Legendary Labs

Secrets of academic researchers who produce excellent science and great scientists

By Adrienne Burke

PHIL SHARP, WHO WON THE 1993 NOBEL PRIZE IN Medicine and trained a scientist who won the same award 13 years later, says he learned from his first mentors how to nurture budding talent. While Sharp was still a grad student in chemistry at the University of Illinois, Victor Bloomfield gave his career a boost by telling other scientists about his work and by sending him to scientific meetings. And his postdoctoral advisor, National Medal of Science recipient Norman Davidson, encouraged Sharp to pursue his own research and engage with other faculty at Caltech.

As he continued his studies under 1962 Nobel Laureate James Watson at Cold Spring Harbor Laboratory, Sharp learned that "if you surround yourself with very exciting people and research projects in an environment where ideas are always percolating and you can add your own perspective, then it's easy to do cutting-edge research."

Sharp certainly makes it seem that way. Progeny of the MIT lab, where 30 years ago he discovered the split gene structure of higher organisms, now populate faculty posts at nearly every major university in the country. Sharp Lab alumni include Howard Hughes Medical Institute investigators, National Academy of Sciences members, and Andy Fire, who won a Nobel in 2006 at age 47. As a group, so-called Sharpies share such fond memories of their days under his tutelage that they organized 20- and 30-year reunions at the lab. Sharp counts them among the happiest days of his life.

Academic scientists such as Phil Sharp, who are as well known for producing excellent science as they are for grooming following generations of top-flight scientists, are a unique breed. Within a system that gives recognition, money, and tenure for scientific achievement, good scientific citizenship generally goes unrewarded. Those who conscientiously nurture their successors' careers are motivated by pure altruism.

And they are largely self-taught. Unlike in industry, where scientists in supervisory roles are typically immersed in management training, few universities offer even basic leadership instruction to newly minted principal investigators.

John Inglis, president of Cold Spring Harbor Laboratory Press, which has published several books on scientific management in recent years, says, "Postdocs who not so long ago did something really great and are given a lot of money and have to set about building a group are immediately faced with all kinds of challenges. Very seldom has anybody talked to them about how to do this leadership thing and how to cope with all the human situations that science throws up when you're dealing with a creative endeavor."

THE DEMORALIZED LAB

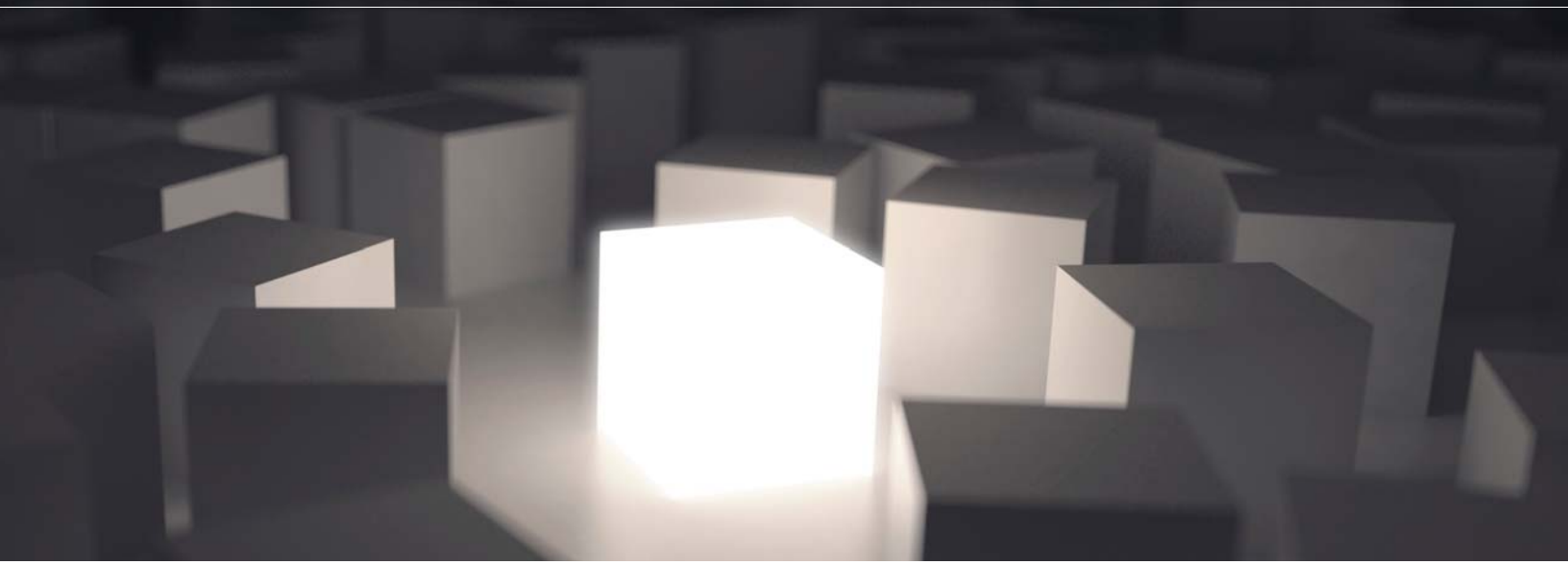
It's no surprise then that the iniquitous university workplace—where senior investigators take credit for students' work, schedule lab meetings on holidays, or provoke postdocs to hoard supplies and lock up their data by pitting them against one another—is no mere myth.

Carl Cohen, president of Scientific Management Associates in Boston and author of *Lab Dynamics: Management Skills for Scientists*, says lousy leadership is rampant in science. "Scientific projects get destroyed, interactions go astray, and students flounder, not because the science itself is wrong, but because scientists are not attuned to personal dynamics," he says.

Maryrose Franko, senior program officer for graduate science education at Howard Hughes Medical Institute, advises students against pursuing postdoc appointments based only on the principal investigator's scientific accomplishments. Franko says many graduate students resolve to put up with whatever misery they must for the chance to work in a prestigious scientist's lab. But, she warns, that strategy can backfire.

One promising young postdoc Franko knows signed on wittingly to the lab of a less-than-supportive P.I. "I warned her, 'He's a shark,'" says Franko. "But she said, 'I don't care, he's the best in the field.'" Now, three years later, the senior investigator has prohibited the postdoc from taking her research to her first faculty appointment. She's dependent entirely on a referral from him to get anywhere.

Kathy Barker, author of the popular lab management advice book, *At the Helm* (see our lab management booklist online), says that people frequently tell her that they wish their P.I. had taken a course or read a book about how to run a lab. "One in three people I talk to have had bad PhD experiences," she says.



But does it matter? "The fact is that very great science can come out of groups that are disasters in terms of human relationships," says Inglis. "A certain amount of money was spent, a certain number of people left science because they were so disillusioned about how the research enterprise works. But does any of that matter if the end result was a significant advance in our understanding of how a cancer cell works?"

David Baltimore, past president of Caltech and Rockefeller University, would say it does matter. "I want to get great science done, but that's not the primary thing. The primary thing is the training, because that's what's going to last," he says. To scientists like him, the advancement of the research ecosystem is more important than any single scientific discovery. And, as Barker points out, providing a future P.I. with an excellent experience can have far-ranging results: "Once you've been in a wonderful lab, you want to make your lab like that."

NO FORMULA FOR SUCCESS

Just what makes a lab wonderful? Even the most highly acclaimed leaders aren't sure of the keys to establishing an excellent research culture. Says Sharp, "It's sort of like cooking. You can follow a recipe, but you only know it works when it works."

Asked to explain his secret to having trained nearly 100 accomplished scientists, including department chairs at Columbia, Duke, Harvard, and MIT, David Botstein says, "It's a reasonable question, but I don't know." Botstein, who taught at MIT and Stanford before becoming director of the Lewis-Sigler Institute for Integrative Genomics at Princeton, says he sees it as his job to produce great students. But he has no formula. "I can only tell you what seems to work for me."

Indeed, conversations with a dozen P.I.s widely recognized as great mentors reveal that few have any scripted approach to mentoring.

George Church, director of the Center for Computational Genetics at Harvard Medical School, has launched some of the most promising young systems biologists in the country. Princeton Associate Professor Saeed Tavazoie, who zoomed from PhD thesis to tenure in just five years and was spotlighted in the New York Academy of Science's New Vistas series for his contributions to gene function analysis, sprang from the Church lab. So did Jay Shendure, an assistant professor of genome sciences at the University of Washington who was named to *Technology Review* magazine's TR35 list in 2006 for a remarkable genome sequencing technology he developed in Church's lab. But like most of his peers, Church candidly reports that he has never studied management or even thought much about it.

Nevertheless, these senior investigators have gleaned and put into practice a certain amount of lab management wisdom over the years. The advice they impart comes down to four simple maxims:

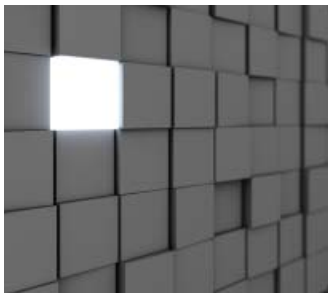
- Hire well;
- Be more guide than boss;
- Do your best to foster an open, congenial, collaborative culture; and,
- Put teaching and your underlings' careers first, your research second.

RELIGIOUS ABOUT RECRUITING

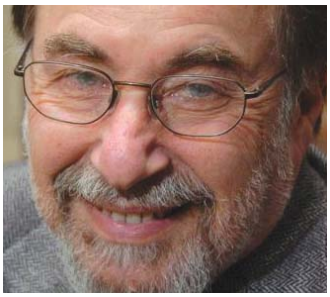
While great lab leaders unanimously disdain micromanagement, hiring is one function they control carefully. "When you try to appear to run a *laissez faire* lab, you have few leverage points," says Church. "The big one is whom you select. That affects tone, ambiance, and subject matters, so you need to exert quite a bit of certitude."

Surprisingly, brilliance isn't necessarily the first trait they seek in postdocs. "I don't look for people who are very smart," says Church. "If you got into grad school at Harvard or MIT, I don't have to worry if you're smart. I'm mainly looking for people who are nice." Church says he is careful to not let his lab revolve around him, and he also shuns candidates who seem most concerned about their own success.

Phil Sharp looks for postdocs with a track record: "They've advanced a problem, can articulate what the problem is, and they have a view of the world that is developed and sometimes different," he says of ideal hires. In grad students, he seeks those clearly "immersed" in science. "They read, they talk science, they work in the lab with a lot of commitment, and they go to lectures and come back with ideas."



NYAS President's Council member Phil Sharp



NYAS President's Council member David Baltimore

Academy member David Botstein

Bob Weinberg, a Whitehead Institute founding member and cancer research pioneer who has trained more than 100 scientists in his MIT lab, says his top criterion for selecting grad students and postdocs is that they be able to get along well with others. "I ask about that before I ask about scientific mettle," he says. "How generous are they with their colleagues? How often do they share? I have turned down an applicant not because they weren't brilliant, but because I'd heard they weren't the most pleasant to have around."

In fact, Weinberg makes it a point to survey candidates' past mentors and labmates before making an offer. "You often have a postdoc around for three, four, five, six years. It's kooky not to invest time in that detective work," he says. "I don't want people in my lab all to be in love, but I would like them to get along and share."

Janet Thornton, director of the European Bioinformatics Institute in Cambridge, UK, goes a step further to have "a group of people who get on well together," she says. She asks existing staff to screen incoming candidates, and takes their reviews seriously. When the feedback was, 'if you recruit this person, the whole group will resign,' she quickly rejected the applicant.

"True grit" is what HHMI investigator Pippa Marrack looks for as "one of the best predictors of future success." What's true grit? "It's about being brave enough to go for the core of the problem, and being persistent and not giving up when something looks like it's going wrong," says Marrack, who has run a lab at the National Jewish Medical & Research Center in Denver with her husband John Kappler for nearly 30 years. "It's being able to persevere when the reviewers say your paper is crap." Marrack says a one-day interview "can occasionally reveal when someone has done something in their lives that lets you see they have courage."

Independence is another sought-after characteristic, especially among senior leaders with multiple responsibilities and overbooked calendars. "As my own life became more complicated running universities, increasingly over the years I have made independence a very important part of the equation," says Baltimore. "The worst thing I can do is accept people who can't handle independence."

EMPOWER AND GUIDE

In fact, the freedom to pursue independent research is what most of these accomplished scientists say they most valued about their own training. "Dulbecco was a hands-off mentor, so I was given as much freedom to do what I wanted to and that made an impression on me," says Bob Weinberg. Everybody in his lab has their own project, and knows up front that when they leave they can take it with them. That way, he says, "They can take pride and ownership in what they're doing."

David Baltimore recalls that Richard Franklin at Rockefeller University "was a wonderful mentor because he gave me the freedom to do what I wanted to within the context of working on problems in virology." Baltimore says the experience taught him the "tremendous importance of allowing young people to find their own way." Over time, he says, "I've just developed great respect for what trainees can do if you support them and provide critical intelligence while letting them define as best they can where they want to go."

Janet Rowley, the 1998 Lasker Award winner, famed for having identified a specific genetic translocation in leukemia, was mentored by 1966 Nobel Laureate Charles Huggins. She says that when she started up her lab at the University of Chicago in 1969 she approached lab management the same way she did child rearing. "You give people a lot of freedom, you're there to help them if they need it, and you let them go," she says.

Rowley also says she prefers flexibility to rules and regulations: "You don't know where creativity is going to come from, and as lab director you have to be open to it coming from an unusual direction."

George Church's lab is so free of rules that he compares it to an artists' colony. "I couldn't be in a cookie cutter mold where the lab was real production-oriented like a factory, or so hung up on dogma and protocol that you couldn't think outside of the box," he says. Having been trained in a research environment that rewarded creativity and interdisciplinary effort, Church says he has adopted the same system.

He is also a fan of equality for people and ideas. "I try to treat everybody as a peer. The lab isn't entirely without hierarchy, but it's historically been pretty flat." As a result, it operates like a free-market system. "If I want to get something done, I have to sell my idea down the line. If it doesn't sell, I realize there's something wrong with my message or it's a bad idea," Church says.

While all of the scientists interviewed for this article talk about the importance of being supportive to their trainees, they also all see value in letting people flounder and learn from their own mistakes. Church says there's a fine line between maintaining a nurturing environment and one that promotes critical thinking. "You don't want to be so supportive that you can't tell someone something is a bad idea, but you don't want to be so critical that they think all their ideas are flawed or that all good ideas come from one person."

Joan Steitz, James Watson's first female graduate student at

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One of the many things you're known for at NYU is fundraising. Is that a talent that you intend to lend to the Academy?

Fundraising will be very important to the Academy. I think it's something that I can help the Academy do. I've been known at NYU for creating, inside the context of the university, the "idea-generated gift," as opposed to the "loyalty-generated gift." NYU is not a university that has a long history of loyalty-generated gifts the way some institutions in the country do. So we had to come up with this notion of the idea-generated gift, which is simply having a good enough outcome created through the philanthropy to make a case that we were worthy of philanthropy.

That idea is transportable to any context and it's the way the Academy has to do its fundraising because there's no such thing, really, as a loyalty-generated gift. The Academy has members, yes. But it doesn't have graduates who owe their careers to the Academy. Quite the opposite: people come because they have careers in science.

Where I could be helpful is in bringing this technique of the idea-generated gift to the Academy and creating a case and a story for the Academy that is powerful enough, in a world where there are a lot of demands on people's philanthropy, to make the Academy one of their investments.

It's my intent to do as much as I can to help Ellis and the Board and the Academy to shape that story. And then, to the extent my energy is wanted, I will help spread the story. Fundraising is not the waving of some magic wand. It's not something that any person's arrival causes in and of itself. That case, in my view, depends upon the quality of the value proposition that can be advanced by the seeking institution. The Academy has got that case. If we have success in fundraising it won't be my success, it will be the success of the Academy in creating for itself a purpose that is compelling to potential benefactors.

Would you describe one crowning moment of your career?

I have said frequently that whatever pride I have in what was accomplished at the law school during my time as dean and in what has been accomplished at the university during my time as president, the single professional achievement most dear to me was achieved between 1960 and 1975. At the age of 17, as a freshman going on sophomore in college at Fordham, for reasons I can't quite explain, I wanted and was allowed to create a high school debating team at St. Brendan's girls' Catholic high school in Brooklyn.

I had been the national high school debate champion myself, and, because I had done it, I didn't think it was remarkable to be the national high school debate champion or to get a scholarship to college or to get to see parts of the country you never would have seen. So, armed with that lack of awareness and utterly oblivious to the fact that, in 1960, Italian Catholic, Irish Catholic, and a few black families in Brooklyn viewed high school girls as having certain roles in the family, I was able to convince a group of nuns to let me try to start a high school debating team.

That work really defined my attitude towards teaching in professional life. I was very proud three years ago when Emory University, celebrating the 50th anniversary of its high school debate tournament, named those girls the top high school debating team of the last 50 years. St. Brendan's won the national championship five times in those 15 years and every girl went to college on a scholarship. Some even went on to be scientists. ■

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Phil Sharp's method for helping students develop their careers is to get them to take ownership of an idea and then to plan and execute a series of experiments that advance the understanding of science in that area. "It works best if that interest is aligned with my interest in the lab. Occasionally it will align to something only distantly related, but I've always found it most important to put the person's development at top."

Church steers postdocs in directions that are most likely to let them taste success. "It's a soft touch," he says. "It's amazing how little it takes to steer, but you don't want any of your postdocs doing something that is so impossible that there won't be milestones or they won't get any credit."

Even before coaching his postdocs on the problems they chose to tackle, Bob Weinberg sees an important role for himself in influencing their thinking. "I want to impart to them a taste for working on problems that are important and will be thought to forge new conceptual paradigms."

In discussions over lunch at least twice a week, and in a journal club where they analyze recent scientific publications, Weinberg teaches his people to think critically about research questions. "Is this an interesting question?" he challenges. "Have they focused on something important, or is it trivial in terms of its heuristic value? Are the data really that interesting? Or are they just filling holes in a brick wall?" He says these questions train people to think about whether or not a topic is worth the investment of time.

Baltimore considers "framing the right question" to be "the hardest thing in science." He says questions have to be audacious enough to be interesting and yet experimentally tractable. "Finding that balance of interest and do-ability is something you only develop with experience and with trying things that are too hard or doing things that are not interesting enough," he says. "I try to help people find that sweet spot. And when we're successful, they do wonderful things and they develop a lot of self-confidence, and when they leave my lab they're ready to establish their own labs and be successful."

Contrary to the supervisor of the hapless postdoc who has no rights to the data she produced, Weinberg makes it a point to ensure that the research his postdocs do in his lab will help launch their careers. He says, "Some labs have rules that when they train grad students or postdocs, the project stays in the lab. When my lab continues in an area of research, I try to stay out of the way of the person who has gone away so they're not being undermined by my lab." To do otherwise, he says, would be very unfortunate. "I'm interested in their soaring, not sinking," he says. ■

Adrienne Burke is executive editor of the magazine.

on the web

For a list of more than 20 books on lab leadership recommended by these scientists, as well as a link to lab management resources from the Howard Hughes Medical Institute, see **nyas.org/legendarylabs**.

Win a lab management book by Kathy Barker or Carl Cohen for yourself or your favorite PI by being one of the first 5 people to share a story—good or bad—about life in your lab. Write to **magazine@nyas.org**.