Profiles in Leadership #11

Robert Langer: From an Ugly Duckling to Singular Swan

Robert S. Langer Jr., Sc.D., New York Delta '70

by **Alan S. Brown**

What does it mean to be a leader? In this series "Profiles in Leadership," Tau Beta Pi is exploring that essential question through the lives of member engineers who attained leadership positions in their fields.

There is a reason Massachusetts Institute of Technology's Robert Langer earned the nickname, "The Edison of medicine." He pioneered such innovative technologies as controlled release drugs, transdermal drug delivery, targeted cancer medications, and tissue engineering and regeneration. He is arguably the person most responsible for making engineering an integral part of biology and medicine.

Langer aims high and uses engineering to change the world. When he won the $1.5 million Queen Elizabeth Prize for Engineering, considered the field's top honor, the award committee estimated that his discoveries saved or improved at least 2 billion lives.

In addition to earning almost every honor an engineer can receive, he has published 1,400 papers that have been cited 230,000 times. This is far more than any other engineer and all but a handful of scientists. His h-index, which measures a researcher's impact, is among the highest of any researcher ever.

Langer is no mere lab magician. His 1,260 issued and pending patents are licensed to 300 companies and 40 companies he co-founded. A recent *Harvard Business Review* profile put the value of his commercial technologies at $23 billion.

Langer's history is the very definition of a black swan, a career so remarkable and unpredictable that it falls outside our expectations. Yet at the start of his career, he was an ugly duckling.

Langer struggled to find a post-doctoral fellowship and engineering jobs before landing in MIT's Department of Nutrition and Food Science. His first nine research grant applications were turned down.

"That story about the professor who sat smoking a cigar and blew smoke in my face and told me I ought to start looking for another job—that's a true story, and he was a very famous guy," Langer said.

Langer doesn't name names, but Michael Marletta, the former head of the Scripps Research Institute, saw it happen. "I thought I was in a Fellini movie," he said.

President Barak Obama awarded Langer the National Medal of Technology and Innovation in 2011. Langer is only one of five people to win the award and the National Medal of Science.

Top-ten Student

According to Langer, there was nothing special about his youth. He was born in Albany, NY, in 1948. His father had a master's in English from Harvard University and owned a liquor store where Langer sometimes helped.

"I was a pretty normal little kid," he recalled. "I played baseball, football, and basketball, and had lots of friends. I was always shy, but not unsocial."

In high school, Langer was a top-ten student in math and science and "not much good at anything else." He did have an ability to visualize solutions to math problems, a chessboard several moves out, or how a hand of bridge might evolve. He was also hooked on the A.C. Gilbert erector, chemistry, and microscope sets his parents gave him.

Upon graduation, his father and guidance counselor suggested Langer study engineering at Cornell. He plowed through classes, but was unsure about his future.

"I really didn't know what I wanted to do," he said. "I got a few offers to run chemical plants, which is what many of my classmates were doing. I was not very excited about that. So, I applied to graduate school to learn things that might be more exciting."

He entered MIT in 1970 and picked an unusual problem for a chemical engineer: the regeneration of adenosine triphosphate, or ATP, the molecule cells use to transfer energy for biochemical processes. Langer thought he might be able to use it for chemical synthesis.

The process he developed was not very practical. His graduate work taught him the importance of precision and reproducibility and how to push deeper and deeper into a problem.

Langer also discovered his love of teaching when he helped start an alternative school for at-risk students. "I loved that, and I was gratified at how well the students did, and how the curricula made a tremendous difference," he said.

Yet in 1974, as Langer was finishing his doctorate, he was still unsure about his future. Like his classmates, he applied for oil company jobs. Every firm made him an offer, but Langer wanted to make a difference in people's lives. He applied for medical research positions, figuring his experience with ATP would help. No one responded. He applied for a faculty position in chemistry education. No reply.

Then someone at the lab mentioned Judah Folkman.

Culture Shock

Folkman was a medical researcher at Harvard University and a surgeon at Boston Children's Hospital. While Langer pursued his Ph.D., Folkman was investigating how to stop blood vessels forming in tumors. If he could block their growth, called angiogenesis, the tumors would starve and die.

Most researchers ignored or belittled Folkman's approach. By 1974, however, his team had identified the first growth factors. This led to an infusion of corporate money and an agreement, the first of its kind, that Folkman could protect his research with a patent. This would become a template for Langer's future success.

"Judah was known for hiring unusual people, and one of the lab's post-docs suggested I write him," Langer said. "Judah wanted this problem solved. A lot of people with excellent medical and biological backgrounds had made little progress, so it made sense to try someone who had a very different kind of background."

Langer's first job was to isolate potential inhibitors for testing. Folkman asked him to look in bone marrow, where blood vessels do not grow. Langer located a slaughterhouse to get bones containing cartilage. Purification yielded hundreds of potential angiogenesis inhibitors. The medical researchers planned to test them on tumors in rabbit eyes, where the blood vessels were clearly visible. However, they had no way to deliver the large inhibitor protein molecules to the tumors. Langer's solution was simple: embed the medicine in a polymer with interconnected pores and attach it to the tumor. Over time, the molecules would percolate through the pores to reach the tumor.

While timed release drugs existed for smaller molecules, no one thought it would work for large molecules. It was like asking a person to walk through a wall.

"I didn't know you couldn't do it because I hadn't read

This Leader In Brief
Full professional name: Robert S. Langer.
Most recent positions: David H. Koch Institute Professor, Massachusetts Institute of Technology.
Birthplace: Albany, NY, 1948.
Highest degree: Sc.D., chemical engineering, Massachusetts Institute of Technology, 1974.
Major career highlights: Assistant professor, nutritional biochemistry, MIT, 1977-81; associate professor and professor, biochemical engineering, MIT, 1981-88; professor, chemical engineering, MIT, 1988-2005; institute professor, 2005-present, MIT.
Board memberships: Co-founded 40 companies and remains a director and/or scientific advisor for many of them. He chaired the U.S. Food & Drug Administration's Science Board, its highest advisory board, from 1999-2002.
Honors: Has received more than 220 major awards. He is only one of five people elected to the National Academies of Medicine, Engineering, and Sciences. Honors include Lemelson-MIT Prize, 1998; Charles Stark Draper Prize, 2002; U.S. National Medal of Science, 2006; Millennium Prize, 2008; U.S. National Medal of Technology and Innovation, 2011; Kyoto Prize, 2014; and Queen Elizabeth Prize for Engineering, 2015. He also holds dozens of honorary doctorates from schools around the world.
Greatest accomplishment: Discovered we could create molecules to deliver drugs of any size or charge, which led to delivery of cancer medications, and my students, who continue to discover new ways to improve health.
Family: Met his wife, Laura, while she was completing her Ph.D. thesis in neuroscience. They married in 1989 and have three children, Michael, Sam, and Susan.
Hobbies: Was an amateur magician, now enjoys finding great restaurants when he travels.
Favorite book: *The Last Lone Inventor: A Tale of Genius, Deceit, and the Birth of Television* by Evan Schwartz. He also enjoys classic television shows and movies.
Personal motto: Dream big dreams, dreams that can change the world. Many times, you're going to run into obstacles. If you do, don't ever give up, just keep trying.
If you could do one thing over: I've been very, very lucky, and learned from the things I haven't done well. My life might be worse off if I didn't experience negatives as well as positives, because I grew from those negatives.

Above: Langer as a baby in Albany, NY. **Center:** Langer as a high school student who was good at science and math but not much else. **Below:** With his wife, Laura, at their wedding. They met while she was working on a Ph.D. in neuroscience at MIT.

the literature," Langer said. "I just kept plugging at it. I discovered over 200 ways to get it to not work. I just kept looking for different things to try."

He never had a "Eureka!" moment. Instead, he developed a complex recipe of polymers, formulations, drying conditions, loadings, and other factors to do the job.

Langer and Folkman published two papers in 1976. The first, in *Science*, showed that angiogenesis inhibitors could kill cancer cells. Avastin, Nexavar, and Votrient are among the many medicines based on that research.

The second, in *Nature*, described the controlled release of large molecules. It eventually became the foundation of the controlled release drug delivery systems used to fight cancer and other diseases.

Publication in two of the world's most prestigious journals should have opened doors. Instead, when Langer was ready to leave Folkman's lab, no one wanted to talk with him. Most biologists and physicians simply did not believe his paper on controlled release. It flouted conventional wisdom and Langer's complex processes were hard to duplicate.

"No chemical engineering department would hire me either," Langer said. "Departments usually want consensus. I was doing experimental biology and that didn't fit in with what chemical engineers did back then."

"Benevolent Dictator"

Nevin Scrimshaw, the "benevolent dictator" who founded MIT's department of nutrition and food science, took him on without asking his faculty for a second opinion. Langer began applying for grants and was turned down consistently.

"I still remember the review from one of the grant proposals I wrote on cancer," he recalled. "It said, 'Dr. Langer is an engineer. He knows nothing about biology and he knows even less about oncology.'"

"I had already isolated the angiogenesis inhibitor, but there was an inherent prejudice against engineers, especially then. I was one of the few engineers doing experimental biology work, maybe the only one. I didn't fit into the box, and they turned it down for that reason."

When Scrimshaw left one year later, the faculty turned on him. The professor who blew smoke in his face was not the only one to suggest he look for a new position. "It was pretty negative, but I had faith in what I was doing and thought it was important, so I kept plugging along," Langer said. "And over time, people began to reproduce my results and the pharmaceutical companies began using my techniques."

MIT rehired Langer. However, it took nearly 10 years after his initial paper for Eli Lilly and International Minerals & Chemicals to call about applying his work. For Langer, that meant consulting fees, research grants, and, most importantly, commercialization. But after the first experiments turned out poorly, both companies gave up.

Langer was frustrated with their lack of tenacity. So, when fellow MIT professor Alex Klibanov suggested they start a company, Langer was ready to take commercialization into his own hands. Their business, Enzytech,

eventually merged with Alkermes, and has since grown into a $750 million biotech firm.

In many ways, this became the pattern of Langer's future success: He developed new ways to manipulate biomolecules at the nanoscale, and commercialized the results through either startups or patents.

Langer built upon controlled release to develop polymers that release drugs through the skin. Recently, working with the Bill & Melinda Gates Foundation, he modified this technology into a birth control system that lasts up to 16 years.

Langer also pioneered tissue engineering by developing a recipe of growth factors and biochemicals that he could embed in a three-dimensional scaffold that prompts cells to organize themselves into living organs. Ultimately, his team hopes to grow replacement organs.

After running the world's largest bioengineering laboratory and setting up companies, Langer has learned a lot about research and business leadership.

"First," he said, "think about important problems that can change the world and make a really big impact."

"Second, you want to have more money than less. I like to have a budget that gives people in the lab the flexibility to think big and do big experiments."

"Third," he added, "it's really important to treat people really well, and to make sure students are learning."

He also has some ideas about businesses. Many startups fail because the principals launch the company before they fully understand their technology. He believes in waiting for a clearer path to commercialization, and protecting that path with strong patent claims that include examples to make them easier to defend.

Business Partners

Choosing the right business partners—venture capitalists and business teams—is also critical. He looks for people who treat others well, though he admits pursuing both relationships and profits is difficult.

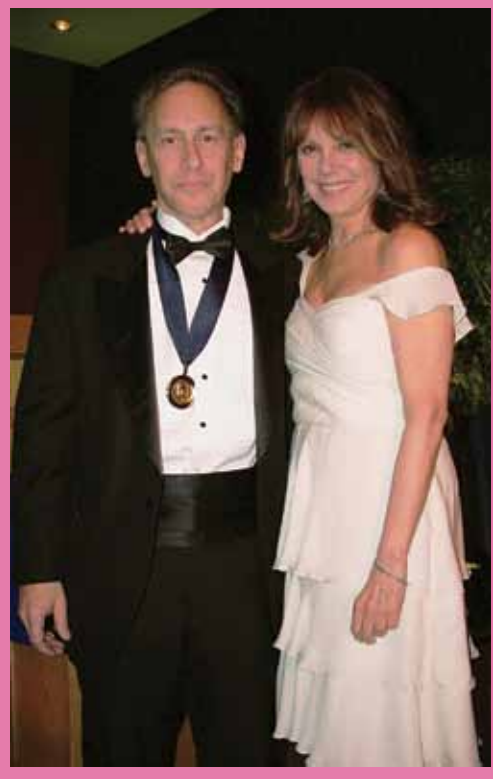
Asked about his legacy, Langer admits that even though he is a pioneer in applying engineering to medicine, his students are the best measure of his success.

"We've had 800 or 900 trainees, and they are professors at some of the best schools in the world and CEOs of companies they've started." He did not win any awards as a young engineer, but several of his students have gone on to win major awards for young investigators.

And if Langer were a young engineer today?

"I don't think I would have done the same thing today. Like that Robert Frost poem, 'The Road Less Taken,' I tried to do something new. I think today I'd be searching for a new way to have the greatest impact on the world and make it a happier place."

Alan S. Brown has been an editor and freelance writer for more than 30 years and lives in Dayton, NJ *(insight01@verizon.net)*. A member of the National Association of Science Writers and former co-chair of the Science Writers in New York, he graduated magna cum laude from New College at Hofstra University in 1974. He is an associate editor of *Mechanical Engineering* and contributes to a wide range of engineering and scientific publications.



Above: Langer in his office at MIT. **Center:** Langer with Marlo Thomas after receiving the General Motors Kettering Prize for Cancer Research in 2004, one of more than 220 honors he has earned. **Below:** Langer with Magic Johnson—both earned honorary degrees at the Mount Sinai School of Medicine commencement in 2009.