THE INDISPENSABLES

THE BACKBONE OF MOST LABS, THESE QUIET HEROES DO IT ALL AND THEN SOME.

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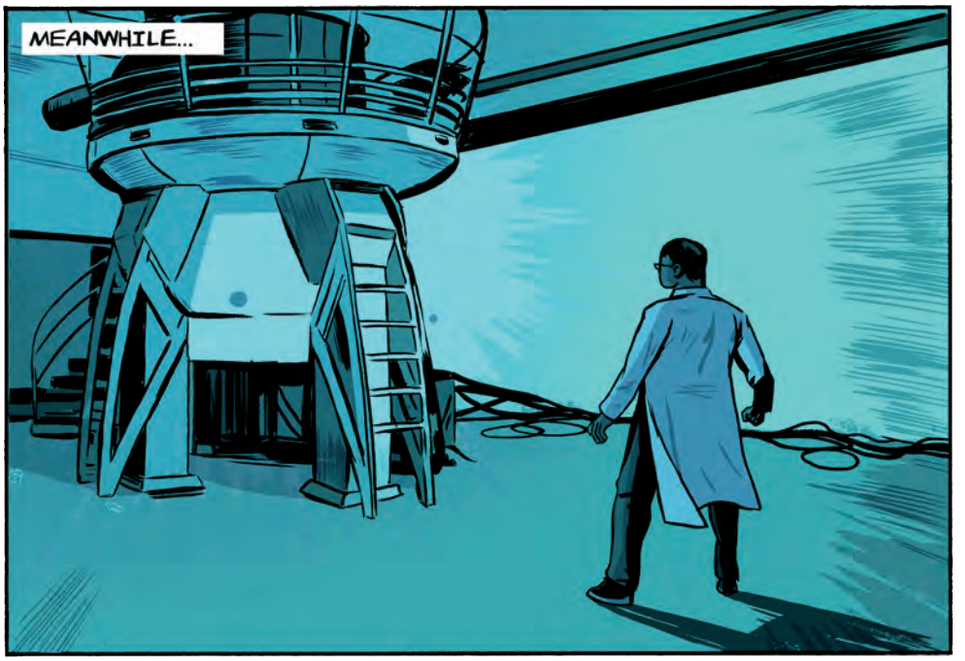
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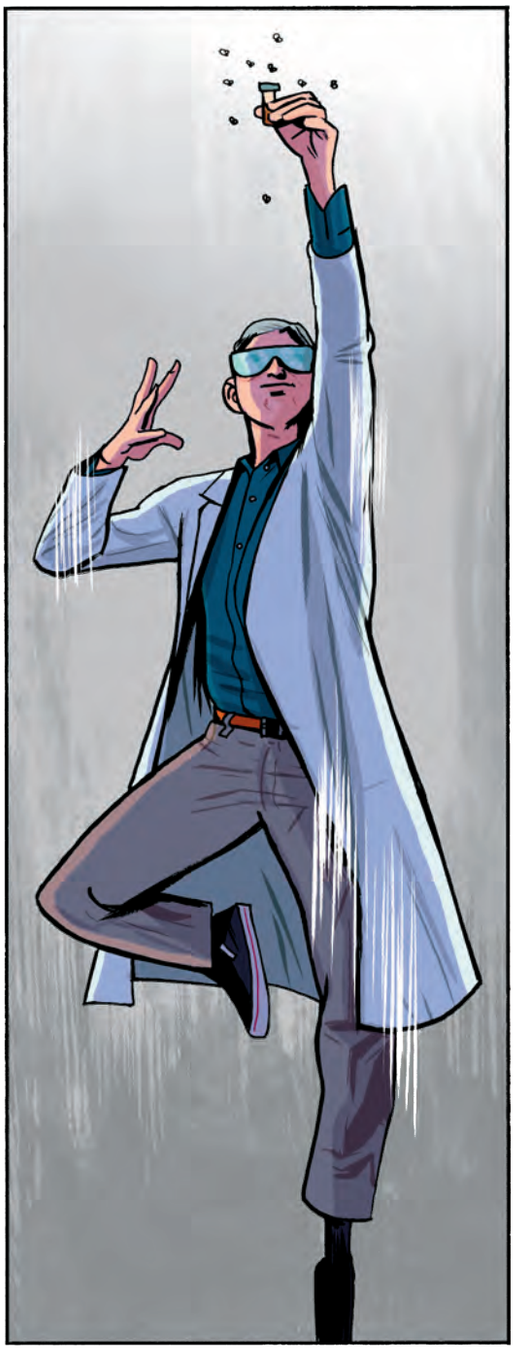


PROBLEM SOLVERS, SHELF STOCKERS, BENCH SCIENTISTS, RECORD KEEPERS, MACHINE FIXERS, WEEKEND WARRIORS, DEN MOTHERS, OLD HANDS, FRESH EYES, MENTORS, MANAGERS. EVERY RESEARCH LAB HAS BEHIND-THE-SCENES SPECIALISTS WITHOUT WHOM MODERN SCIENCE COULD NOT GET DONE.

Their bland bureaucratic titles—research technician, resource manager—belie their vital contributions. These women and men are not wannabe principal investigators (PIs) or discouraged academics. Some have specialized expertise; others are jacks-of-all-trades. They are ambitious, not for fame, but for personal excellence and the chance to make a lasting contribution, however unheralded, to science.

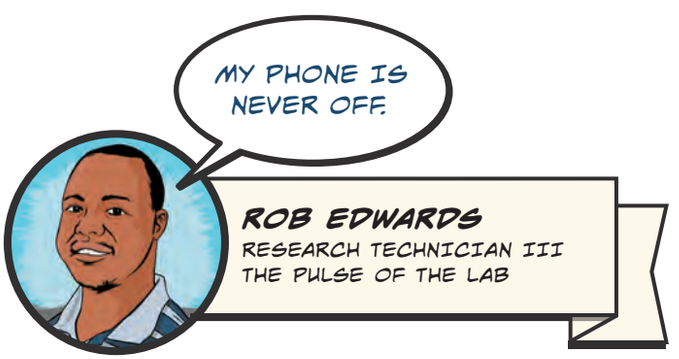
"There are very few laboratories that do not have at least one technician who often plays the role of lab manager, making sure the trains run on time, the supplies are ordered, the equipment gets repaired. It would be very hard to run a lab without such a person," says Shirley Tilghman, a molecular geneticist and president of Princeton University.

It's a career option that needs serious consideration, according to Tilghman, who cochaired the National Institutes of Health Biomedical Research Workforce Working Group. The group's June report calls for professionalizing the crucial research-affiliated roles of lab specialists and paying them accordingly. "Make them a professional category that academic medical centers and research institutes and universities recognize as valuable—in fact, invaluable—parts of the biomedical workforce."

A little recognition wouldn't hurt, either. "As in most areas, credit flows up the hierarchy," explains Gerry Rubin, director of HHMI's Janelia Farm Research Campus, in Ashburn, Virginia. "The people at the top get way too much credit. And the technicians and managers don't get enough. Academia very much rewards individual achievement—less so, team achievement."

Adds Rubin, "Labs are full of students and postdocs who come and go every three to four years. It's important to have somebody with a sense of continuity and context."

Here are the stories of five indispensable lab team members, among many acknowledged by grateful HHMI investigators.



Seventeen years ago, Rob Edwards noticed an ad for a radio frequency engineer in the HIV-focused laboratory of HHMI investigator Michael Summers. On paper, Edwards may have

seemed an odd fit for the lab: no academic experience, just lots of work for defense contractors. "I don't want to say this, but my old job depended on war—and sometimes, on destroying people's lives," he says. Today, after nearly two decades working alongside Summers, Edwards' career has been recast. "What we do here saves people's lives. It has a purpose."

At the University of Maryland, Baltimore County, Summers and his team are studying the architecture of HIV to understand how it and other retroviruses assemble, and how the viruses package their genetic material to infect other cells. This scientific pursuit hinges on nuclear magnetic resonance (NMR) spectroscopy—which is where Edwards enters the picture. He is responsible for two 600-megahertz NMR machines and a mammoth 800-megahertz instrument with a cryogenic probe. "There are so many things that can go wrong," he says. "The magnet, the probe, the platform, the software, the console, the amplifiers."

But NMR machines are just part of Edwards' job. He designs the electrical and mechanical components of laboratory upgrades and ensures the continuous operation of centrifuges, water purification systems, electrical generators, and other critical research tools. "I keep everything up and running, because you never know when a grad student or a postdoc will have that sample—the protein they've been working on for a year," Edwards says. "When they're ready to roll, there can't be any obstacles on the instrument side."

Edwards also mentors young scientists in Summers' lab—including a large number of minority grad students and postdocs, who may not have received ample encouragement in the past. "He has served as a positive force for about 50 high-achieving minority students who have worked in my laboratory," says Summers, "often privately enforcing his own interventions to challenge the students and support them during times of academic struggles."

As Edwards explains, "I'm a minority also; I know you can get down on yourself. So I always say, 'I believe in you.' That's what Mike said to me when I first started here: 'You can do it, I hired you for a reason, just be confident.' Now that I have that confidence, when I see someone without it, I try to instill it."

Edwards brings this sense of purpose to every facet of his job. "My phone is never off. My vacation time is maxed," he says with a laugh.

"Embryonic stem cells have to be tended and fed every day. They don't know about weekends or holidays," says Phil Smallwood, a research technician for 18 years in the laboratory of Jeremy Nathans, an HHMI investigator at the Johns Hopkins University School of Medicine who studies the mammalian visual system.

"When I'm actively working with the cell cultures, I'm here seven days a week. I have been here Christmas Day, New Year's Eve, New Year's Day," says Smallwood. "This is why Jeremy trusts me: he knows that it will get done and it will get done correctly. These cells are going to be turned into a mouse. I won't cut corners, because Jeremy is basing his reputation on the conclusions that he will draw from these mice."

"Extraordinary experimentalists" is how Nathans describes Smallwood and research specialist Yanshu Wang, another essential lab team member (see Web Extra, Lab Heroes). "They have the same relationship to doing experiments that Itzhak Perlman has to playing the violin."

For Smallwood, who has created 40–50 mouse lines in Nathan's lab—transgenics, knock-ins, knockouts—the musical analogy is apt: away from work, he is an accomplished flutist. "You always have to practice—you can't rest on your laurels. It's the same in science. You always have to keep learning new techniques, advancing with technology, or you'll get left behind."

Smallwood also draws on another analogy to explain the craft of science: cooking. "The first time you make a cake, you follow the recipe. It's the same with an experiment: you can't change a variable right away. But after doing it for many years, you get a feel for how the cell behaves, for what works and what doesn't. Take something as simple as pipetting an enzyme back and forth, such as in trypsinization, a process to chemically separate cells. I was originally taught that you add the trypsin once and place the colonies in the incubator. But the colonies don't completely break up. I found that if you pipette the trypsin back and forth a few times and then put the colonies in the incubator, it's like night and day. It's a little trick that goes a long way."

The co-inventor of 10 patents—beneficiary of Nathan's uncommon largesse in sharing professional recognition—Smallwood doesn't feel like an unsung hero. Yet while he appreciates the recognition, he doesn't crave it. "The students, they come in, find a project, get published, go on for a postdoc, look for a job. I'm content to be in the background. Jeremy arrives in the morning and there I am at my bench. I'm a constant. I'm with Jeremy for the long haul."

Among the many niche communities in the giant enterprise of science, worm experts are a special cadre. *Caenorhabditis elegans*—the slender and sinuous nematode—may be a model organism, but it also requires model experimental techniques. And in the small guild of *C. elegans* specialists, Peggy Kroll-Conner is a star.

Judith Kimble, an HHMI investigator at the University of Wisconsin–Madison who studies the fundamental controls of animal development, has for 16 years relied on Kroll-Conner's finesse. "Peggy is the heart and soul of all our genetics," says Kimble. "She has become the person who generates some of the most finicky strains in the lab. In the worm community, she is known as being exceptionally fastidious—her strains always have the correct genotype and, just as important, are not contaminated."

According to Kroll-Conner, the key to ensuring that frozen worm stocks are free of mold and bacteria is good sterile technique. She vigilantly labels items to prevent strain mix-ups. Once the worms are frozen, she thaws a portion to make sure the animals are viable and the stock pristine. She returns test thaws to the scientists who created the worms, so they can validate the strains. She also revalidates her own strains. "In other words," says Kroll-Conner, "we do a lot of quality control."

Alongside the ever-present threat of contamination is the challenge of fashioning strains with multiple mutations. "Mother Nature doesn't give up her secrets easily," says Kroll-Conner. "I try to figure out a way to balance the mutations in a user-friendly way, to minimize the work needed to maintain the worms." Certain mutations are more challenging than others, she says. In one experiment, she had to set up a mating with a strain of worms whose reproductive systems quickly developed tumors. "I set up numerous mating plates with large numbers of worms and ended up with only three cross-progeny. Only one of those had the genotype that I was looking for."

Such perseverance and attention to detail is essential in her role. It's also about mutual support, she says, a concept that seems to have been bred into the *C. elegans* world by Janelia Farm senior fellow Sydney Brenner, a molecular biologist who shared the 2002 Nobel Prize in Physiology or Medicine. "When Brenner started this science in the 1970s, he said that the worm community should work together in a spirit of cooperation. He felt that science would advance much faster that way," she says. "I like that philosophy."

"A lot of things go on behind the scenes to make science happen," says Todd Laverty, who for 29 years has supported the work of Gerry Rubin, director of HHMI's Janelia Farm Research Campus. For 23 of those years, Laverty managed Rubin's lab at the University of California, Berkeley. For the last six, he has overseen the *Drosophila* and Media Prep shared resources at Janelia. His specialty is feeding, sheltering, moving, breeding, and otherwise nurturing fruit flies, as well as preparing meals for other laboratory animals. "It was obvious, right from the beginning, that I had found my niche."

At Janelia, Laverty manages some 18,000 fly stocks—that is, 36,000 vials of flies, 50 to 100 flies per vial, each a unique genetic line. He shepherds the stocks through a 28-day lifecycle: egg, three larval stages, pupa, and hatched fly. Each morning, peering through a microscope at flies dozing on a pad suffused with carbon dioxide, he selects virgin females for genetic crosses. Each week, he starts new generations in fresh vials, using a duck feather to gently transfer the prospective parents from one plastic abode to the next. And each month, he manages the production of 130,000 vials of fly chow: a mixture of cornmeal, molasses, agar, and yeast—and gets four-star reviews from lab managers for quality and consistency.

"I can remember telling people, when I started out, 'What I'm going to be doing 20 or 30 years from now, I don't know. But I'm happy now doing what I'm doing,'" Laverty says. After he'd worked for Gerry four or five years, he remembers riding in an elevator with a gray-haired co-worker. "I teased him: 'Who gets gray hair working in a lab?' Funny thing: now *I'm* that gray-haired guy!"

Laverty is the only person Gerry Rubin brought from his Berkeley lab to Janelia. "There was no one better than Todd to set up a facility to support all the *Drosophila* labs here. He is very calm, and he's very good at managing people and building a team," says Rubin. "In my Berkeley lab, at times he had to deal with as many as 15 postdoctoral fellows, all with different needs and demands. He does a remarkable job of keeping everybody happy." In a high-pressure laboratory setting, Rubin adds, "That's a very unusual ability."

Laverty describes himself as "a pleaser by nature. I get satisfaction out of starting a task and following through. PIs get the big ideas: 'This is really cool, let's figure this out. I'm not going to worry about the little steps right now.' It's those little steps that I worry about."

In Rubin's lab at Berkeley, Laverty played a supporting role in more than 100 different research projects, including sequencing the *Drosophila* genome. Published in 2000, the sequence marked a scientific milestone because of the fruit fly's pivotal role as a model organism in research, in areas ranging from aging and cancer to learning and memory. "There were hundreds of people in the field who could do the same thing that I was doing. But I had the opportunity to do it every day in the Rubin lab—and it was the Rubin lab that was sequencing the fly genome."

In 1989, Bruce Walker, an infectious disease specialist at Massachusetts General Hospital, sifted through a tall stack of applications for a technician's job in his lab. He immediately noticed the application from Alicja Trocha, a recent immigrant from Poland who had joined the anti-Communist Solidarity movement as a student in the 1980s. Trocha had worked in a lab on the rabies virus—like HIV, a deadly pathogen. She had earned a veterinary degree. And she had done field work with farmers, suggesting a level of real-world maturity not always seen in hothoused science majors.

Walker interviewed Trocha in German, which she had picked up in an internment camp in Munich after fleeing Poland in 1986. Immediately impressed, he offered her the job. But Trocha, overwhelmed by Walker's laboratory operation and by the technical terms she would need to master, initially declined. He persisted, and the result has been a professional match made in heaven.

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"Alicja has been invaluable to my career," says Walker. "There is nobody in the world who can clone T cells better, and as my lab manager she has not only set the highest standards for performance and integrity but has done it in the most collegial way." Today, Walker leads an international research effort to understand how some rare individuals, known as long-term nonprogressors—infected with HIV but never treated—can fight off the virus with their own immune systems. Insights into their biology could lead to a vaccine or new treatments for the disease.

Trocha supports this effort at the lab bench. "Tissue cultures are like animals or kids," she says. "You have to tend to them, not when you want, but all the time. My colleagues tease me that, since I was a veterinarian, I think of the cultures as my sheep. You may feed them twice a week, but some of them like to eat more, some less. I look at each flask and each culture individually, because they differ in their ability to proliferate. That variability in proliferation might be a clue to why some T cells are effective in inhibiting HIV in the body—and some are not."

As a lab manager, Trocha also deals with the minutiae of administration, regulatory requirements, and the exhaustive task of tracking a large repository of biological samples with bar codes. She documents growth and maintenance of the T cell clones (T cells derived from one "mother" cell that are 100 percent genetically identical), and she teaches fellows and postdocs how to do the same. She also catalogs the clones and the details of how they were established, so that when clinical questions arise years after, she has the answers.

"I believe in myself because Bruce gave me that chance. I would have never known what I could do if I hadn't come here," she says. That brimming confidence extends to the science. "It is bigger than life to be with a group of people who have such bold plans and high aspirations. But this is what I like: trying to make the impossible possible. An AIDS vaccine would change the world."

■ –MADELINE DREXLER

WEB EXTRA: Read about other indispensable lab heroes from HHMI labs by visiting www.hhmi.org/bulletin/Fall2012.