting that this novel drug-delivery system will one day allow millions of diabetics to discard their pumps, meters, and monitors. The acquisition drew notice because Merck reportedly will pay out more than a half-billion dollars if certain milestones are met; a company representative said last month that a phase I clinical trial in humans has begun.

"Todd was a very good scientist, although he was by no means my best student," Ying says. "But he had very good business acumen. And that's essential in running a company."

For Zion, becoming a full-time entrepreneur was the obvious next step once he realized the value of his discovery. "I suppose that somewhere in the recesses of my subconscious, remaining in academia was a possibility," he says. "But it's hard to go out and be an entrepreneur with a Plan B. You gotta tell yourself that this is the only way the company can move forward, and we're going to make that work."

Zion's business savvy made an impression on Lita Nelsen, the longtime director of MIT's technology licensing office. Biotech startups are common at MIT, she says, but SmartCells stuck in her mind because Zion managed to avoid what she calls "diluting the company." By running a tight operation and not asking for more money than he needed to reach a succession of technical milestones, Zion was able to retain control of the company rather than trade away a lot of equity for cash. That strategy resulted in a huge windfall for Zion, his small team, and a handful of early investors, including MIT, when Merck acquired the company.

Zion immediately spent some of his profits to buy a struggling private Montessori school that his three children were attending. Then, he took some time off. But within a year, Zion reunited with some of his former SmartCells colleagues to start another company. Largely self-funded, Akston Biosciences Corp. is testing technologies for clearing the body of unwanted material implicated in various diseases, like the  $\beta$  amyloid protein that forms abnormal deposits in the brains of Alzheimer's patients.

Ying says that roughly one-quarter of her MIT students have founded companies or gone to work for a startup. But she has chosen not to take that path. "What interests me," Ying says, "is bringing the technology to a certain level where you can spin it off, and then playing an advisory role to make sure that things are running smoothly."

"She's an educator at heart," says Andrey Zarur, who as one of Ying's first graduate students developed the initial technology

### *"It's hard to go out and be an entrepreneur with a Plan B."*

Todd Zion, Akston Biosciences Corp.

that Zion later modified to create SmartCells. Now a partner at Kodiak Venture Partners in Boston and CEO of Greenlight Biosciences in Medford, Massachusetts, the latest of 15 companies he has started, Zarur says Ying "would take me with her on visits to companies to get funding for the lab. And I would make the presentation. People thought she was taking advantage of me because she made me do three Ph.D. projects. But I was like, 'Dude, you're crazy. She is preparing me for the life I want to have.'"

By the time Zion launched SmartCells, Ying had left MIT to become the founding director of the Institute for Bioengineering and Nanotechnology (IBN) in Singapore. She says the job gave her a chance to return to her roots—born in Taipei, she grew up in Singapore before coming to the United States as a teenager—and to spread the twin gospels of top-flight research and entrepreneurship that she had learned at MIT.

Her record over the past 12 years suggests she has done exactly that. IBN has generated more than 300 patents, 80 licenses, and eight startup companies. But basic research with commercial potential doesn't just happen, she notes. Faculty members have to buy

into the goal—and sometimes they need some help in finding a project with commercial promise. Ying recalls coaxing a scientist who was studying epigenetics to shift to cell and tissue engineering. "She got very interested in that and she wanted to work on liver tissue. But I persuaded her to work on kidneys, because it's a much less crowded area."

Ying also weighed in when the researcher began to think about developing an artificial kidney. "That would take a very long time," she told her. The institute had recently developed new ways to produce stem cells from a person's kidney tumors, so Ying persuaded her colleague to instead turn

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such cells into a toxicity assay for potential cancer drugs. Ying hopes to find partners in the drug, consumer care, and food industries who are interested in developing the in vitro technology, which she says is more efficient than having to use animals.

Overall, she envisions creating a different entrepreneurial model than simply having lab members leave to spin off a technology. “We don’t have a steady supply of new students like at MIT,” she notes, “so a spinoff can mean losing five or 10 good people” from a staff of 160 researchers and 20 graduate students.

Instead, Ying hopes to find a way for IBN to help nurture new companies without losing all the scientists who did a technology’s foundational work. “We will continue to help [the firms] with the research,” Ying says, “and maybe they will give us not just royalties but some shares to the people involved. So it would be win-win.”



Howard Schulman

**THE ROUGH ROAD TO A PRODUCT**

Howard Schulman has experienced the roller coaster ride familiar to many scientists who try to turn an academic discovery into a drug. More than 2 decades have passed since he and Mark Anderson demonstrated that inhibiting an enzyme Schulman had co-discovered, calmodulin-dependent protein kinase II (CaMKII), could block heart arrhythmias.



Mark Anderson

And for the past 6 years

Schulman has been president of Allosteros Therapeutics, a tiny company the two men created to translate their knowledge into helping heart patients. But so far it hasn’t happened.

Schulman and Anderson, now director of medicine at Johns Hopkins University School of Medicine in Baltimore, Maryland, began their collaboration in the early 1990s at Stanford University in Palo Alto, California, where Schulman, a molecular pharmacologist, was a professor, and Anderson, an M.D.-Ph.D., was doing a postdoc and medical residency. Their work offered an alternative to antiarrhythmic therapies based on ion channels, a once-popular idea that had proven to cause more harm than good. But Schulman was happily ensconced at Stanford, and Anderson was just beginning his career as a physician-scientist. So instead of commercializing the discovery themselves, the two scientists obtained a use patent on it and hoped that a

company would license their work.

It was a long wait.

“Stanford made a minimal effort to find a partner,” Schulman says. “They might have done more if I had already been a successful founder or if I had chosen to be more aggressive.” Stanford finally struck a deal with a nearby biotech company, Scios Inc.

Scios designated CaMKII inhibition as one of its three lead programs in cardiovascular medicine, and Schulman and Anderson became consultants. But the arm’s-length relationship prevented Schulman from using his expertise in medicinal chemistry. “I didn’t get to see the compounds or help them on assays,” he notes. “It was not an entirely satisfactory relationship.” In 2003, Scios was purchased by Johnson & Johnson, and 3 years later the pharma giant shut down its entire preclinical cardiovascular effort, including a gleaming building that housed its research on CaMKII. “So we got the license back,” Schulman says.

He and Anderson had continued to work on CaMKII, and so they took matters into their own hands. “It’s actually not that hard to start a company,” Schulman says. “All you need to do is go on the Web, register it in Delaware, and create a post office box. It doesn’t cost very much.”

What costs lots of money, of course, is turning a molecular drug target into an actual therapy. The Leducq Foundation, a family philanthropy based in Paris that supports basic research on cardiovascular disease and

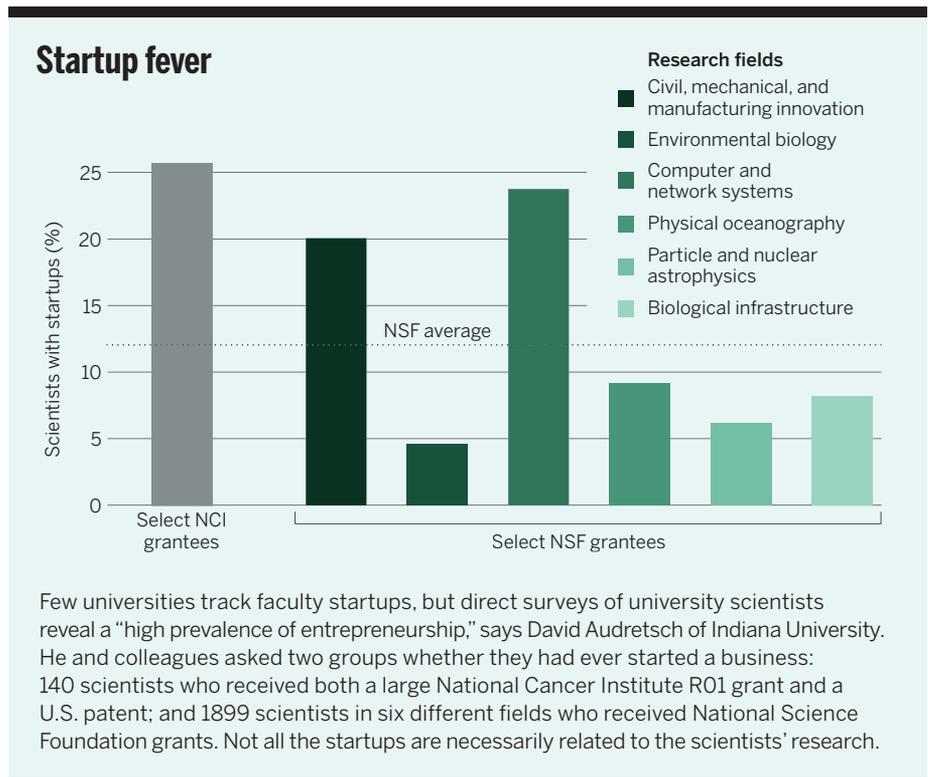
stroke, was already funding Anderson to lead an international collaboration on CaMKII. As luck would have it, the trust decided to create a philanthropic venture company—a for-profit entity with the mandate to invest in promising treatments against heart disease—just as the two men formed Allosteros.

“We competed successfully for seed money,” Anderson says. The \$1.3 million that Allosteros received enabled Schulman to set up a small lab in nearby Sunnyvale, California, and subsequent federal small business grants and other funding have allowed the company to outsource some needed chemistry work and refine two compounds into potential candidate drugs. This spring, the two men came within a whisker of inking a deal with a major pharma that would have taken those compounds through clinical trials.

“At the last minute, they told us they were no longer interested in heart failure,” Schulman says. “Being part of a multibillion-dollar cardiovascular program would have been nice. But not yet.”

Schulman remains optimistic that the stars will eventually align for Allosteros. In the meantime, he’s trying to maintain a basic science program and has applied for another small business grant.

For Schulman, 66, seeing CaMKII become the basis for a range of heart treatments would establish his credibility as an entrepreneur and fulfill a careerlong urge to help bring a drug to market. For the 55-year-old Anderson, the stakes are not



so high. “I think entrepreneurs are people who put their livelihoods at risk by placing bets on a particular business concept,” he says. “That’s not me. I’m a physician scientist, and I live mostly in a world of mice. Howard’s been living Allosteros for 6 years. I still have a day job.”



Michael Weiss

### THE BUSINESS OF DOING GOOD

Michael Weiss has carved out a successful research career unraveling the complex structure and inner workings of insulin. But Weiss, a biochemistry professor at Case Western Reserve University in Cleveland, Ohio, has more than just an academic interest in understanding the hormone that helps the body regulate blood glucose levels.

In 1980, as a Harvard Medical School student on a travel fellowship across the Middle East and Africa, Weiss was shocked to find out that millions of diabetics in the developing world couldn’t manage their disease properly because they lacked access to a version of the hormone that doesn’t need to be kept refrigerated. “That problem should be easy to solve by engineering an ultra-heat-stable insulin,” he remembers thinking.

It wasn’t. It took Weiss nearly 3 decades to come up with a solution, one that relies on single-chain analogs of the natural protein, which has two chains. Since founding Theralin Diabetes in 2009, Weiss has been simultaneously publishing papers in top journals and getting up to speed on what it takes to make a synthetic form of heat-stable insulin available commercially.

One important lesson came in 2007 from Richard Klausner, then the head of global health programs at the Bill & Melinda Gates Foundation and a friend from Weiss’s medical school days. “Rick told me two things: One, you need a business plan that makes sense to Western investors, including how to win FDA [Food and Drug Administration] approval for the drug; and two, don’t tell me anything more until Case Western has secured the IP [intellectual property].”

“Those were new words to me,” Weiss admits. “I was very naive about business and the commercialization process.” Weiss decided to make up for lost time, taking a 2-year sabbatical so he could earn an MBA in 2010—at the age of 53—from Case Western’s Weatherhead School of Management.

Weiss also reached into his past to find someone to run the company: Rick Berenson, a college roommate turned venture capitalist. In line with Klausner’s advice, Berenson decided to target diabetics in the industrialized world. One niche, he

says, is the many people who suffer from a marked insulin resistance and need a large dose of insulin before meals to help manage their bodies’ reaction to the glucose. The company’s first product is likely to be Fluorolog, an ultraconcentrated, rapid-acting biosynthetic version of insulin. “Insulin is sticky, so you can’t just concentrate it,” Weiss explains. “So we put fluorine in it so it’s not so sticky.”

Weiss has raised \$11 million from investors and garnered \$9 million in grants, mostly federal small business research grants. He needs at least that much again to take just that drug candidate into clinical trials. “I was hoping to do consecutive clinical trials [on several candidates], with several years of really interesting science coming out of all this,” Weiss notes. “But the venture capitalists have a different perspective. They want to know how quickly we can create value, and then exit.”

Weiss knows that “creating value” will also hasten progress toward solving the problem he encountered on his travels 35 years ago. “I want to move insulin analogs out of the lab—from mice and rats and pigs—and into humans,” he says. “And the only way to do that is company creation. I have [entrepreneurial] friends who don’t really care what the product is. But my goal has always been to meet the unmet clinical needs of diabetics.”



Paul Romer

### LOOKING BEYOND ONE’S RESEARCH

Not every company founded by an academic springs from what he or she is studying. For 2 decades, economist Paul Romer probed how a nation’s investments in

education and research can spur long-term economic growth, an important question in macroeconomics. But in 2001, he left his faculty position at Stanford University to launch a company aimed at solving a very prosaic problem: getting students to do their homework.

Romer had noticed that students in intro economics courses were blowing off homework assignments. And even when the students did do the problem sets, many faculty members couldn’t provide much feedback because the classes were so large.

Romer thought that technology could solve the problem. His chance came when Skandia, a Swedish life insurance company, offered to finance an endowed chair at Stanford so he could extend his work on innovation. “Why not fund a new venture instead?” he asked them.

Skandia said yes, and its \$11.2 million

investment bankrolled Aplia, an educational software company that lets students go online to work on material aligned with their textbooks. The software gives immediate feedback on wrong answers and allows students to participate in interactive group exercises that simulate market conditions—

*“As an entrepreneur, you have to be willing to walk away with nothing if you don’t succeed.”*

Paul Romer, New York University

“it’s like lab experiments in the natural sciences,” Romer explains.

Romer also wanted to fix what he calls a “broken” publishing model: Textbooks were getting more and more expensive, but they weren’t helping students master the subject. Aplia offers a menu of online supplemental materials so that students can choose what fits their needs—and their budgets.

Although lacking any formal business experience, Romer chose not to work with Stanford’s technology transfer office. Instead, he took a 2-year leave from the university—“they weren’t very happy”—that eventually stretched to 6 years. Romer initially hired a CEO to run the company, but he eventually grabbed the reins, believing it necessary to remain “cash positive.” At one point he even sold his house and poured the proceeds into the company.

It took Aplia a few years to regain its footing, by which time Romer realized that he missed doing research. “I had proven my original point: It was possible to get students to learn more by doing homework, and to change the textbook-based model of education.” So in 2007 he sold the company. Romer’s current research focuses on the role of cities as an engine for innovation, and in 2010 he joined the faculty at New York University in New York City, where he directs the Urbanization Project at the Stern business school.

Would he ever want to be an entrepreneur again? “It was very exciting and intellectually stimulating, and the closest friendships I ever had were part of that experience,” he says about Aplia.

Starting the firm also taught him an important lesson about entrepreneurship, he says: Don’t risk more than you can afford to lose. “Things were touch-and-go for a while—we didn’t have much in the bank. As an entrepreneur, you have to be willing to walk away with nothing if you don’t succeed.” ■