on the mistake of referring to a research lab as a workplace around cell biologist William Wickner, M.D., DMS’s Chilcott Professor of Biochemistry. He considers his lab “a great big playground,” where he gets to choose the “games” (scientific experiments), select the “toys” (lab equipment), and pick his “pals” (students and postdoctoral fellows). As long as he continues to attract funding—something he’s been quite successful at throughout his career—he’ll be able to keep “playing” as long as he likes.

Wickner’s enthusiasm is infectious, says colleagues. “He is an eternal optimist, with boundless enthusiasm and energy for science,” declares Janet Shaw, Ph.D., who was a postdoc in his lab at the University of California at Los Angeles (UCLA) in the early 1990s. “I cannot remember a day in his lab when he did not come in whistling—usually ‘Jeremiah was a Bullfrog’—with a big smile on his face and three or four new ideas for experiments.” Shaw, one of many Wickner-lab alums who sing his praises, is now a professor of biology at the University of Utah.

Wickner still whistles while he works, but his favorite tune nowadays is “Foggy Mountain Breakdown,” a lively bluegrass number. And he’s as excited by his work—oops, play—as ever.

“He’s total love of science was inspirational,” says Pamela Silver, Ph.D., a postdoc in his lab from 1978 to 1982. “Bill is one of the people I admire most in science and is also a close friend.” Now, as she runs her own lab at Harvard, she’s her “role model for high experimental and intellectual standards [and] ethical and fair behavior to colleagues.” And, she notes, his attitude serves as “a constant reminder that one should extract as much pleasure as possible from every moment in the lab, as well as from life in general.”

Wickner, who grew up in the apple-farming town of Wallkill, N.Y., has been extracting pleasure from science for as long as he can remember. He was inspired by his father, a country doctor who had a “real interest in the science that lay behind medicine,” and by a high school science teacher. But it wasn’t until he enrolled in Harvard Medical School (after getting a degree in chemistry from Yale in 1967) that he found his true calling—that of a medical researcher.

During his first year in medical school, he encountered biochemist Eugene Kennedy, Ph.D., who gave “a wonderful series of lectures on lipid metabolism,” Wickner recalls. “The way he showed how the discoveries were made, I found fascinating.” So fascinating, in fact, that he approached Kennedy about working in his lab. Instead of saying yes or no right away, Kennedy gave Wickner several journal articles. He “asked me to read them and come back to him with what experiments I would do to follow up the scientific questions,” Wickner says. “In the ensuing sessions, Gene led my reading in a sort of Socratic fashion.” But the young Wickner was itching to get into the lab, and after several sessions, “I finally blurted out that this was great fun, but I sure as heck hoped I could do research in his lab that summer. And he said, ‘Oh, of course, I wouldn’t have been spending this amount of time if you couldn’t.’”

Wickner enjoys telling that story. He’s relaxing on the couch in his office, which is connected to his lab. He can see his own bench from where he’s sitting and hear the quiet hum of activity in the lab. So, he continues, “1968 was a great year for me. I fell in love twice. Once with doing biochemistry and once with Hali. I was completely enchanted.” He’s been doing biomedical research ever since. And he’s still married to Hali Wickner, director of communications for DMS. In fact, both Wickners have a knack for translating complicated scientific topics into plain English. Kennedy, now an emeritus professor of biochemical chemistry and molecular pharmacology at Harvard, finds it remarkable that his protégé, in addition to being a talented researcher, is such a gifted communicator.

Being able to convey complex information to scientists and nonscientists comes in handy when you’re teaching students or trying to explain your research to reporters. Wickner is a master at adding color to what would otherwise be drab explanations. He talks about enzymes being “well behaved” or “crashing out of solution,” about calcium being “released back into the cytoplasm in little puffs.”

When he was still in Kennedy’s lab, Wickner made a surprising discovery that became the foundation of his own career. At the time—the late 1960s and early 1970s—it had been determined that “the enzymatic machinery of protein synthesis of the cell . . . was all water-soluble,” he explains. Scientists typically used a detergent to extract an enzyme from a cell and then chemically disentangled the detergent from the enzyme afterwards. But when Wickner tried that process on a protein from the cell membrane, the enzyme “would come crashing out of solution and form a precipitate and become inactive.”

Wickner finally realized that the prevailing scientific knowledge might be wrong—at least as far as membrane proteins were concerned. They turned out to be water insoluble. “So this gave me an idea which I nursed throughout my postdoctoral time—to study how membrane proteins were synthesized and how they got into and across membranes.”

From 1971 to 1974, Wickner did a postdoc at Stanford with Nobel Laureate Arthur Kornberg, M.D., known for elucidating the mechanisms by which DNA molecules are duplicated. Wickner remembers him as “a great teacher of how to do science.”

On a corner of his desk, Wickner has what he calls “a little shrine”
to his mentors—Kennedy, Kornberg, and Paul Boyer, Ph.D., who directed the institute at UCLA where Wickner got his first job in 1976. “In the back of the shrine you observe a picture of Gene Kennedy,” he explains. “And just in front of him . . . is a small glass and porcelain filtration device used in an organic chemical synthesis of lipids, which he gave me.” Wickner cherishes that piece of glassware. He even had Kennedy—and Kennedy’s longtime research associate—sign it. “Then in front of that is an acid filtration device from my postdoctoral advisor’s lab, Arthur Kornberg. And [there’s also] a picture of Paul Boyer . . . accepting the Nobel Prize.” Boyer won the Nobel in 1997 for deciphering the chemistry of the enzyme that synthesizes ATP, adenosine triphosphate, “the energy currency of the cell,” Wickner explains. “Paul was also a wonderful mentor. He had a tremendous love of science and a verve for it. He was enthusiastic in his support for the young people in his institute,” adds Wickner.

Just as Wickner is enthusiastic in his support for those who have worked for him. “Typically, [my] students and postdocs have gone on to start their own labs,” he says proudly. “This is another really rewarding part of scientific careers—the extended family of people who’ve been to the lab.”

Janet Shaw even uses the same phrase in echoing the thought: “He genuinely cares about his extended lab family and takes great delight in seeing them mature and become independent scientists.”

At UCLA, Wickner helped determine how portions of the cell membrane are assembled and how chemical guides direct proteins to the membrane. By the time he joined the DMS faculty as chair of the biochemistry department in 1993, Wickner had established a reputation for his contributions to understanding how cell membranes function. In 2000, he stepped down as chair so he could devote more time to his research. By then he was well into what he calls the second phase of his scientific life, following some advice from Kennedy. “He told me that you should work on two separate topics during a scientific life,” Wickner says. “That gives you about 20 years to work on each. It will keep you much fresher in the second half to have a separate topic to work on.”

Kennedy chuckles on being reminded that his protégé took the advice to heart. But he says not all scientists agree with him. In fact, one researcher tried several times to change topics but says “he was like a man with a boomerang”—he kept returning to the same subject.

But Wickner has managed to stay focused on his new interest—organelle movement and fusion. It was originally suggested to him in the 1980s when he was doing a sabbatical in Switzerland. He and a Swiss colleague were sitting in a train station when Wickner asked him, “What’s the next big thing in mitochondrial research?” Mitochondrial research was his colleague’s specialty. “He said, ‘Why the mechanisms of fusion and fission and inheritance. . . . Nothing is known and it’s gotta be a really interesting story. . . . But I’m not going to work on it.’ I said, ‘Do you mind if I work on it?’ He says, ‘Be my guest.’” Once back at UCLA, Wickner started working on organelle fusion and fission and inheritance in the yeast vacuole.

He even drew one of his postdocs into the new field—Lois Weisman, Ph.D., now an associate professor of biochemistry at the University of Iowa. “I think he had the biggest impact on my scientific life,” she reflects. On her Web site, a caption next to her photo reads: “According to Lois, she was not born until she met Bill Wickner, under whom she did a postdoc at UCLA.” Weisman says studying yeast vacuole inheritance is her passion. “Yet it is hard to imagine how I would have come to this project if Bill had not said that vacuole inheritance would be a topic worthy of serious investigation.”

Yet Wickner weaves fun into even the most serious investigations. He admits to being “an unabashed lab rat.” He laughs. “I love it. I love coming in to work. I love the excitement of trying to get a good experiment done.”

Barbara Conradt, Ph.D., was inspired by that excitement. “I was completely caught by his liveliness and enthusiasm for his work,” recalls Conradt, who worked in his lab from 1990 to 1994—both at UCLA and at DMS. She later worked at MIT with Robert Horvitz, Ph.D., who shared the Nobel Prize in Physiology or Medicine in 2002, and at the Max Planck Institute in Germany. Now she’s back at Dartmouth as an assistant professor of genetics.

Wickner has so much fun that he says he would keep doing research even if “someone waved a magic wand and cured all disease—which would be wonderful,” he says. “I would come to the lab the next morning still wanting to understand how membranes fuse.”

continued on page 63