



January 2007

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Recommended Citation

Heacock, Steve (2007) "Cell Mates: David Bodine enlists Colby researchers in a bid to unlock the genetic mysteries of blood disorders," *Colby Magazine*: Vol. 95 : Iss. 4 , Article 8.

Available at: <https://digitalcommons.colby.edu/colbymagazine/vol95/iss4/8>

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CELL MATES



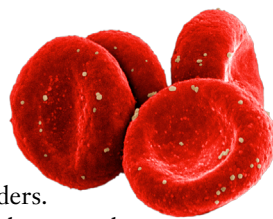
David Bodine enlists Colby researchers in a bid
to unlock the genetic mysteries of blood disorders

By Steve Heacock

Tucked away in glass-sheathed Building 49 on the sprawling 300-acre home campus of the National Institutes of Health, in Bethesda, Maryland, David Bodine '76 stalks the halls—examining slides, studying results, and exhorting his colleagues as they divine the mysteries of blood cells.

Bodine is rangy and fit; it's apparent that he has kept up his running (he ran track and cross country at Colby). Don't expect a white lab coat. If you see him at work, he will likely be wearing Nike running shoes, baggy gray sweats, and a faded tennis shirt. "As you probably noticed," said one colleague at the National Human Genome Research Institute (NHGRI) with a wry smile, "fashion is very important to Dave."

What *is* important to Bodine is the diligence and the professional collegiality of his "section"—his laboratory. Bodine's team is figuring out why blood cell development doesn't always work properly—and how to fix it when it goes wrong. The team's focus is a group of diverse inherited blood diseases (most are anemias) having to do with faulty or reduced production of red blood cells that develop from stem cells in bone marrow. Red cells contain hemoglobin, the essential protein that carries oxygen to the cells of the body. He is clearly energized by his work and by the science going on around him, and he is eager to mentor young scientists—many of whom are from Colby.



Don't let the sweatpants fool you. Bodine is a leader in his field, and his research could lead to groundbreaking ways to treat serious blood disorders.

Next year will be Bodine's 23rd at the NIH, where he recently was named chief of the Genetics and Molecular Biology Branch. The promotion last fall is the latest in an accomplished career that began in 1984 at the NIH's Clinical Hematology Branch of the National Heart, Lung, and Blood Institute. As a senior staff fellow, he launched his own lab in 1988, and five years later he was recruited to the NHGRI's Hematopoiesis Section of the Genetics and Molecular Biology Branch. He received tenure in 1995. He has won a slew of awards, including the NIH National Research Service Award and the NHGRI Mentor of the Year Award.

This is no small thing, coming from one of the largest and most esteemed centers of biomedical research in the world, an organization that employs more than 19,000 people. The NHGRI alone employs 750. Bodine's branch consists of approximately 60 researchers and scientists, and his lab is made up of a dozen scientists.

He clearly has put his stamp on his lab.

"He has this saying, every day," said André Pilon '03, one of a long line of Colby students and graduates who have gone to work with Bodine. "He walks in every morning and asks us, 'What are you doing to thrust back the boundaries of ignorance today?'"

It appears that Bodine and his colleagues are doing plenty.

They are hard at work studying the genetic underpinnings of hematopoiesis, the process of blood formation. Hematopoietic stem cells, found in bone marrow, turn into red blood cells and the many different types of white blood cells. Anemia, leukemia, and a variety of other blood diseases disrupt the process.

"Very broadly, we're talking about red cells that are arresting their maturation just short of being *good* red blood cells," Bodine said one blustery November day, as windswept rain lashed Building 49. "We are learning how to regulate red cell production in animals. Gene therapy? Someday, I hope. But a drug that would do an end run around invasive gene therapy would be just as desirable. Our job is to come up with the targets, understand why the cells work and don't work, and determine what is correctable."

One of the curious aspects of some of these blood disorders is their propensity to afflict certain populations. Some African, Asian, and Mediterranean populations are more prone than others to hereditary blood diseases like thalassemia and other anemias. Approximately 100,000 babies are born worldwide every year with severe forms of thalassemia, which most often limit life expectancy to between 20 and 30 years but also can cause death in newborns. Genetic evidence suggests that in Sicily, for example, 6 to 12 percent of the population could transmit thalassemia to their children.

"Some of the broader questions," Bodine said, "are why are there so many people with this disease gene in these particular geographical areas? And why doesn't natural selection make it go away?" In the case of thalassemia, the affected red blood cells provide a poor host for the parasite that causes malaria, which is endemic to these parts of the world, so it is an evolutionary tradeoff.

Pilon's work focuses on gene regulation, figuring out which genetic "pathways" are wrong in defective red blood cells. He studies mice that are missing a key protein called a transcription factor. He analyzes red blood cell maturation in these mice to determine why the hematopoietic cells do not generate the proper number and quality of red cells.

He has discovered that these cells do not divide correctly and cannot mature (or differentiate) into the cells they need to become.

"My work is to find out the molecular biology that lies under all of that," Pilon said. "The DNA is the genetic material or code in the cells. RNA is the message that tells the cell to make the transcription factor that, in turn, triggers production of other proteins needed for cell division. Certain genes are 'turned on' when this process happens, and I'm trying to figure out why they *aren't* turned on in these defective cells. I have to see how the transcription factor causes a gene to be activated or repressed."

Pilon has been in the Ph.D. program at George Washington University since 2004, part of the NIH Graduate Partnerships Program. At Colby he worked in the research laboratory of Julie Mil-



PHOTO BY ROBERT VISSER

David Bodine '76, center, confers with researchers Serena Vayda '03, left, and André Pilon '03 at the National Institutes of Health's Genetics and Molecular Biology Branch laboratory. Vayda and Pilon are members of Bodine's team, which investigates causes of red blood cell disorders.

lard, the Dr. Gerald and Myra Dorros Professor of Life Sciences and chair of Chemistry, and discovered that the biochemistry program was a feeder for Bodine's NIH lab. Once Pilon started working for Bodine, he recruited one of his Colby classmates, Serena Vayda '03.

On the face of it, Vayda, a biology major with an environmental science concentration, was perhaps not an obvious natural fit for Bodine's lab. But she has flourished. Working in the Flow Cytometry Core Facility, her work is highly specific and technical. Using flow cytometry, Vayda can analyze single cells, determine their size, and analyze proteins on the cell surfaces. The flow cytometer scans 10,000 cells per second. "We're trying to come up with a new way to correct defective cells, and that could mean gene therapy," she said. "You could introduce a therapeutic gene into a cell using a virus. But you have to know just what cells you have targeted. Eventually, a corrected non-stem cell just dies, but a corrected stem cell will keep making blood cells forever."

Vayda plans to enter medical school next fall, perhaps to pursue hematology.

The Colby-Bodine connection has also benefited Emily Devlin '07, a Colby senior from Pennington, N.J., who managed to spend eight months in Bodine's lab. She worked with the Biology Department to turn her Washington Semester into NIH lab work, tacking Jan Plan on the front end of that semester and a summer internship on the back end. She plans to return after graduation, work in Bodine's lab again, and eventually enter an M.D./Ph.D. program.

Supervised closely by Bodine, Devlin was given two projects to work on by herself. "That was really fun," she said. "He is involved with everyone in that lab. He is constantly educating everyone. He trained me and taught me a tremendous amount." One project Devlin worked on was generating a mouse model for a rare blood disease, Diamond Blackfan Anemia. This is the project she will return to later this year. Devlin's other project focused on DNA regulatory elements in the beta-globin gene clusters. Her father, with a Ph.D. in toxicology, and her mother, an engineer, were enthusiastic about Devlin's NIH opportunity.

Pilon and Devlin, with encouragement and guidance from Bodine, traveled to Orlando in December to present at the 48th annual meeting of the American Society of Hematology. Both researchers gave 10-minute talks in front of approximately 200 people. Their work had been chosen from nearly 7,000 submissions for about 875 oral presentations. Word got back to Bodine, he said, that Pilon and Devlin were the most polished and poised presenters in their sessions.

"It impresses me that Colby trains these students in a certain way," he said. "The hands-on approach is really there in Julie Millard's lab. We have students and graduates from other schools here, too, of course. But the Colby kids start so much faster. The day they get here they are doing the science. The others are great, too, but they have to ramp up. The Colby kids come here knowing how to keep a notebook, organize their time, and keep data."

Pilon agreed. "The amount of research and hands-on science is really rigorous [at Colby]," he said. "Even in the first years, you're not just staring down the barrel of a microscope sketching pictures of cell structures. You're doing real science and learning important techniques in the lab courses. And then you move on to Julie Millard and it's a research-mentor relationship. ... Then to get the opportunity to

THE COLBY-NIH PIPELINE

Professor Julie Millard, the Dr. Gerald and Myra Dorros Professor of Life Sciences and chair of the Chemistry Department, and her colleagues know "Bodine material" when they see it. But the honor, which goes to especially promising, budding scientists, carries an admonition.

"I tell each one before they go to Bethesda," Millard said, "'Don't mess it up for the next one.'"

It seems to be working. André Pilon '03, in the Ph.D. program at George Washington University and currently working with Bodine in the lab, says it's obvious that people are "coming here for a reason. Dave has a genuine interest in us doing well."

"He knows research and good academic training are the building blocks," said Whitney King, the Dr. Frank and Theodora Miselis Professor of Chemistry and associate chair of the department. "On the reaccreditation committee, we are looking at outcomes, and in the sciences he was a logical person to talk to. Dave gave us very high marks and helps us with external reviews of all kinds. He is helping us become a better institution as an outside evaluator. His professional credibility is just tremendous. The unspoken qualification to get into grad school is research. It's not required, but it's a qualification. Dave's mentoring and encouragement go a long way in helping us step up in that area."

Millard, now in her 16th year at Colby, stresses undergraduate research as an integral part of the Colby chemistry experience.

"Working in a lab and presenting at a conference or meeting are goals for us here," she said. "We've provided research opportunities for as long as anyone can remember. And David Bodine has been extremely helpful. He came up to do a chemistry seminar, the Howard Hughes Medical Institute grant overseers invited him as an outside expert—he's just been a great resource. When we were starting to do work with cells, he sent us a whole line of cells and all the media we needed. If I recommend someone, he takes them. He's just brilliant at letting them blossom there. They all come back with rave reviews about the lab—and they all love David Bodine."

NIH/COLBY ALUMNI

Laurie Girard Eidt '93: Graduate of Washington University, Physical Therapist, Stamford, Conn.

Stephanie Andriole '98: Graduate of Sarah Lawrence College, Genetic Counselor, New York City

Claire Overgaag '98: Graduate of Massachusetts General Hospital Institute for Health Professionals, Nurse Practitioner, San Francisco area

Douglas Nilson '99: Graduate of Northwestern Medical School, Emergency Medicine, Providence, Rhode Island

Tiffany Frazier '01: Graduate of University of Vermont Medical School, Resident in Pediatrics, Boston, Mass.

Lindsey Rowland '01: Graduate of St. George's University School of Veterinary Medicine

Jessica Weisbein '01: Graduate of University of Pennsylvania Medical School

André Pilon '03: Currently serving in NIH lab

Serena Vayda '03: Currently serving in NIH lab

Nicholas Markham '04: Attending Vanderbilt Medical School, M.D./Ph.D. Program

Erin Parry '06: Attending the Johns Hopkins School of Medicine, M.D./Ph.D. Program

Emily Devlin '07: Currently at Colby, slated to return to NIH lab

work with Dave here and go to Orlando, where we can hit up the big names in hematology, the ones who write the books. It gives us a chance to give our talks, maybe attract the attention of someone whose lab we might want to visit. It gives us a chance to line up our post-doc experience.”



Before Millard and her colleagues Frank Fekete and Judy Stone from the Biology Department started sending students to Bodine, there was Professor Art Champlin. Champlin, who passed away unexpectedly in 2003, taught Bodine at Colby in the early '70s. And it was Champlin, along with a fellow biology professor, the late Miriam Bennett, who mentored Bodine and gave him the support and encouragement he needed to thrive. “I never can repay them for the time and trouble they took with me,” said Bodine.

Bodine double majored (biology and environmental studies) and graduated cum laude with distinction in both. He also won the Webster Chester Biology Award. Bodine earned his master's in human genetics at Rutgers and his Ph.D. in zoology and genetics at the University of Maine, followed by research at the Jackson Laboratory in Bar Harbor. In between his course work at Orono and the beginning of his research at the Jackson Lab, Bodine returned to Waterville, living briefly with Champlin and his wife, Betsy '65 (now Betsy Stark Roberts, who returned in 1971 to work in the Biology Department for 33 years).

Bodine volunteered to work in the Biology Department and, in his spare time, built a garden for the Champlins; the garden was still intact when Roberts sold the house in 2005. His interest in gardening continues. When spring bulbs are blooming at his Chevy Chase, Maryland, home (where he lives with his wife, Susan, a lawyer and assistant administrator in the EPA's Office of Solid Waste and Emergency Response, and their two sons, Christopher and Steven), Roberts is sure to find out by e-mail. Living

inside the Beltway and gardening in Hardiness Zone 6 haven't turned Bodine into an Orioles or a Nationals fan, though: his NIH e-mail handle remains tedyz— for Red Sox legends Ted Williams and Carl Yastrzemski.

Bodine received his Ph.D. in 1984 and did his post-doctoral and staff fellowships at the NIH's Clinical Hematology Branch of the National Heart, Lung, and Blood Institute in Bethesda. And, as his career has progressed, he's focused some of his considerable energy on Colby.

“He is very devoted to Colby and to Colby students,” Roberts said. “He thinks of that as a very important part of his work and he's always looking for more. He would write to Art, to me, asking what we thought about certain students at Colby. I think it goes back to the mentoring he got while he was a student at Colby. He is dedicated to providing it to other Colby students.”

He also is dedicated to his profession, and that means publishing at the highest level and taking leadership roles in professional societies. He has long held leadership positions in the American Society of Hematology, the International Society of Experimental Hematology, the Leukemia and Lymphoma Society, and the American Society of Gene Therapy, where he will serve as president beginning in 2008. He has been published widely throughout his career and has served on the editorial boards of *Experimental Hematology*, *Gene Therapy*, the *British Journal of Hematology*, *Molecular Therapy*, and *Blood*, the official journal of the American Society of Hematology and the most-cited peer-reviewed journal in the field.

His curriculum vitae runs more than 25 pages.

But throughout his distinguished career, one of Bodine's experiences at the Jackson Laboratory has stayed with him—and speaks to the essence of his love for his work.

“One Saturday morning I was doing an experiment that everyone thought was dumb,” he said. “I had a good hypothesis, though, and I really believed in that experiment. It required forty or fifty vials that had to be analyzed individually by a scintillation counter. I remember waiting by the counter so that I could see each value as it was recorded. I could have gone away and come back for the printout at the end of the analysis, but I was so excited to see the result, I could not wait. If anyone had seen me, they'd have thought I was nuts. But, I thought, ‘I'm the only one in the world doing this and I can't wait to see the results. This must be the right place for me.’”



PHOTO BY ROBERT VISSER

David Bodine '76 at the National Institutes of Health in Bethesda, Maryland.