Patrick Brown

Even when the chips are stacked against him, microarray pioneer Patrick Brown remains an incurable optimist. After defeating dogma in biochemistry and genetics, Brown is taking on the world of publishing—and he still hasn't run out of breath.

In the spring of 1995, Stanford University researcher Daniel Herschlag introduced his friend and colleague Patrick Brown to the joys of running. The two researchers began jogging regularly on the Stanford campus.

"Almost as soon as [Brown] started, he said, 'I want to run a marathon,'" recalls Herschlag. Just four months later, on the cold and damp day of the Sacramento Marathon, Brown woke up with the flu and a temperature of 102 F, and missed his bus to the starting line. Undaunted, he began running directly from his hotel and finished the race near the head of the pack in just under 3.5 hours.

That same indomitable spirit has allowed Brown to go the distance as a scientist, Herschlag says. Brown is perhaps best known for his work on microarrays and HIV integration, but his eclectic interests run the gamut from basic science to translational medicine. With a network of some of the best scientists in the world—his website lists 36 collaborations—he has examined the genetic signature of cancer and other diseases, used microarrays to analyze chromosome breakage and gene copy number, and dived into RNA dynamics.

"Pat tends to create an atmosphere where people feel empowered to go out and do things and explore—that leads to a lot of new discoveries," says Herschlag. "His intellectual force and personality really make people gravitate towards him."

In academic circles, Brown is famous for his unconventional approach to science, his tendency to talk in superlatives, and his unbending opinions. In person, he can be surprisingly shy and unassuming—until he begins talking about one of his pet projects.

"One of the things I like about Pat is that he has a great combination of imagination and enthusiasm on one hand, and very hard-core, solid principles on the other," says Richard Tsien, Brown's collaborator and colleague at Stanford. "There is an almost messianic zeal about the way he does things."

Throughout his career, Brown has taken stances that challenge the prevailing ways of thinking. While still in graduate school, he found that the enzyme topoisomerase II slices DNA before passing a double helix through the break. Initially met with skepticism, the finding has since earned a solid place in textbooks.

"He's very iconoclastic—he's always been that way," says Nick Cozzarelli, his graduate advisor. "And a surprising number of times, his ideas have turned out to be correct."

Perhaps the most telling illustration of Brown's unerring instinct is his work on microarrays. In 1992, he submitted a grant proposal to the US National Institutes of Health (NIH) that included a piece on microarrays. "I had the whole thing laid out," Brown recalls. "I was just so sure [they would fund it]." Much to his chagrin, the NIH specifically nixed the part about microarrays. It wasn't until he took out that part that the agency agreed to fund his proposal.

Brown's vision has been more than validated since then. His 1995 paper on the technology has been cited more than 1,700 times. He says the episode taught him a valuable lesson: "If people tell you [a project] is a waste of time, it's going to be good."

Despite what anyone else may think, Brown says, his unshakeable faith is the key to his success. His oft-repeated phrase—"Blast ahead!"—has

inspired his students and colleagues when their own faith was in short supply.

"When you are in the middle stages of the project and things are not going well, and you go to see Pat Brown—when you come out the door, things are rosy again," says Joe DeRisi, a former graduate student, now a researcher at the University of California in San Francisco.

Faced with an obstacle, Brown does not hesitate to venture outside the life sciences to surmount it. Building the first microarray required engineering expertise, for instance. Brown enlisted the help of Dari Shalon, then a graduate student in mechanical engineering at Stanford.

In the mid-1990s, Brown stumbled across a different kind of problem. He found that analyzing microarray data from thousands of genes involved long, tedious sessions with cumbersome PDF files and massive tomes in libraries. He came to the conclusion that to mine the literature systematically, published results would need to be easily accessible to anyone. "Suddenly, the problem for research was this kind of political, social problem," Brown says. "But as far as I'm concerned it's fundamental to [science]."

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Along with such scientific heavyweights as Harold Varmus (*Nat. Med.* 7, 10; 2001) and Michael Eisen, Brown helped found—and spends a significant amount of time promoting—the business model of the Public Library of Science (*Nat. Med.* 9, 154–155; 2003), which published its first open-access journal in October. He now refuses to publish in journals that don't fit his criteria for open access. "It bothers me that a good paper winds up in a journal that doesn't deserve it," he says. Although his first microarray paper appeared in *Science*, "I would die before I publish a paper in *Science*," he now says.

Brown also expects his collaborators, students and postdoctoral fellows to publish in a select few journals. He says he "bends over backwards" to promote his students' careers in other ways, but his zeal has made for some tense situations (*Nature* 425, 334; 2003).

Brown can afford to turn his nose up at publications such as *Science*, *Nature* and *Cell* because he has already established a reputation as a solid researcher, notes Larry Steinman, Brown's colleague and collaborator at Stanford. But young researchers need to publish in high-profile publications to launch their careers, Steinman says. "When it comes down to thinking of what [Brown] wants or what they want, [his students] might first have to think of themselves."

These days, Brown is training for his eighth marathon. He is a familiar figure on the Stanford campus, jogging with his three children or his dog. "He finds a way to enjoy almost any situation," says Herschlag. "Nothing will slow him down."

Charlotte Schubert, San Francisco, and Apoorva Mandavilli, New York