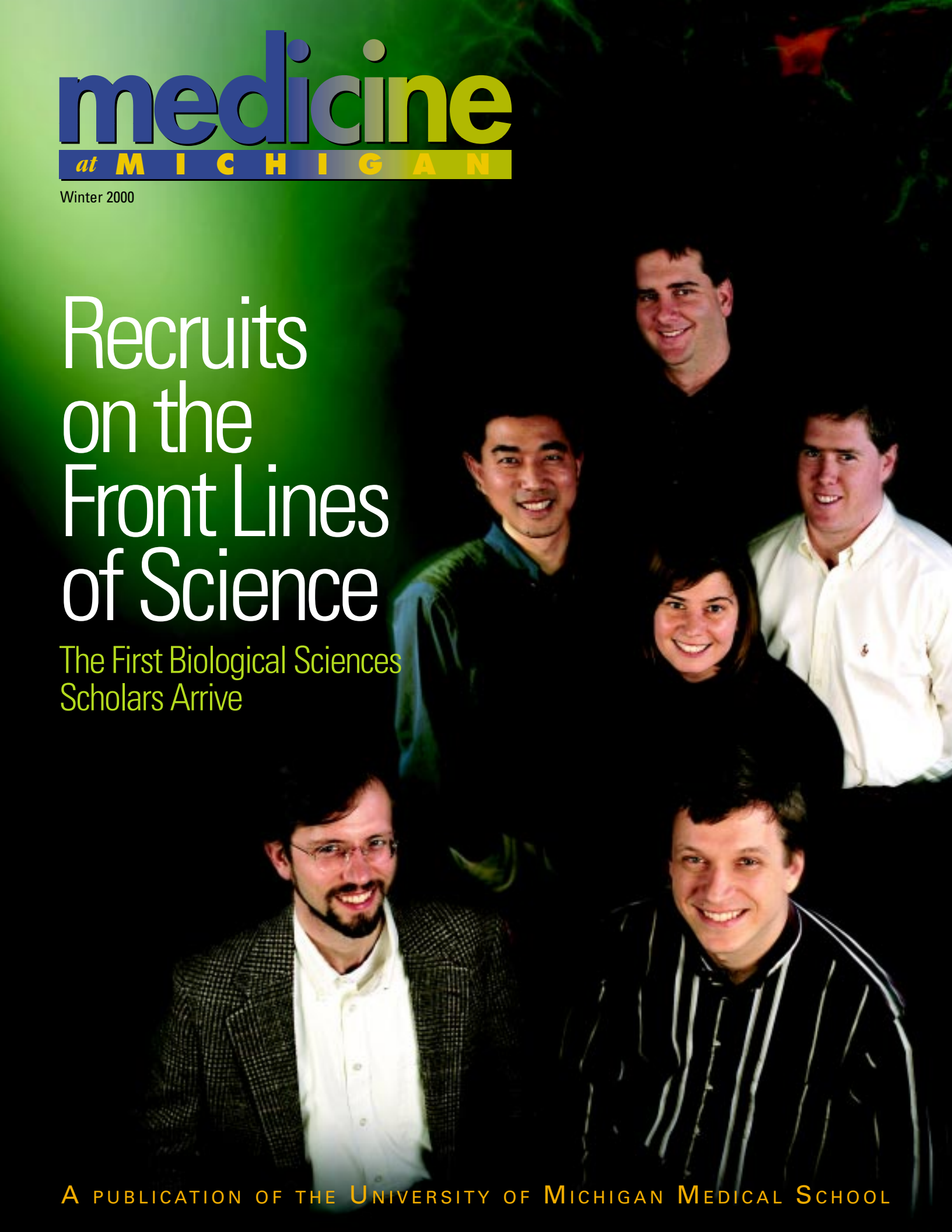
medicine at MICHIGAN
Winter 2000

Recruits on the Front Lines of Science

The First Biological Sciences Scholars Arrive



A PUBLICATION OF THE UNIVERSITY OF MICHIGAN MEDICAL SCHOOL

Wanting to **Know** What No One Has **Ever** Known **Before:**

Six Young Stars Chase Their Dreams at Michigan

By **James** Tobin

The surfaces in Sean Morrison's brand-new office in the Cancer Center are utterly clean and bare. In the nearby labs of Zhaohui Xu and Tom Wilson and Brian Akerley in the Medical School, research benches and storage shelves are only beginning to accumulate their loads of beakers and flasks. Even the quarters of Kathleen Collins and John Moran, who arrived at Michigan a year ago, harbor little of the clutter that grows only from long labor in one spot. Each of these six places says: "Something is starting here. This is the beginning."

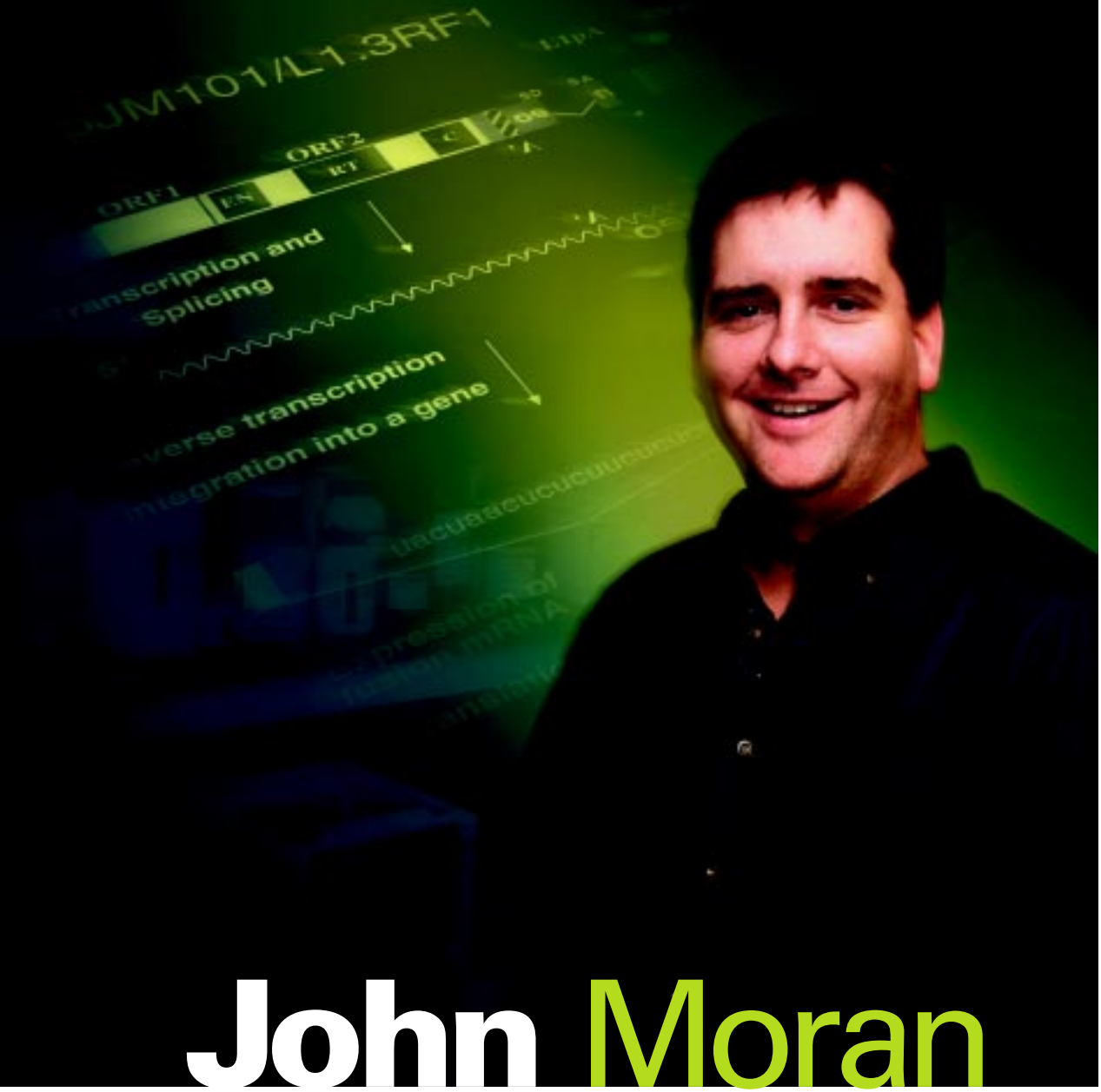
Together, these six beginnings make up a milestone. Collins, Moran, Xu, Akerley, Wilson and Morrison are the first University of Michigan Biological Sciences Scholars — the fruit of an annual commitment of up to $2.5 million by Gilbert Omenn, CEO of the Health System and the University's executive vice president for medical affairs, to recruit, in his words, "the equivalent of the 'best athletes in the draft,' the most promising faculty candidates from top labs at top institutions."

The appointments of these six are in the Medical School; future "classes" of Biological Sciences Scholars may include appointments in departments outside the school as well. They are among the first recruits to the University's emerging Life Sciences Initiative, an intense, long-term effort to lead the world in the momentous advances in biological understanding that are only beginning with the nation's Human Genome Project, directed by U-M Medical School geneticist Francis Collins. No one knows, of course, which scientists in which nations will do the work that makes 21st-century scientific history. But the interdisciplinary research committee who chose these young scholars believes they stand as good a chance as any. (The committee is currently headed by Michael Marletta, Ph.D., professor of biological chemistry in the Medical School and the John Gideon Searle Professor of Medicinal Chemistry in the College of Pharmacy).

While these sparsely furnished workspaces may be portals to the future, they also represent six culminations. They are the prizes at the end of six long paths of persistence and inspiration and perhaps especially of a rare form of devotion — and of joy. In academic training, no trail is longer than that of the medical scientist, and without a "joyful sense of superior intellectual power," as Albert Einstein once described the pleasure of being a scientist, they might not have come this far.

They share with all young biological scientists of the day a special luck of timing: that of coming to the world of medical science when it is poised on the brink of fabulous new discoveries. University of Michigan President Lee C. Bollinger, who is determined to change the landscape of the life sciences at Michigan in the coming years, has compared the postgenomic world of the biological sciences to the ferment in physics in the early decades of the 1900s, the flurry of intellect focused on constitutional law, his area of study, in the 1960s.

But their stories also encompass the inspiration and triumph that have been a part of science forever: the college student who almost became a millionaire but kept right on going when he didn't; the 10-year-old who decided to become a scientist when he overheard the groans of the dying woman who had taken care of him for many years of his childhood; the experiencing by a beginning scientist of an unexpected "eureka" moment in the quiet of a late December eve, with the accompanying certitude that an entirely new idea had just found its way to formulation in her head.



John Moran

"BIOCHEMISTRY FLOATED MY BOAT."

In the late 1960s, John Moran's family moved from their blue-collar Queens neighborhood of Jackson Heights out to the more suburban Holtsville, Long Island, 45 minutes east of the city. But his dad still did the work he'd always done — commuting back to the city every day to supervise crews fixing Manhattan's underground phone lines.

That was the prototypical career path among Moran's childhood friends—toward the practical jobs that keep the world running. "We didn't use a lot of big words," he says. "Not many people said 'extemporaneously' where I grew up." Up to high school, he and his younger brother either studied or played sports in the street. It was one or the other, their father said. When the boys turned 16, he gave them a choice — find a job on their own or go to work in the sewers. So the teen-ager spent his summers ripping out and refitting the insides of old buildings.

But his dad also saw his older son's remarkable grades in science and math, and he made it clear that Moran was headed for college. He chose the Rochester Institute of Technology, sight unseen, because it offered him the most scholarship money. Except for a senior trip to Washington, D.C., he'd never left metropolitan New York in his life. He packed his car while his dad reminded him: "You're not going there to party."

Rochester's commitment to preparing students for technical careers might be called ferocious. In four years Moran was allowed four electives. Students at Rochester take classes for a term, then work for a term, so he found a job at a pharmaceutical plant, mixing anti-fungal compounds for medicinal chemists. In class he had to compensate fast for a shortage of high school lab experience. In one early outing he mistakenly set the room on fire. ➤

John Moran continued

In organic chemistry, he and a friend got into a pattern with a professor named Kay Turner. She would hand back a test, point to one of their solutions, and say, "This is right, but my way's quicker." Moran and his friend would look it over, produce a faster route to the answer, then hand it back. Turner would glance at it again and say, "Your way's quicker, but my way gives a higher-percent yield." To Moran, it was just fun. Then one day Turner said, "You know, you guys think this is a game. But not everyone can do this." "That's when I started to realize, 'Wow, maybe I got a knack for this stuff,'" Moran recalls.

He had chosen to major in medical technology by flipping through the Rochester catalog and pointing a finger. When another professor invited him to switch to biochemistry, Moran discovered an infinitesimal realm of cause and effect that appealed to him immensely. "At the molecular level, biochemistry was telling you how things work," he says. "You were going into the nitty-gritty. Plus, it was just generally cool. It floated my boat. It was concrete. There were answers."

When Kay Turner told him there was a good Ph.D. program in biochemistry at Ohio State University, he applied and was accepted. When somebody called to tell him some paperwork was needed, he got in his car, drove all night to Columbus, slept in the car outside Ohio Stadium, woke up, walked into an office, filled out the papers, got back in the car and drove home to Rochester. "I wasn't a big guy on, like, planning out where I go in life," he laughs. "I was just kinda like, okay, I get in the car and I go there."

He arrived in Columbus in the fall of 1986. A few months earlier he had met the woman who would become his wife — Robin Sullivan, an electrical engineering student at Rochester. Now he fell in love again, with genetics.

"It made sense," he says. "It was really, purely logical. When you looked at genetics, it was like — the traceability of it — wow, that's cool. The problem-solving was cool — how you could play with DNA, cut DNA, sequence DNA, do recombinant DNA work. You could get a handle on what actually was occurring."

At long last, Moran was becoming aware that his grasp of science was not like everyone else's. When his mentor at OSU, Philip Perlman, suggested that Moran follow him to the rarefied environment of the University of Texas Southwestern Medical Center at Dallas, home to three Nobel laureates, Moran got back in his car. In Dallas he studied mobile introns in yeast mitochondrial DNA — that is, pieces of DNA that move from one place to another in the yeast's genetic sequence. He took his Ph.D. in 1994. For his postdoctoral work, he set his sights on the mysteriously shifting pieces of human DNA called Long Interspersed Nuclear Elements, or LINES — distant descendants in the human genome of the introns he had studied in yeast.

LINES are often classified among the genetic elements called "junk DNA" because they seem to have no clear function. Yet scientists are intrigued by their ability to leap from one place in a genetic sequence to another, sometimes dragging adjacent genetic elements along with them. These movements are thought to hold promise for understanding and possibly for treating a host of inherited diseases, including cancer.

So in the spring of 1994, Moran was back in his car — first to Baltimore, where Haig Kazazian ran a leading LINES laboratory at Johns Hopkins University, then to the University of Pennsylvania when Kazazian moved his lab there. Understanding LINES became Moran's obsession — why some leap and some don't, how they move and how often, and what these characteristics might imply for medicine. While he acknowledges that the mapping of the human genome is a revolutionary step, he notes that a map, after all, is only a tool for exploration. "The thing that people are still gonna need to figure out is how things work," he says. "There's not gonna be a simple solve to the how-things-work problem. There'll be inferences, but until you get down in the trenches and figure it out, you won't know how it works."

Moran, who looks and sounds like an affable ex-Marine, fills his speech with its own kind of junk DNA — a lot of New York-inflected "and-stuff-like-thats" and "Hey, whatevuhs." But when the conversation moves deep into his work, the street riffs give way to precise blends of scientific sophistication and pithy simile, as when he likens genetic strands to Lego blocks, the tiny plastic children's blocks that can be shaped into structures of infinite variety. All of a sudden, the thick-necked guy who says things like "I didn't walk around and start sitting there and expousing like I knew something" is saying: "Our hope is that a true understanding of the biochemical and molecular mechanisms by which these elements move will ultimately help us better understand human disease processes."

Clearly, the professors who recruited Moran to U-M's Departments of Human Genetics and Internal Medicine were charmed by the combination. "John's enthusiasm for, and excitement about, his research—and about science in general — were impressive and infectious," says Thomas Gelehrter, M.D., chair of the Department of Human Genetics. "The clarity with which he was able to describe complicated genetic experiments reflected the clarity and incisiveness of his scientific thinking."

Moran shrugs. "Once I start talking about science, I get excited, you know? I get pumped. I like the stuff. I work at my hobby." As for his back-door path to a position that any product of Caltech or Yale might envy, he says, "Look at Kurt Warner for the Rams right now. The guy played arena football for the Iowa Barnstormers and now he's, like, the most prolific passer in the game. If you keep doing it, you don't have to be at the elite schools, coming up. If you're into it and you love what you do, you'll get there." ■

Sean Morrison

It seems to violate some unspoken protocol for scientists to talk about the competitive nature of what they do. Overt discussion of competition is for athletes and entrepreneurs. Which, no doubt, is why talk of competition in science comes more easily for Sean Morrison, who has been all three — scientist, athlete and entrepreneur.

Entrepreneur came first.

Growing up outside Halifax, Nova Scotia, Morrison was a hands-on science guy from an early date. "The older I got, the more excruciating it was to sit there and listen to people talk about science rather than doing it," he says. In his science fair project in his senior year of high school, he and a friend studied *mycorrhizae*, a fungus used in agriculture to increase nutrient uptake in plants — an earth-friendly fertilizer, but expensive to grow. When they found a better way to grow it — hydroponically (in water) — a profit-making enterprise was born. Dalhousie University, which had already recruited the two as students, lent them a lab. The Canadian government gave them a grant. They hired staff. When his partner dropped out of the company to focus on his classes, Morrison quit school to work on the company full-time.

He spent a quarter-million dollars on research. He needed $3 million to bring the fungus to market. By the time he was 20, he had talked to every significant investor in agricultural biotech in North America. But it was the late 1980s. The American stock market had just crashed, and no one was investing in agricultural biotech. Morrison closed the door on Endogro Systems, Inc., packed two years of college courses into 12 months, and sent off his applications to major graduate programs in immunology. "I wanted to get into medical research," he says, "because medical research is more competitive than agricultural research. I wanted to spend time on things that people considered important problems, and where, if you were successful in solving a problem, it would be something that people felt really mattered. And I really enjoyed the competition."

He chose Stanford over Harvard and Oxford, not just for the California weather but to work in the lab of Irving Weissman, who was doing pioneering work with hematopoietic stem ➤

"I wanted to get into medical research because medical research is more competitive than agricultural research. I wanted to spend time on things that people considered important problems, and where, if you were successful in solving a problem, it would be something that people felt really mattered."

Sean Morrison continued

cells, the rare cells in bone marrow that generate all the other cells in the blood and immune systems. By the time he finished, he was considered one of the most promising students in his field in the world. But he wasn't the type to spend every night in the lab. After all, the Stanford club hockey team played every Tuesday, Thursday, Friday and Saturday night, not to mention road trips, and Morrison was its regular right wing. "I wasn't good enough to play varsity hockey in Canada, but I was good enough to play in California," he says. He married halfway through his fourth season and hung up his skates when his first child arrived. "It was forced retirement, and it's still painful," he says with a wry smile, "but it was time to move on."

Next came post-doctoral work in David Anderson's lab at Caltech, where Morrison used techniques he had learned in Weissman's lab to isolate the stem cells that give rise to the peripheral nervous system. That set up the work he is now preparing to do at Michigan, where he will investigate whether stem cells from various types of tissues use the same set of genes to replace themselves. If that's the case, the implications may be profound. If, for example, all kinds of stem cells use a common genetic program to make more of themselves, it's possible that a misfiring of that program is related to the deadly proliferation of cancer cells. Identifying the genes involved in that malfunction could produce new targets for genetic treatments in cancer. His work is stirring real excitement among his new colleagues in the Department of Internal Medicine's Division of Molecular Medicine and Genetics. "He is without a doubt one of the brightest, most innovative researchers I have ever met," says Michael Clarke, M.D., professor of internal medicine, who worked with Morrison for a time at Stanford. David Ginsburg, M.D., Warner-Lambert/Parke-Davis Professor of Medicine and chief of the division, calls Morrison simply "a superstar."

Describing what drives him, Morrison reaches for an analogy to his second-favorite sport. "Science is like golf," he says. "It's not like hockey or football. In hockey and football, you want to go out on the field and destroy your opponent and beat him physically as well as on the scoreboard. In golf, you're basically playing against yourself, and no matter how well you do, there's always room for improvement. I don't sit in my laboratory and I don't stand on the golf course trying to beat so-and-so. I just am trying to do better and better, to improve the quality of the science I do and the types of experiments that I do. And while some people just go out and enjoy playing easy golf courses, if I'm successful, then I want to be successful on tough courses." ■

Zhaohui Xu

Zhaohui Xu (pronounced ZHOW-way SHOO) grew up in the city of Suzhou, an hour's train ride west of the great Chinese port of Shanghai. In his housing complex, families lived close, both physically and emotionally – so close that while his parents were away at their jobs (his father as an engineer in a textile plant, his mother as a teacher of the deaf), an elderly neighbor woman looked after him and his younger brother. And when the doctors said the woman's breast cancer was beyond treatment, Xu, at age 10, would lie in bed at night and listen to her cry with pain. That was when he decided to become a doctor.

Compassion alone, of course, doesn't make a career in medicine. As Xu finished high school, he learned that the nation's best medical college would not admit students from his city that year, but only from Shanghai and Beijing. So, instead of settling for a second-best medical school, he applied for a place in biology at the elite University of Science and Technology of China, thinking he could shift to medicine later.

From his province of 70 million people, 50,000 students took the entrance exam. Xu placed eighth. At the university, he competed with China's best students in science, including four who had scored first on the entrance exam in their respective provinces. Yet here, too, he did extremely well, ranking second in his class without working terribly hard. "I had this belief in myself," he says simply. "I think I can catch not-so-obvious things more quickly."

As he moved from class to class and lab to lab, his ideas about the future changed. In medicine, he would be one doctor helping one person at a time. In bench science, his intellectual gifts might create knowledge applicable by thousand of doctors. "Gradually, I realized that I could learn something that nobody had ever learned before," he says. "I could be the first person to discover something or to reveal something or to visualize something. And I think that being the first is a fascinating thing for me – not just repeating what other people have done, but doing something unique, becoming a source of knowledge."

By 1989, he had decided to pursue advanced studies in the United States. As an undergraduate, he had met vis-

thing for me."

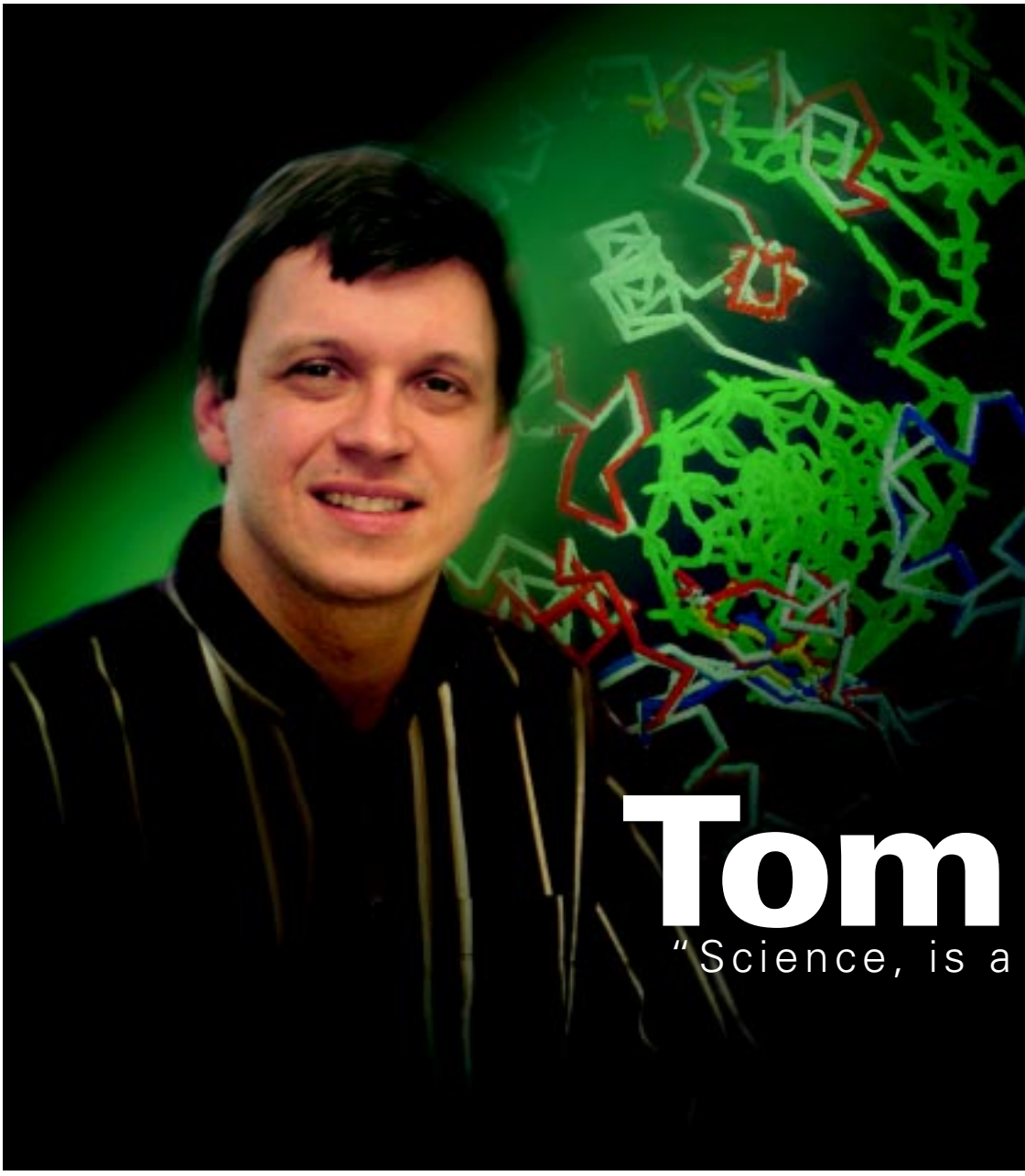
iting American students and teachers and found them to be "ordinary people like us, nothing mysterious about them, very normal." Despite his contacts with Americans, he knew virtually nothing of life in the U.S. "There was just a sense of curiosity," he says. "I wanted to go there and see what it looked like."

Armed only with an acceptance letter from the University of Minnesota, Xu boarded an airplane in Shanghai on September 8, 1989. On the flight he slept for many hours. When he awoke, he saw green mountains beneath him, and the enormity of the step he had taken struck him like a blow: "These were not the mountains I was used to seeing. It was a completely different place. I just felt so strange. I really didn't know what would happen, and I didn't want to know what would happen." That night, as the roar of a Los Angeles freeway invaded the room of his nameless hotel, he thought, "Why am I here? I shouldn't be here. So lonely."

In Minneapolis, it took long months for Xu to adjust to a new culture. Gradually, he says, "my confidence came back. I knew I could do a great job." In fact, he took his doctorate in biochemistry in three years, a record for his department. His strengths in chemistry and physics had led him to protein x-ray crystallography, an abstruse and highly technical sector of biological chemistry in which scientists study proteins in crystalline states, examining the spatial relationships of individual atoms in a given protein with extremely high-energy x-rays. From Minnesota, he took his work eastward for postdoctoral study at Yale, where he broke ground in understanding so-called molecular chaperones — molecules that help various proteins to fold themselves into their native structure. In Michigan's Department of Biological Chemistry, Xu hopes to learn how proteins are moved from one place to another within cells with the help of another class of molecules which he calls molecular "buses."

At a school of Michigan's caliber, he notes, he can maintain "scientific sharpness." The scientist must make many judgments, he says; his fortunes depend on his ability to choose wisely, to capture what is important, what is practical, what are the risks that are worth taking and the risks that are not worth taking. "To be good but not to be overly ambitious," he says. "Asking the right questions, but not asking the question that cannot be answered." ■

"A lot of times, the questions you need to answer and the problems you need to solve are small-scale. It's not 'how to cure cancer.' It's 'how do we get this one molecule to do this one thing we want it to do?' And using your creativity to make that happen is something that I enjoy very much."



Wilson

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"Science," says Tom Wilson, "is a bunch of toys. And in one way of looking at it, scientists are just a bunch of kids in a toy shop." Understand that this opinion comes from an explorer of structures that are among the most infinitesimal and unknowable in nature; from a young scientist of whom Peter Ward, M.D., chairman of the Department of Pathology, says, "Dr. Wilson's work has substantial implications for human diseases," including cancer.

A bunch of toys? One appreciates the insight only if one believes that play is at the heart of human creativity. Certainly it's a key to Tom Wilson's career as a medical scientist. Which started, in a way, with music. He may have been the only kid in the history of Neena-Menasha, Wisconsin, to be told that he played jazz saxophone well enough to make a living at it. "You'd be surprised to find how many scientists are frustrated musicians," he says. The non-scientist sees the two endeavors as utterly unlike, one "hard" and rational, the other "soft" and whimsical. But there's common ground between them — the intricacy of the structures, perhaps, or the free play of experimentation, or both. "I suppose you could approach science as a matter of rote and say, 'What we need to do is apply a set of established techniques to this, that, or the other thing,'" Wilson says. "But there's no question that the most successful and important scientists have done nothing of the kind."

As it turned out, he traded the sax for an elite undergraduate program at the University of Wisconsin that guaranteed admission to medical school. Music became his hobby; he taught himself how to play the Celtic-Irish tin whistle, then turned to lutherie, the hand-crafting of stringed instruments. But in medical research he found his true vocation. He searched out a job as an undergraduate assistant in a lab, and here he first saw the appeal of science as a highly challenging game — "to formulate a question, and through your own wits and guile, come up with something which will help you answer that question."

By the end of four years, Wilson had come to believe he was ill-suited to a career as a pure clinician, though he still wanted an M.D. degree. He switched to Washington University in St. Louis, which offered an M.D.-Ph.D. At first, he saw the latter as supportive of the former. By the time he finished, it was the other way around. "I loved medical school," he says. "Without the medical training, you miss a lot of what disease is really about. But it also became clear to me that what I liked about medicine was the science — the mechanical aspects of disease." Through his Ph.D. training, his residence in clinical pathology, and his post-doctoral work (all at Washington University), the study of disease mechanisms led him through ever more minute processes until he was studying the links between the rearrangements of chromosomes and cancer. Scientists have long known that such a link exists. Now Wilson is exploring precisely how one affects the other.

Wilson had a friend in graduate school who gradually tired of medical research in the lab. The process of solving the step-by-step problems of bench research, each of them only a tiny step toward a distant answer, left his friend cold. Wilson found himself having precisely the opposite reaction. Though intent on his ultimate goals, he loved the day-to-day problem solving. "A lot of times, the questions you need to answer and the problems you need to solve are small-scale," he says. "It's not 'how to cure cancer.' It's 'how do we get this one molecule to do this one thing we want it to do?' And using your creativity to make that happen is something that I enjoy very much."

That, like the saxophone, is a kind of play — constantly fooling and fiddling not with the keys of a musical instrument but with ideas, even when one's away from the research bench. "It's the constancy of being there with (the problem)," Wilson says. "It's not so much being there in the laboratory, but the science being with you. I would wager that you're probably going to find that most scientists are like this, that it's not a 9-to-5 job. It's all-encompassing. I mean, you are what you're trying to do in the laboratory. When you're at a play or playing with your children, it doesn't go away. When you're with a problem and spend time with it and work with it so much that eventually it becomes a part of you, that's when the moments of realization come in." ■

"I followed a path based on things I enjoyed and

Kathleen Collins

At the age of seven, Kathleen Collins informed her parents that she, like her mother, had decided on a career in nursing. "No, no, no," her father replied. "You need to be a doctor." It was 1971, before most fathers had learned to talk that way to their daughters. The senior Collins was a school administrator and former English teacher in the small Massachusetts shore town of Norwell. Put your mind to it and you can do whatever you want, he told his daughter. "I really distinctly remember that, so I think it did have an impact on me," she recalls. "Because of the way I was brought up, I didn't feel restricted to any particular field. I followed a path based on things I enjoyed and things I seemed to be good at."

She was very good indeed in science and math, and she nurtured an image of herself as a doctor through the first two years of a pre-med curriculum at Wellesley. Then one of her professors, a biologist named Andrew Webb, invited Collins and

things I seemed to be good at."

a few other students to help him in his lab. Webb, working with colleagues at nearby MIT, had just cloned a copy of the human gene for interleukin-one, a protein thought to play a major role in activating the human immune system. Collins' assignment was to clone not just a copy of the gene, but the gene itself.

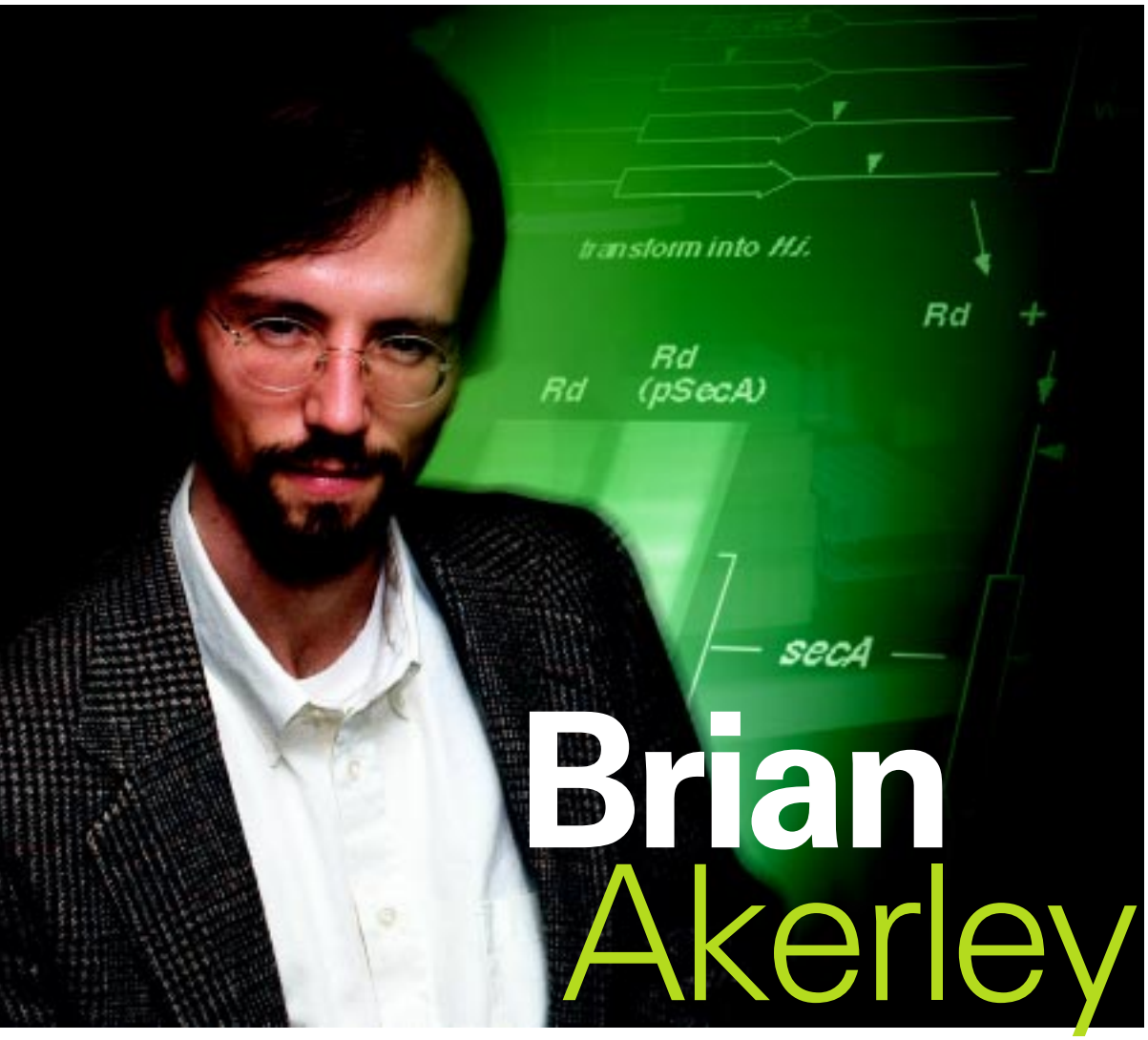
Month after month, she went to Webb's lab. As she worked, her conception of science itself changed. Science, she began to realize, was not a settled body of knowledge that one looked up in a book. It was an unfolding mystery — a conversation between investigators and nature in which nature clung jealously to its secrets. And her conception of herself changed, too: "I gained a view of myself as someone who could contribute to better understanding those unknowns."

In the spring of her senior year, she received acceptance letters from the medical schools at Johns Hopkins and Harvard. She picked up her summa cum laude degree, went home to Norwell and told her parents she didn't want to go to med school, not yet. She wanted to keep working in Webb's lab.

"They looked pretty worried," she says. "But they let me do it." The next year, she and her colleagues cloned the gene for human interleukin-one. From there it was on to the combined M.D.-Ph.D. program at Hopkins, where she developed an interest in HIV while working with AIDS patients, then to the MIT lab of David Baltimore, the Nobel laureate who is now president of Caltech. Hers was a textbook example of the virtues of combining training in the clinic and the lab. "I enjoyed thinking about virology at the time that the AIDS epidemic was in full bloom," she says, "and I felt that studying HIV would be an important contribution. A research career studying AIDS, I decided, would nicely combine my research and clinical interests, plus it would allow me to do something I felt was important for society."

"I was working really late and all of a sudden I saw the answer. I saw that the cells weren't being killed by the immune system when they expressed this gene, but when we altered the gene so that it wasn't expressed, the cells were being killed. I was the only one in the world who knew that. That was the best."

When she describes her work at MIT on a gene involved with HIV called Nef, it becomes clear that Collins, despite the M.D. half of her training, never lost the love of solitary lab work that she discovered at Wellesley. She is a person who chooses words with extraordinary care, but a thrill still resonates in her voice when she describes the night she looked through her microscope and realized that her theory about the Nef gene's effect on the human immune system was true. "I was working really late, and all of a sudden I saw the answer," she says. "I saw that the cells weren't being killed by the immune system when they expressed this gene, but when we altered the gene so that it wasn't expressed, the cells were being killed. I was the only one in the world who knew that. That was the best." To have that "only one in the world" knowledge, even if briefly — "Oh," she says. "It's amazing." At Michigan, where she holds joint appointments in internal medicine and in microbiology and immunology, she's pursuing more knowledge about the Nef gene. Already, she says with the same low note of excitement in her voice, "We've had some interesting results. It's too early to say for sure what will happen, but we're excited about the possibilities." ■



Brian Akerley

"You realize that there's so all of it. And you to do science, I think — you don't

Brian Akerley recalls the exact moment of his first encounter with the fact that DNA exists. It was in a high school science class at St. John's, a Catholic prep school in Massachusetts. The teacher's name was Hook. "You remember the person who tells you these things," he says. Even as a younger kid, he'd had a touch of science fever, demanding that his parents drive him from store to store for chemistry supplies. But his main aim at that early age, he explains with a twinkle in his eye, had merely been bigger and better "exothermic reactions" — explosions and fires, that is. But Mr. Hook, drawing open the curtain on DNA, excited a far deeper fascination in the young Akerley.

"The concept that there's a molecule that encodes everything, and we can read it — Ha! From then on, I just…." Though Akerley is 33, his voice trails off for an instant, a tiny echo of adolescent wonder still audible. "That molecule — not only does it template all these proteins, but it's set up in a way that they can direct the entire development process of an organism! That was pretty amazing."

He went through two years at Bates College telling people he was pre-med, but after just a couple of weeks in the lab of his faculty advisor, the pre-med talk ended. Soon, he was leaving parties at 2 a.m. to run to the lab. "There he goes," his pre-med buddies would say, "reading that oncogenes textbook again." He was hooked. Molecular madness. A genetics junkie.

Next came graduate school in immunology and microbiology at UCLA, where his only question about the big city, noted for the glamour of its entertainment industry, was how to find an apartment closer to the lab. For his dissertation, he studied signal transduction in the bacteria

much more to the story that you can't encompass may never know everything. That's what drives people the fact that the more you find out, the more you realize you don't really know what's going on."

Bordetella pertussis, which causes upper-respiratory infections. The simplicity of the organism allowed him to trace signal pathways down through the cell to the genetic level. That work led to Akerley's postdoctoral work at Harvard and now to Michigan, where he continues to study signal transduction in bacteria. Beyond its immediate utility in treating diseases, his work has helped to illuminate the much larger problem of how bacteria exchange information with their host organisms — a basic question that gets to the root of how cells "talk" to one another.

Some variation of the awe that Akerley felt at his "discovery" of DNA probably ignites most scientific careers. But a quality much different from sheer wonder is required to propel such a career over the long haul, Akerley found. Awe comes unbidden; understanding requires repeated acts of intellectual will. Akerley calls the process "demolition and reconstruction" — building up a theoretical structure to explain a natural process, then blowing the structure to smithereens with contrary data, then laying one new brick on another to build a new structure for testing.

"Science is not easy, and in reality it's not that pretty," he says. "Scientists have to make it sound good, but it's hard work." He'll be pleased if his work helps lessen the burden of disease. But he can't honestly say this is more than a pleasant consequence of his obsession. It might even be wrong to say he pushes farther into the genetic mists in pursuit of ultimate understanding. For ultimate understanding is a will-o'-the-wisp, receding even as it beckons the explorer onward. "You realize that there's so much more to the story that you can't encompass all of it," Akerley says. "And you may never know everything. That's what drives people to do science, I think — the fact that the more you find out, the more you realize you don't really know what's going on."

Yet whenever Akerley and his colleagues break new ground on the far frontier, they'll leave maps in their wake, maps that will help others toward new cures and new treatments. "Scientists study what's interesting, not what's important," he says. "But what people don't realize is that later on, what was interesting to a scientist becomes important. If you take an unbiased view, you're more likely to find something useful than if you tried to grab what you think is useful. It takes a few people figuring out how everything works, and then some other people taking a look at it and finding out what you can do with it. It's the engineer versus the physicist. If you don't know what electricity is, it's going to be very difficult to make a light bulb." m

Seventh Scholar Named

A seventh Biological Sciences Scholar has now been named: Jorge Iñiguez-Lluhí, Ph.D., whose primary appointment will be in the Department of Pharmacology. A native of Mexico City, Iñiguez-Lluhí earned his doctorate at the University of Texas Southwestern Medical Center in Dallas in 1994 and did postdoctoral work at the University of California at San Francisco. His primary research focus is on cellular signal recognition, transduction and response. Five more scholars are expected to be named in the current academic year. The search committee has selected 10 candidates for final consideration from the more than 200 applicants.