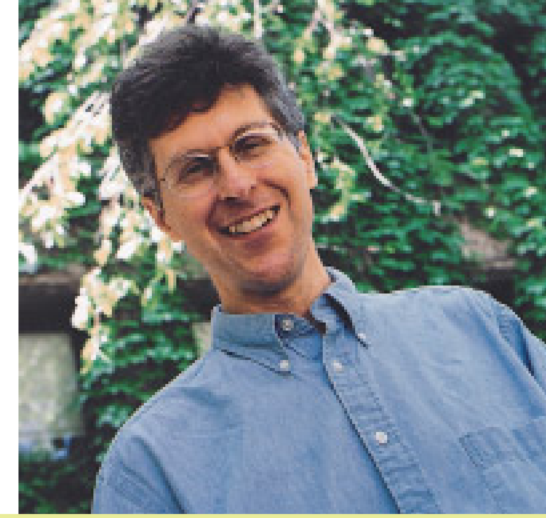
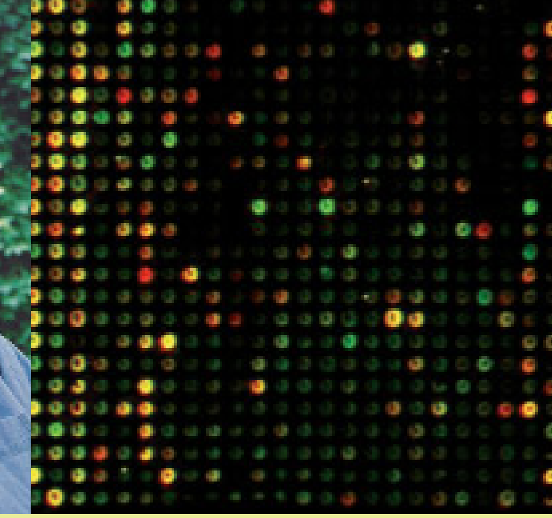
# The Everyman **of Science**

by Frank Stephenson


**Chicago alumni have a reputation for the unconventional,** the quirky — sometimes the oddball. But even by Chicago standards, Patrick Brown, AB ’76, PhD ’80, MD ’82, stands out.

Brown developed what *U.S. News & World Report* once called “one of the hottest tools in the field of biotechnology” — but then walked away from a chance to make millions from his invention.

Or consider that the Stanford University biochemist has published widely in the world’s premier academic journals on groundbreaking work in AIDS and genetics — but then launched a nonprofit enterprise to compete head-to-head with those same publications.

Brown’s career is infused with such contrasts, the type of life that the *San Francisco Chronicle* last year described as a “throwback to the days when prestige was the main payoff” for scientists who “raced to make knowledge public.”

That was, in fact, precisely what he did after developing the “gene chip,” a simple, cheap and fast way to analyze genetic activity in cells. After reporting his findings in *Science* (1995), in characteristic egalitarian fashion he put his notes on the Internet for the world to see. A short time later, he declined an invitation to join a startup company that aimed to commercialize his invention — a company that since has sold for a reported $90 million.

Today, Brown’s technique is one of the most widely used diagnostic tools in life science. In many research circles, it’s become the tool of choice in drug discovery and in disease diagnosis.

Gene chips — more technically known as DNA microarrays — are little more than pieces of glass specially coated with thousands of microscopic bits of DNA. Armed with an assortment of these inexpensive “chips,” scientists can get a quick and highly accurate snapshot of which genes are active in almost any biological sample. This reveals clues about how cells are genetically configured and how they react to various substances, from toxic chemicals to natural proteins.

“It’s like being able to read the molecular script that’s being played out in every cell,” Brown said. “It can tell us what the cells are like and what they’re able to do. That’s why it has such useful applications for anything in biology.”

In presenting him with its 2002 innovation award, *Discover Magazine* cited Brown’s invention as “a research tool that has fundamentally changed our understanding of genetics and has transformed genetic research.” Microarrays thus raise “new possibilities of dramatically improving treatment and cure rates for various diseases,” according to the article.

They also raised the possibility of making Brown a very wealthy man, but he said going into business would have been “a complete conflict of interest” and “undermined a lot” of what he was pursuing in basic research.

“I love what I do. Being able to do basic research — that’s such a precious opportunity,” he said. “I wouldn’t want to trade that for anything.”

Quirky? Unconventional? Maybe. But over the years, remarkably consistent. Brown has served on the Stanford biochemistry faculty since 1988, a full professor since 2000. In 2002, the Howard Hughes Medical Institute honored him with its prestigious investigator award. All his many honors and accolades showcase much of the same thing — a drive borne of an insatiable curiosity and an idealist bent.

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Born in Washington, D.C., among the last of the baby boomers, Brown would be a teenager before he knew his dad was an analyst for the CIA. But his father’s work led the family to travel, exposing the young Brown to life in such faraway places as Paris and Taipei and teaching him “the true scope of possibilities,” he said.

Brown’s father graduated from the University of Chicago, and his son would follow in his footsteps to begin his academic odyssey. Brown took three degrees from his dad’s alma mater: a bachelor’s in chemistry in ’76, a doctorate in biochemistry in ’80 and an MD in ’82. He left college with more than just three degrees. It was at Chicago that Brown met his future wife, Sue Klapholz, PhD ’80, MD. The couple has since added three children to their family.

Although he did a pediatric residency at Children’s Memorial Hospital in Chicago, a career in medicine didn’t materialize for Brown, mainly because of his keen interest in research. After he completed his residency, he landed a coveted research post at the University of California-San Francisco working in a lab run by J. Michael Bishop and Harold Varmus. This biochemistry duo would go on to share the 1989 Nobel Prize in Medicine for their discoveries about how genes can ignite cancerous tumors.

When the offer came to join Stanford in 1988, Brown’s reputation had him pegged as a rising star in AIDS research. He’d published a groundbreaking paper showing how the AIDS virus invades the genetic apparatus of cells and plants its destructive DNA. The paper held the promise of pointing drug designers in the direction of an effective compound to fight the disease.

But once at Stanford, Brown surprised everyone but himself by changing gears. He soon became immersed in a dogged pursuit of a simplified way to build and use DNA microarrays, recognizing their enormous potential in genetic research and the implications for advancing almost the entire scope of biological science.

By refusing to become defined by a narrow field of research, Brown revealed his true character as a scientific explorer. He spent most of the early 1990s working with Stanford engineers to design a robot that would make the tedious work of building what he called his “home-brew” microarrays nearly as simple

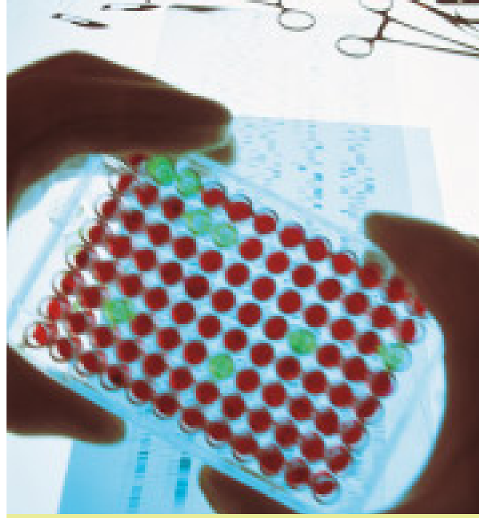

Photo by David Joel


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as turning on a switch. When the robot was perfected, he published a "how-to" manual on the Web that helped these robotic devices become standard equipment in life science labs throughout the world.

As he watched his invention mature and proliferate, he also began to see how the free flow of information affected its use.

From almost the day he set foot on the path to a career in science, Brown had nursed a bone in his throat over what he considered to be a fundamentally flawed process of scientific publishing. In the "publish-or-perish" world, academics routinely publish the results of their publicly funded research through private, commercial publishing houses. In the bargain, Brown felt ordinary citizens are largely denied access to the information their taxes pay for because of the eye-popping subscription costs for many of the best scientific journals. The system grated on Brown's sensibilities as a self-styled Everyman of science.

"We viewed this entire process as being patently unfair," he said. "Not only were scientists in poor countries being denied access to the latest and best information out there, but the public who supports this research was being denied access as well. We felt there simply had to be a better way to do it."

From the start, Brown and his like-minded colleagues (including Varmus, who had become director of the National Institutes of Health) realized they were taking on a Goliath. Western methods of publishing scientific literature were well entrenched and largely in the hands of a few for-profit publishers with decades of academic tradition on their side.

But the printed page still dominated as the disseminator of science discovery; the Internet was an afterthought. Brown and his cohorts felt a fresh breeze blowing across the scientific landscape, especially the free exchange of information.

In 2000, Brown, Varmus and one of Brown's former post-doctoral fellows, geneticist Michael Eisen of the Lawrence Berkeley National Laboratory, led a grassroots effort to reform the system. They wrote an open letter calling for the creation of a new model for releasing scientific papers to the public. The central idea: Scientific publishers should profit from newly published material for only six months, after which the content would be available in a free, online database.

"We expressed our view that scientific publications are intended by the research sponsors and by the scientists themselves to be as freely available as possible and further, that we believe that society is best served by putting this [literature] into the public domain," Brown said.

The appeal, which drew more than 34,000 signatures from scientists in 180 countries, ultimately failed. But the effort revealed a genuine hunger throughout the scientific community for reform.

Brown's answer: Launch a nonprofit publishing enterprise that would go head-to-head with the best commercial models in scientific publishing. To pay for publishing costs — mainly digital page production — scientists or their institutions would pay a modest fee, typically $1,500 per accepted article. Digital versions of publications would be available online to the public for free and print versions at cost.

Backed by a $9 million grant from the Gordon and Betty Moore Foundation, Brown, Eisen and Varmus (now president and CEO of the Memorial Sloan-Kettering Cancer Center in New York) established the Public Library of Science. PLoS — as it's best known — rolled out its premier publication, *PLoS Biology,* in October 2003. The following fall, *PLoS Medicine,* billed as an "international medical journal," made its debut. In time, Brown said, the new publishing venture will branch into all life science fields and eventually embrace the humanities, social sciences and economics.

First, though, PLoS has to prove itself. By large measure, Brown said, the venture's launch has been a success: A rigorous peer-review process is in place, increasing numbers of top-drawer papers are showing up, reviews in *The New York Times* and other newspapers have been favorable, editorial staffing has been beefed up — including three editors based in Europe — and the new medical issue. Cooperation among universities is growing as well, with a consortium established of supporting campuses, Brown said.

On the whole, things are progressing much as he and his partners predicted two years ago, he said.

"We're fighting inertia. Scientists are just like everyone else in one sense — they get into habits in how they do things. It takes energy and courage to buck the status quo," Brown said.

"Because we were new, we always felt it would be a struggle to win over the entire scientific community, but we're getting there," he said. "And the public is beginning to take notice and see the value of what we're doing. We're still totally confident we're on the right track."

Perhaps there's no better proof of that than the recent revelation that PLoS — and similar open-access publishing efforts in Europe and elsewhere that have sprung up in recent years — clearly have some of the biggest publishing houses worried. Last June, the London-based *Guardian* reported that the CEO of the Amsterdam-based company Reed Elsevier, the world's largest publisher of scientific journals, denounced the move toward "open access publishing" as a threat that could wreck "the entire academic publishing industry." That same month, *The New York Times* reported that pressure from PLoS is beginning to have an impact, offering as evidence recent policy changes at some houses that soon will open their databases to the public six to 12 months after initial publication — precisely what Brown and Varmus had called for initially.

To add to the bandwagon, NIH recently proposed to make all agency-funded research papers publicly available six months after journal publication. It's asking all authors receiving NIH funding to send electronic copies of their final manuscripts to the agency, which would make them freely available on the NIH Web site, PubMed Central, six months after official publication.

Meanwhile, Brown muses slaying other dragons. He's starting a new assault on the AIDS virus, employing his gene chips and a world of new knowledge that technology has brought to the task. Remarkably, somehow he still manages to dream, and when he has lately it's been about innovative approaches to developing sustainable, nonpolluting sources of energy.

"That's a very complicated problem, I know, but it's something I'm very interested in," he said. "I'm trying to educate myself right now, just trying to figure it out."

"I think most scientists are optimists, really. Given tough problems, we realize there's probably no perfect solution. But if you work hard enough, you can usually come up with practical steps to make things better."