Alan Eastman, Ph.D.: Lab lover

By Amos Esty

A word of advice for applicants to the DMS Program in Experimental and Molecular Medicine (PEMM): When Alan Eastman asks about your hobbies, don't talk about your love of travel or the latest addition to your stamp collection. "Your answer is supposed to be research," says Eastman, a professor of pharmacology and toxicology. "If your research is not your hobby, you'll only work 9:00 to 5:00. You cannot do research working 9:00 to 5:00."

Of course, he continues, that "doesn't mean you can't go party hard, doesn't mean you can't walk the Appalachian Trail. But it means you've got to be thinking about science while you're doing it."

Grew up: Outside London, England

Early interests: Music and running

Education: Brunel University, London (B.Sc.); Chester Beatty Research Institute (Ph.D.)

Favorite author: Neal Stephenson, author of *The Baroque Cycle*

Hobbies: Playing acoustic guitar—and doing research

Thoughts on his move to the U.S.: "Science was easy to adapt to. But the style of life, the appearance of the towns, the lack of a town center, that sort of thing was different."

Eastman acknowledges that most scientists find setting up a clinical trial more daunting than working in a lab.

Eastman follows this dictum himself, which helps to explain how he can find the time for all of the various roles he fills. In addition to being the director of PEMM, Eastman is the codirector of Norris Cotton Cancer Center's Molecular Therapeutics Program and a devoted researcher. "I spend about 40 hours a week running the grad program, 40 hours a week running the molecular therapeutics program, and 80 hours a week in the lab," he says, laughing. That might be a slight exaggeration, but Eastman clearly enjoys his work, especially his time in the lab.

His passion for science arose early, while Eastman was growing up in the countryside south of London. "As a kid, the thing that intrigued me more than anything else was probably all those nature shows, the safari shows," Eastman says. "I got really interested in that, which I guess got me into biology."

As an undergraduate, Eastman did manage to find time for a few diversions. His interest in music took him to a recording studio in Switzerland, where he played his own small role in Mick Jagger's success—making coffee for Jagger at a recording session. While he was in graduate school, Eastman met another musician, a guitarist named Brian May. Eastman and some friends convinced May's band to put on a concert at a high school outside London. The name of the fledgling band was Queen. "Three months later they were touring with Mott the Hoople, and three months after that they were topping the bill," Eastman says.

He eventually decided he stood a better chance of success in science than in music, but like any aspiring musician he wanted to take his show on the road. So when he finished his Ph.D. in 1975, he applied for a number of postdoctoral positions in the United States. He heard back from only one: the Medical College of Georgia, in Augusta. In 1976, Eastman arrived in Augusta to work with Edward Bresnick, Ph.D., who became Eastman's scientific mentor.

What Eastman didn't know—and what Bresnick had failed to mention—is that Bresnick already had plans to leave Georgia. Four months after Eastman settled into Augusta, Bresnick moved his lab to the University of Vermont (UVM), taking Eastman with him. Eastman found the landscape more to his liking in Vermont than in Georgia. He and Bresnick remained at UVM until 1983, when Bresnick accepted a position at the University of Nebraska, and once more Eastman relocated with him. Eastman enjoyed his work in Nebraska, but he and his wife, whom he had met and married in Vermont, missed the northeast.

So in 1989, when Bresnick was offered a position as chair of the Department of Pharmacology and Toxicology at DMS, Eastman accepted Bresnick's offer to relocate yet again. But the next time that Bresnick moved—in 1995, to the University of Massachusetts—Eastman stayed put at Dartmouth.

Throughout all the changes of location, one constant for Eastman was his research. He is proud of the fact that he has been continuously funded by the National Institutes of Health since 1980. One of his longtime research topics has been apoptosis—a form of cell death. In the 1980s, when Eastman started work on apoptosis, the subject wasn't getting much attention from other scientists, many of whom weren't convinced of its importance. Part of the problem was that not much was known about how apoptosis worked. All that was clear was that the end result was the death of the cell.

So Eastman took a different approach. "When you're doing a maze, the easiest way to get the answer is to go backwards," he says. And that's what he did. "We started asking the question, When is the cell dead?" he says. "What did it look like the day before? What did it look like the day before that?"

Eastman and other researchers were eventually able to outline a clearer picture of the events leading up to apoptosis, identifying steps such as the degradation of DNA. By the early 1990s, the field was starting to take off, as scientists realized the potential it offered to tar-

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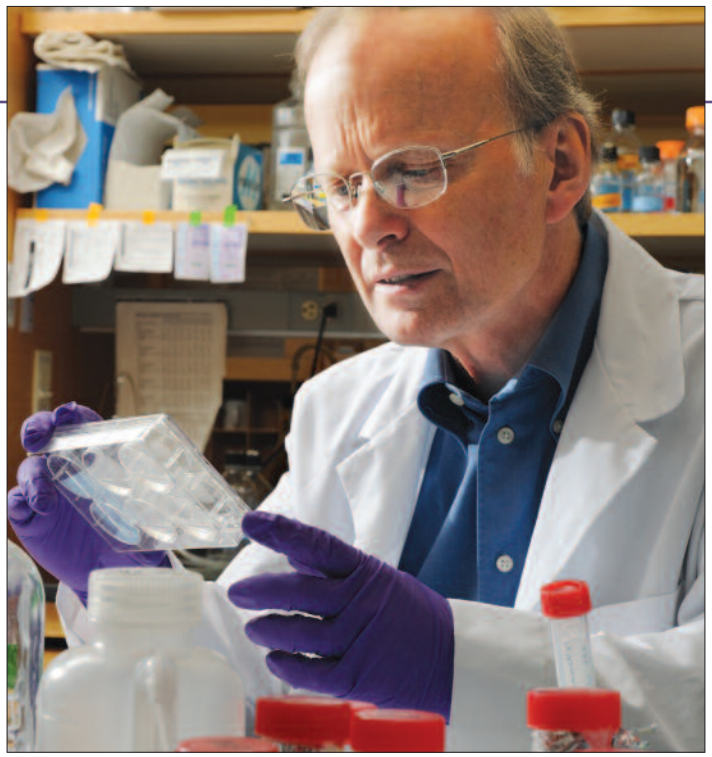

JON GILBERT FOX

Alan Eastman continues to love working in the lab, but he also runs one of DMS's graduate programs and oversees the translation of basic research into clinical trials.

get diseases such as cancer. "All of a sudden you could genetically manipulate the cell," Eastman says. "You could turn death on or off by putting genes in or taking them out."

Eastman has also worked on manipulating the cell cycle in order to kill cancer cells. Several years ago, with the help of a number of colleagues, he initiated a Phase I trial of a drug that prevents cancer cells from repairing DNA damage by inhibiting a gene that stops the cell cycle at a key checkpoint, leading to the death of the cells. This work got Eastman increasingly involved in the clinical side of translational medicine, pushing him to do more to bring scientific research into the clinic.

"I can publish my observation and nobody will act on it," Eastman says. "Unless I take that observation through and start moving into the clinic myself, it's never going to happen." But he realizes that it's easy for a scientist to be overwhelmed by the long process of turning an observation into a possible treatment. "I think a lot of people are scared of it," he says. "I've had a number of basic scientists say they'd like to do it but don't know how. And I've said, 'Well, this is how you do it. Let's take it one step at a time.'"

Even with guidance, Eastman says, most scientists find setting up a clinical trial more daunting than working in a lab. "They're trained to clone genes or do cell biology, and they're not trained to go that step further," he says. "It's something I wasn't trained to do. It's something I've learned over many, many years." As codirector of Norris Cotton's molecular therapeutics program, his job now is to share that knowledge. "I keep saying to people, 'I'll help you,'" he says.

One part of that assistance is getting people to talk to one another. "If you want to be a basic scientist and clone genes, you can do it very easily in your own lab," he says. "If you want to do translational work, you have to nurture relationships with other people in other disciplines."

An example of that type of work is a clinical trial that started enrolling patients in May, to assess the safety of a potential treatment for breast cancer. William Kinlaw, M.D., found that a nutritional supplement called conjugated linoleic acid can turn off a tumor's ability to synthesize fats, which are needed for tumor growth. The finding was promising and had clear clinical implications, but Kinlaw says the process of moving it into a clinical trial has been a lot of work. "It has been very interesting," he says. "I've never done anything like this before."

Eastman, says Kinlaw, has been one of the people responsible for helping to move the supplement into the trial. "He has been a major advocate of this work on tumor metabolism from the day I showed up at the Cancer Center," Kinlaw says. "He has been kind of behind the scenes, pulling the strings, making everyone do what they need to do to get this done."

Eastman tries to promote translational research among graduate students as well. That's why, for example, a core PEMM course involves teaching the scientific basis of disease. "You do the molecular biology, but you do it for a clinical reason," he says. "You actually see that disease, you understand the pathophysiology." Students in the program even have the opportunity to go on clinical rounds, to see firsthand how treatments end up affecting patients. "We're trying to train Ph.D.'s at the cutting edge of translation," Eastman says.

He does his best to stay current on the research projects being carried out by all the PEMM graduate students, whether they work in his lab or another one. "I think the graduate programs are actually underappreciated for the amount of information they relay," he says, which is why he tries to attend as many student presentations as possible.

But despite all these other duties, Eastman always finds time to get back to his own lab. "I would be lost if I wasn't working in the lab," he says. "It's too easy to get out of the lab and tell somebody in the lab to do this experiment. You don't see the errors, you don't see why it doesn't work, because you're not there."

Even today, research remains Eastman's first choice of hobbies. On weekends, he and his wife like to head for their house on a lake in northern Vermont, where he can kayak, do landscaping, and, of course, think about science. "Every weekend, I get up in the morning at 7:00," he says. "And I do three hours of work or so. So by 10:00, 11:00 in the morning, I feel I've worked hard."

After all—as he tells his students—it's simply not possible to do research by working just 9:00 to 5:00. ■