endeavors

Research and Creative Activity • The University of North Carolina at Chapel Hill
Fall 2010

How old are you? The answer may depend on your levels of a protein called p16. page 6

endeavors
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Endeavors engages its readers in the intellectual life of the University of North Carolina at Chapel Hill by conveying the excitement of creativity, discovery, and the rigors and risks of the quest for new knowledge.

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On the cover: Your birthdays may be coming more—or less—often than you think. Photo by Donn Young.

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THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL

My grandfather gave me this wallet. He bought it, like most of the presents he gave for Christmas, at a flea market. The leather inside is dyed bright red. The outside is stitched together with some kind of plastic cord. When it was new, two cowboy boots were embossed into the leather on one side. The other side had a pony. Both sides are worn smooth now.

My grandfather used to make up stories about a little red Volkswagen Beetle that outwitted a mean black Cadillac. He would pay for our McDonald's Happy Meals with exact change: handing the cashier the coins, he'd say, "Here's your cost," and then—forking over the bills—"and here's your profit." He didn't say hello when he answered the phone. He'd just announce his name, *James*, as if the caller should get down to business. He would say that his garden was doing pretty well, but the macaroni he planted still hadn't come up.

He gave me the wallet when I was eighteen or nineteen. I've carried it every day since. It was in my right front pocket the day I helped carry his coffin from the funeral home to the hearse, and from the hearse to his grave. We unpinned the carnations from our lapels and left them on the lid of his coffin. He was eighty-eight. In the last few years of his life he'd struggled with diabetes, a bladder infection, kidney stones. He had elevated levels of the marker for prostate cancer, but because of his age, the doctors decided not to investigate. One day a diabetic coma put him in the hospital. The doctors there found more and more things that were going wrong. They said he'd likely had several small heart attacks and not realized it. The prostate cancer had probably spread. They gave him a pacemaker, but he wouldn't need it for long.

Eighty-eight may be ripe enough, as old age goes. Would he have lived longer if he ate better? Was all that black coffee good for him? Did he wait too long to give up cigars? What if he could have taken some kind of blood test years ago to see how his body would react to getting older? Or to see whether he'd make a good candidate for a particular kind of prostate cancer treatment? Would he want to know? Would we?

The wallet is starting to fall apart. Receipts and little slips of paper sometimes fall out through the cracks in the leather. When money and credit cards start to slip out, I'll probably have to retire it. For now, though, I'll keep it right here in my right front pocket.

—Jason Smith

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The stage is set for My Boy Rascal's album release party in March 2010. Story on page 20. Photo by Tang Yi.

overview

FAMILY MEDICINE

Is there a doctor on the air?

by Mark Derewicz

Adam Goldstein and Cristy Page make it sound so easy—they discuss the latest research and interview experts without slip-ups or awkward pauses. They have an affable, conversational style even when they cover the most serious topics. They're the antishock jocks. And they have a purpose.

Every week Goldstein and Page, doctors in UNC's family medicine department, take a break from their routines to tape a radio program in a tiny, windowless studio in north Chapel Hill. The show is called *Your Health*. You can listen on WCHL 1360 or on the web. Chances are you will benefit from it, whether you love research, have a family member with a serious illness, or even if you're just battling a viral infection.

"Often people can't afford to see top experts," Goldstein says. "Or they might not have time to read a new book. Maybe they're turned off by a complex subject such as nanotechnology in medicine. I know I didn't understand why we should invest in nanotechnology or what the risks might be until we interviewed Joe DeSimone at UNC. I had a lot of 'Aha!' moments during that interview."

When Goldstein and Page explain research and talk to experts, they cut through scientific jargon. When they answer listener questions, they give advice as though talking to their patients.

During one show, a listener said her doctor prescribed antibiotics for strep throat even though the medicine might have little impact on the sore throat; he'd said it prevents rheumatic fever. "If that's true," the listener asked, "do I really need the antibiotics? Isn't rheumatic fever really rare?"

Page responded, "Great question. Yes, it's true that your body might fight strep on its own—and yes, it's true you need antibiotics."

JASON SMITH

Goldstein chimed in, "You'll get rid of strep throat sooner by taking antibiotics. And that doctor was correct: if you don't take antibiotics, you can get rheumatic fever. One reason rheumatic fever is rare is because we treat strep with antibiotics."

Goldstein, who's been at Carolina since 1993, has always been interested in media and translating research for the public. He teaches a course on media advocacy, writes op-ed pieces for newspapers, and helped create a statewide program to limit teenage smoking. *(See* Endeavors, *Spring 2007*, *"Facing Facts.")* So when colleagues in the Department of Family Medicine wanted to start a radio program in August 2008, Goldstein volunteered.

The first episode of *Your Health* aired in October 2008, and soon it will be syndicated across North Carolina. Goldstein's team is negotiating with corporate sponsors to increase the show's budget, which could allow for even wider syndication. The team would also be able to buy better sound equipment or build a new studio. A larger staff could develop special show segments. Or they could take the show on the road. "One of my dreams is to set up the show in the lobby of UNC Hospitals," Goldstein says. "That would make the show more visible, and I think it would be a lot of fun."

Adam Goldstein is a professor and Cristy Page is an assistant professor in the Department of Family Medicine, both in the School of Medicine. The department funds the program, which family medicine program director Julea Steiner produces. UNC Health Care is a sponsor. Your Health *is broadcast Saturdays and Sundays at 9 a.m. and Mondays at 6 p.m. and 10 p.m. Find archived shows at www.wchl1360.com.*

PUBLIC HEALTH

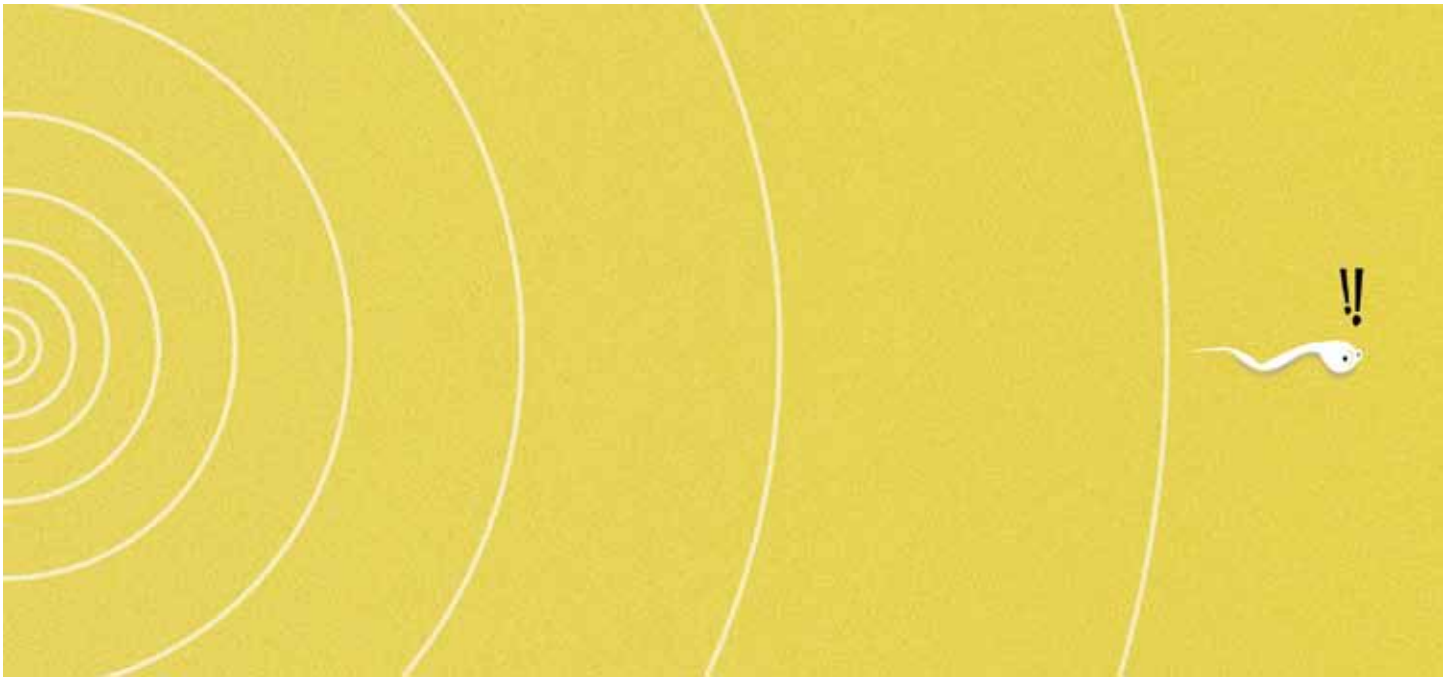
Strike up the ban

by Ramona DuBose

In January 2010, North Carolina became the first tobacco-producing state in the nation to ban smoking in restaurants and bars. Now, the latest poll conducted by the Survey Research Unit at the Gillings School of Global Public Health shows the ban is supported by just over 72 percent of adults in the state. Almost 26 percent opposed the ban, and just over 2 percent were undecided.

CAROLINA FINDINGS

Autistic behavior is the result of many rare and small genetic changes. Doctors often unnecessarily treat irritable bowel syndrome with narcotics, which may further compromise their patients' health. Corporate boards in North Carolina are increasingly diverse, but they are not as diverse as the boards of Fortune 100 companies. Men who are infected with human papillomavirus (HPV) are at greater risk of becoming infected with HIV than men



Ultrasound wipes out sperm. It causes infertility in rats, and may one day prove effective as a safe, long-term contraceptive for men. Illustration by Jason Smith.

CONTRACEPTION

A sound decision

by Ginnie Hench

Therapeutic ultrasound—which uses a different frequency from the ultrasound that gives us our first images of a growing fetus—may be able to prevent pregnancy by depleting sperm reserves in men. James Tsuruta and colleagues have shown that one therapeutic ultrasound treatment eliminates developing sperm cells in rats. The potential contraceptive effects of ultrasound are long-term, reversible, and inexpensive, without the use of hormones.

Tsuruta studied cellular communication as a grad student. He became an expert on Sertoli cells, supportive "nurse cells" essential for sperm development. That expertise attracted the attention of the Parsemus Foundation, a group dedicated to finding low-cost medical solutions that the pharmaceutical industry neglects. Reports published in the 1970s stated that rat sperm could be depleted with ultrasound. The reports were not well-received by the scientific community and were largely forgotten. Parsemus invited Tsuruta to help lead a team trying to verify the published experiments.

The conventional thinking is that one egg is an easier target than millions of sperm. But in fact, "it takes millions of sperm to provide the few that are strong enough to fertilize an egg," Tsuruta says. In fertile men, sperm production cycles constantly. Ultrasound depletes all stages of developing sperm, from the youngest spermatocytes to the mature spermatozoa. Once sperm reserves are eliminated, fertility is impossible. Tsuruta hopes that spreading this information about sperm biology will change the misperceptions that support a funding bias in favor of contraception research that focuses on women.

Efforts to understand how ultrasound depletes sperm could open up new avenues for research. A single sperm takes seven weeks to mature; yet experiments from the 1970s found that ultrasound confers infertility for twenty-four weeks. Tsuruta speculates that the low number of resident sperm stem cells may temporarily alter the sperm stem-cell instruction program. Another effect could be structural. Tight junction bridges between Sertoli cells form a barrier against infiltrating immune cells. If ultrasound ruptures the barrier, the Sertoli cells may need time to repair the tight junctions.

Tsuruta's team is trying to find the minimal dose of ultrasound that can safely cause infertility in rats. Long-term, Tsuruta wants to comply with strict regulations in wealthy countries while keeping the treatment inexpensive for developing countries.

Tsuruta points out that ultrasound contraception won't stop HIV exchange between sexual partners, but he says it could limit the number of new babies born HIV-positive. Pregnancy-related deaths common to resource-poor areas would be prevented by effective contraception. And if ultrasound proves to be a viable male contraceptive, men will have another option for sharing responsibility for family planning.

James Tsuruta is an assistant professor of pediatrics in the School of Medicine.

BIOCHEMISTRY

King Tet

by Tom Hughes

Yi Zhang found that the protein Tet 1 helps stem cells renew themselves and stay pluripotent—able to become any type of cell in the body. "This may be one component of a cocktail to reprogram a specialized cell to go back to the undifferentiated, embryonic stem-cell state," Zhang says. Scientists are now one step closer to understanding the genes, proteins, and reactions that control embryonic stem cells.

Yi Zhang is a professor of biochemistry and biophysics in the School of Medicine.

who are not HPV-positive. Focusing on certain post-traumatic stress disorder symptoms may be key to treating anger among Iraq and Afghanistan veterans. Deaf children who receive a cochlear implant before eighteen months of age eventually develop nearly the same abilities as normal-hearing children to hear, understand, and speak. A protein called Ku is particularly adept at healing damaged strands of DNA. A six-gene signature can help predict whether pancreatic cancer will metastasize.

GENETICS

Is smoking in your genes?

by Noor White

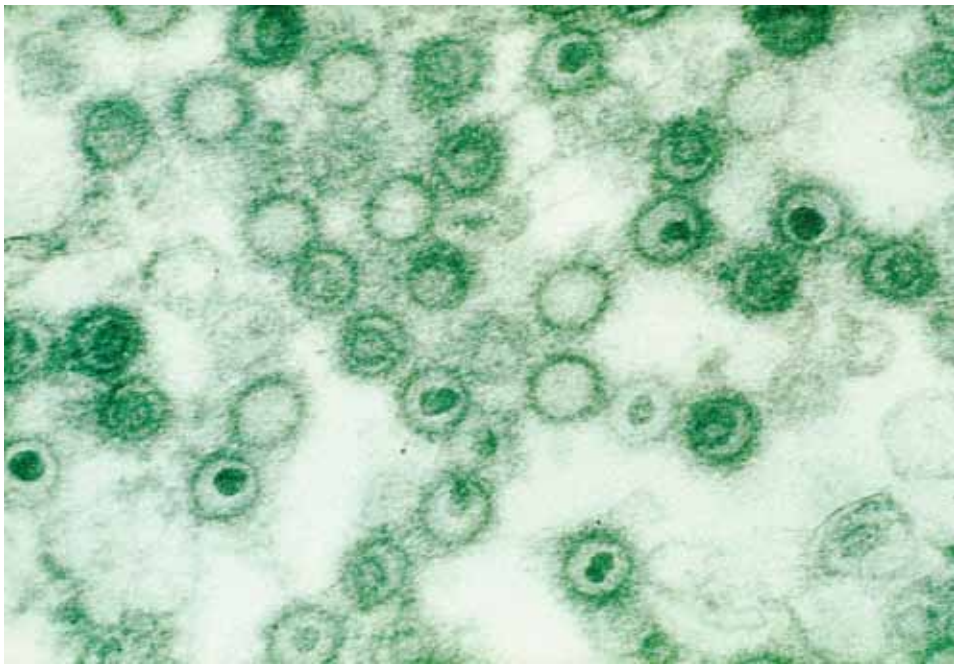
Have you ever wondered why it takes some people years to quit smoking, while others can stop cold turkey? According to UNC geneticist Helena Furberg, the answer is in our genes. Furberg led the Tobacco and Genetics Consortium to bring together genetic and lifestyle data from sixteen independent studies. They used data about whether people began smoking; if so, how old they were at the time; the number of cigarettes they smoked per day; and whether they were able to quit for more than a year.

Furberg and the consortium identified several genetic changes associated with smoking habits. Three of the changes are associated with how much people smoke, and the strongest of them is a single base-pair change, or single-nucleotide polymorphism (SNP), in a nicotine receptor gene. Eight other SNPs are associated with starting to smoke, and one is identified with whether a person was able to quit.

Furberg believes that the next step is to conduct research in other disciplines to translate this genetic information into practical public health measures. "Right now, the results are most useful to addiction biologists, who can start looking at these genetic regions and figure out what they do," Furberg says. She hopes this research can be used to develop personalized clinical treatments to help smokers quit for good.

Helena Furberg is an assistant professor in the Department of Genetics. Furberg and the Tobacco and Genetics Consortium partnered with the European Network of Genetic and Genomic Epidemiology, Oxford University, and GlaxoSmithKline to do analyses that identified the SNPs.

FABIO FROSIO



The Epstein-Barr virus, part of the Herpes family, is one of the most common viruses in humans. It causes several different kinds of cancer and autoimmune diseases. Image courtesy of UK Clinical Virology Network.

PATHOLOGY

The EBV virus: a trojan horse to kill cancer

by Lee Langer

Researchers for the UNC Project in Malawi have made an advance in the treatment of Burkitt lymphoma, using a common virus associated with the tumor as a Trojan horse to kill tumor cells. This is a significant step forward in the management of Burkitt lymphoma, a deadly childhood cancer prevalent in sub-Saharan Africa.

Previous studies have found that Burkitt lymphoma cells in sub-Saharan African patients are almost always infected with the Epstein-Barr Virus (EBV). EBV infections can switch between two states: a latent state in which the virus is not dividing and an active state in which the virus takes over the host cell's machinery, replicates, and kills the host cell. When EBV is active in a cell, that cell and nearby infected cells can more easily be destroyed by antiviral medications. A theoretical way to aggressively treat Burkitt lymphoma would be to use chemotherapy to activate EBV and simultaneously use an antiviral agent. But until now it wasn't known whether chemotherapy could effectively activate EBV in humans. In a clinical trial of twenty-one children with Burkitt lymphoma in Lilongwe, Malawi—home of the UNC Project—researchers report that EBV apparently activated less than a day after treatment with a first-line chemotherapy. "We were shocked by how quickly an effect was seen," says pathologist Margaret Gulley. "We had a feeling that the virus would be activated but thought that it would take days or weeks."

The next step will be to determine whether a double-pronged attack with chemotherapy and antivirals will result in better outcomes for children with Burkitt lymphoma. Carol Shores, who visits Malawi three times a year and is the senior author of the current study, will be leading a Phase I safety trial of simultaneous treatment with chemotherapy and antivirals beginning this August. Although both drugs are approved in the United States, Shores says the study will verify the safety of the drug combination in Malawian children, many of whom

Giving babies in sub-Saharan Africa an antiretroviral drug once a day during their first six months of life drastically reduces the rate of mother-to-child HIV transmission. Just over 47 percent of North Carolina residents favor increasing the tax on a pack of cigarettes from the current 45 cents to the national average of $1.34. Increasing certain proteins in the blood vessels of mice lowers the animals' blood pressure. In high-school sports other than basketball and ice hockey,

have potentially complicating health concerns including malaria and malnutrition. If the trial goes well, a Phase II trial of the efficacy of the two drugs in treating Burkitt lymphoma will be next.

Lee Langer is a graduate student in neurobiology in the School of Medicine.

Margaret Gulley is a professor of pathology and laboratory medicine, and Carol Shores is a surgical oncologist and associate professor of otolaryngology/head and neck surgery, both in the School of Medicine. This study appeared in the April 2010 issue of Clinical Cancer Research.

PEDIATRICS

When parents understand, kids are healthier

by Tom Hughes

Parents of overweight or obese children often don't recognize that their children have weight problems. But Eliana Perrin found that a simple intervention can help change parents' assessments of their children's weight and can influence behaviors at home. Perrin gave pediatricians a color-coded chart to help explain body mass index to parents and a series of questions and suggestions to help them counsel parents to make behavioral changes.

In initial visits, only 57 percent of overweight children's parents accurately perceived their child's weight. That improved to 74 percent at a three-month follow-up visit. Also at the follow-up, children who were overweight were more likely than healthy-weight children to drink lower-fat milk and showed the largest reduction in the frequency of eating out. Overall, children increased their fruit and vegetable consumption, decreased their consumption of sweetened beverages and unhealthful snacks, drank lower-fat milk more often, and reduced the time spent playing video games and watching television.

"A lot of studies have shown that parents don't see their overweight children as overweight," Perrin says. "This is the first time we've seen a changed perspective from parents. We hope that parents who know their children are overweight will be empowered to help them achieve more healthful lifestyles."

Eliana Perrin is an assistant professor of pediatrics in the School of Medicine.

WOMEN'S HEALTH

Menopause sooner?

by Jason Smith

Women who were exposed as fetuses to a synthetic estrogen called DES reach menopause about a year sooner than women who were not exposed, according to a study of twenty thousand women in the United States and Puerto Rico.

The number of eggs in a woman's body declines as she ages, and menopause begins as her egg supply starts to run out. Girls born with fewer eggs should reach menopause sooner. (In the womb, a baby girl will have about five million eggs in her ovaries; by birth she'll only have about two million.)

This medical journal advertisement encouraged doctors to prescribe desPLEX® "to prevent abortion, miscarriage and premature labor." The ad recommended the drug "for routine prophylaxis in all pregnancies," and promised "bigger and stronger babies" and "no gastric or other side effects."

Anne Steiner studied middle-aged women to find out how the time they spent in their mother's wombs may have influenced the number of eggs they were born with. Steiner controlled for factors such as race, education, income, and smoking status, and found that DES—prescribed by many doctors from the 1940s to around 1970 to reduce the risk of pregnancy complications—seemed to have the greatest effect on the age at which women hit menopause. Steiner found that low birth weight and whether the mother was diabetic hastened the arrival of menopause by less than a year, though the association was comparatively weak. And she found that birth order, breastfeeding, and exposure to smoke seemed to have no measurable effect on the age at which the women reached menopause.

Anne Steiner is an assistant professor in the Department of Obstetrics and Gynecology in the School of Medicine.

PEDIATRICS

Trained to deliver

by Mark Derewicz

Every year, 3.7 million babies die within days of birth, and 3.3 million more are stillborn. Ninety-eight percent of these deaths occur in developing countries. A research team that included UNC's Carl Bose tested whether interventions common in developed countries could save lives.

The researchers trained caregivers from Argentina, Guatemala, India, Pakistan, Congo, and Zambia in routine newborn care—identifying common illnesses, keeping babies warm, resuscitating babies who haven't taken breaths on their own. Those caregivers then trained thousands of rural birth attendants in their home countries.

Bose and his colleagues provided handheld pumps and masks that birth attendants could use to help fill the lungs of babies who weren't breathing at birth. They gave caregivers scales to measure birth weight, and medical kits to help prevent infections.

The research, which involved more than 110,000 births in rural regions, showed a 30 percent reduction in stillbirths: a decrease from twenty-three per one thousand births to sixteen. (In the United States there are fewer than ten stillbirths per one thousand births.) Bose and his colleagues say that basic interventions helped save babies who hadn't drawn breaths on their own after birth: those babies would have been assumed to be stillbirths had birth attendants not helped the babies breathe. "This is a simple intervention," Bose says, "and it can be effectively taught to traditional birth attendants who deliver most of the babies born in developing countries."

Carl Bose is a professor of pediatrics in the School of Medicine.

girls are no more susceptible than boys to concussions. Urine tests might help identify people who are prone to liver damage from the popular over-the-counter drug acetaminophen. Black patients are less inclined to choose surgery for early-stage lung cancer than white patients, often because of communication gaps between them and their doctors. A shift in the balance between the good bacteria and the bad bacteria that populate our gut could be a harbinger of colon cancer.

HOW OLD ARE YOU, REALLY?

THE ANSWER IS IN YOUR BLOOD, AND NED SHARPLESS CAN TELL YOU.

STORY BY
MARK DEREWICZ

PHOTOS BY
DONN YOUNG

I'm thirty-nine years old. But after going to RealAge.com and typing in a bunch of lies—I mean, information—about my diet and habits, it turns out I'm actually thirty-five. My diet is pretty good, the site tells me. And I'm wise for not smoking. Who knew? But my real age would be even lower if I'd spend more time exercising and less time eating cheese-filled pastries. Guilty as charged.

I should eat more fish, broccoli, cranberries, apples—anything high in omega-3 fatty acids, flavonoids, or antioxidants. Green tea is a must, of course. Oh, and tomatoes. I should eat more of them. Or tomato paste, juice, sauce, soup, ketchup. Tomatoes are high in lycopene, the site tells me, which is supposed to prevent prostate cancer.

The site leaves a lot to the imagination. For instance, how does it know how long I've not been exercising? What if eating pounds of blueberries every week is actually bad for me? Has anyone studied that? And the site didn't ask me about my salt intake; I add it to stuff here and there.

Still, people seem to love RealAge.com. A friend bragged that he was really thirty-two, not forty-two. Good for him.

Unfortunately, oncologist Ned Sharpless is old. "I took that test in my thirties and it said I was in my forties," Sharpless says. "That really ticked me off."

You see, Sharpless doesn't eat enough ketchup. "Yeah, it's good that I don't smoke and I exercise regularly, but I don't have enough lycopene in my diet," he jokes. "I swear that thing is run by the ketchup industry."

Sharpless says there's no real proof that lycopene is so beneficial that it adds years to our lives, no proof that it slows the degenerative process of aging. Same with highly touted wonder foods. That said, he'd love to know how old he really is, down to his blood and bones. He'd especially like to know how old his patients really are.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Wouldn't it be best if we could peek inside the human body and measure something that tells us how old we really are, or whether our lifestyles and habits hurt or help us? That's what Sharpless did. He can tell you how old you really are and—in some cases—why. And someday he might even be able to tell us whether eating blueberries and tomatoes really does add years to our lives.

Generally speaking, the younger we are the better we respond to treatments such as chemotherapy, radiation, and organ transplant. But that's not much more specific or scientific than RealAge.com. Wouldn't it be best if we could peek inside the human body and measure something that tells us how old we really are, or whether our lifestyles and habits hurt or help us?

That's what Sharpless did. He devised a blood test to measure a protein called $p16^{INK4a}$, a tumor suppressor that builds up in cells as we age. (We'll refer to it as p16.) He can tell you how old you really are and—in some cases—why. He's already found out how old he really is. And someday he might even be able to tell us whether eating blueberries and tomatoes really does add years to our lives.

In UNC's Lineberger Comprehensive Cancer Center, at the end of a long hallway lined with posters of colorful cells and carcinomas and confusing equations, is a small office where Sharpless spends a lot of time talking with students and postdocs about what makes a good scientist. He's put a few photos on his walls to make his points. One is of the devil tempting Jesus. "Get thee behind me, Satan," he tells students. Don't let the less challenging path tempt you. "There's a lot of easy stuff we could do that's not the right stuff to do." There's a postcard of George Washington. "When you run a lab, you have to be a good leader," he tells students. "You have to remember what's in it for your people." Next is St. Thomas More. "He was uncompromising. You gotta stick to your principles." And there's a large poster of the cover of *London Calling* where The Clash's Paul Simonon is destroying his bass guitar. "There are established paradigms in science, and if all you do is work within them, you won't make progress," Sharpless says. "Don't be afraid to do something that someone else says is dumb. Don't be afraid to break a guitar." (Also, he really likes that album.)

Scientists have known for several years that p16 increases with age—in rodents, at least. "That was interesting," Sharpless says, "but no one could say whether the increase was twofold or twentyfold." And no one knew which cells were important to p16 expression. Not all cells have the protein, and it doesn't work the same way in all cell types.

Sharpless, curious, decided to break a guitar—he dedicated part of his lab to aging when he arrived at Carolina in 2002. "Not all of my colleagues were enthusiastic," he says. "At that stage of my career it might have been better to focus solely on cancer." (His lab does study p16 as it relates to cancer. We'll get to that.) "But there wasn't a lot known about p16 in aging. My interest has always been the cell cycle: what makes cells divide. That's important for cancer, but there's more to it than cancer." And, Sharpless says, "my first graduate student, my first postdoc, and my first technician all conspired to study p16 in rodent aging."

First, they measured RNA molecules for the p16 gene to figure out which cells in rodents expressed p16. And one of their first findings was that rodents with low p16 were younger and fitter.

In one experiment, Sharpless restricted the diets of rats and then studied different organs to see what happened. He got a provocative result: caloric restriction didn't do much to p16 levels in some organs, but p16 expression in the kidneys and in a few other tissues was almost completely stifled as the rats aged. And rats don't need a lot of p16 in their kidneys: they don't usually die of kidney cancer; they die of kidney failure.

Sharpless knew from other studies that calorically restricted rodents seemed much younger than normal rats. The dieting rodents performed better in dozens of ways, including on the classic maze test. They had better brain function, heart function, muscle and kidney and immune functions. "They live longer, more robust lives," he says. And now he had proof that they are molecularly younger—at least in some tissues, including kidney tissue.

In later experiments, Sharpless used RNA-based tests to show that p16 doesn't increase in every kind of cell as mice age. "It *does* go up in lots of cells, but we found it doesn't do much in many of those cells," Sharpless says. "We think p16 is unimportant in some cells. But in a few cells, it's *very* important."

For instance, he found that the protein hinders the division of pancreatic beta cells, which produce insulin in rodents—and in humans. If we can't make enough insulin, we get type 2 diabetes. Previous to this work, diabetes researchers had thought that beta cells didn't divide—or if they did, that they didn't replicate fast enough to matter. "That's what we were taught in medical school," Sharpless says. "Turns out that's wrong." Sharpless and Harvard scientist Susan Bonner-Weir showed that beta cells divide, and p16 stops that division. High levels of p16 are not good for beta cells, which rarely turn into cancer and have to divide so that the pancreas can produce enough insulin.

So what does p16 do in humans? It's not easy to harvest cells from human organs. But in 2006 Sharpless worked with hematologist David Scadden to find that p16 hindered division in hematopoietic stem cells as rodents got older, a clear sign that p16 levels correlated to the aging process. So Sharpless thought he'd study human hematopoietic stem cells. But he ran into trouble: you have to extract those cells from bone marrow. And that hurts. A lot.

"When we tried to get this study off the ground, I pitched the idea to cancer doctors," Sharpless says. "They said, 'This is awful. You gotta do *three* bone marrows? Who's gonna do that? Why can't you just test the blood?'" Sharpless thought, "Oh, you stupid clinicians. We smart scientists have elegant reasons for why we need to use marrow."

Sharpless (who, by the way, is also a clinician) contacted anyone in the country he thought could help him find bone marrow donors. Over three years colleagues in Seattle gathered eighteen people—too few to conduct a full study. But his lab did find that human stem cells always have low levels of p16, no matter how old or young someone is, and that makes the protein harder to study. It would be better to study a line of cells with a wide range of p16 expression.

"We gave up," Sharpless says. Well, they retreated. His lab decided to heed the advice of the stupid clinicians and use T cells in blood. Sharpless's team set up a blood-drawing station in the lobby of UNC Memorial Hospital and paid volunteers ten dollars for a sample of blood and answers to a few questions.

This is where I first heard of Sharpless's research. His team took my blood while I filled out a questionnaire about my general health, disease history, and exercise and smoking habits. The idea, according to a white-coated lab tech, was to see whether certain behaviors help keep people molecularly younger. Sounded interesting.

"I really didn't think this would work," Sharpless says. "As a mouse geneticist, I thought these questionnaire-based studies were just the softest stuff you could imagine. If I asked you how much you exercise, would you answer that question the same today as you would six months from now? It just didn't seem very precise."

For my part, I'm confident I gave him good data: I've been consistently lazy and a devout nonsmoker for a good decade.

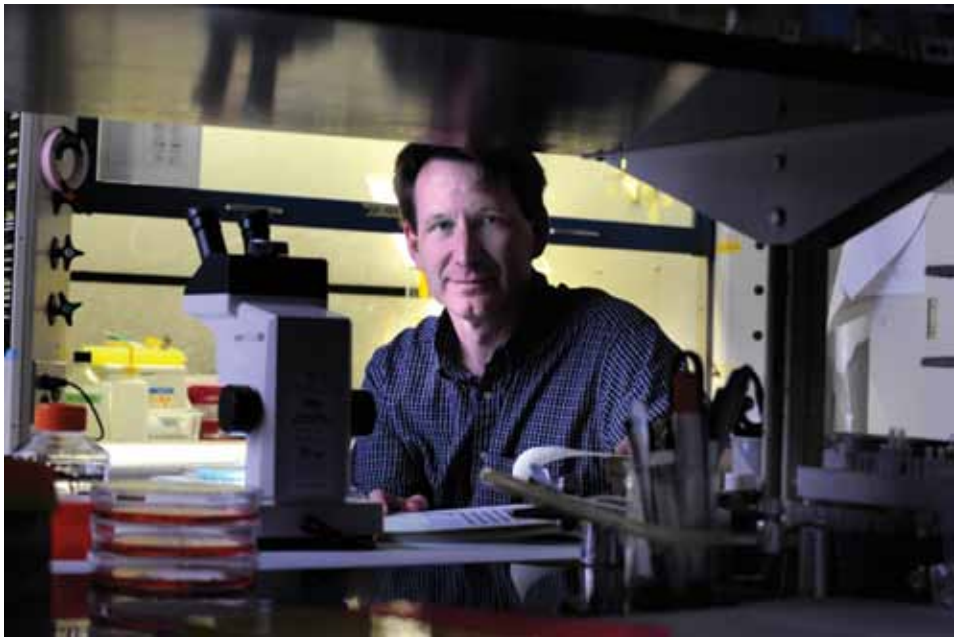
Team Sharpless collected two hundred blood samples and used a common technique—polymerase chain reaction—to analyze the p16 gene in T cells. To Sharpless's surprise, the results were robust. P16 expression in T cells increased exponentially with age, and T cells allowed for a much purer measurement of age than did hematopoietic stem cells. Smokers who didn't exercise had higher levels of p16. Sharpless says doctors have known that longtime smokers seemed physiologically older—they looked older than their stated age. It seemed as if smokers were molecularly older. "And now we have proof of that," he says.

Now, the elephant on the page: if p16 is a tumor suppressor, and smoking increases p16, how does smoking cause tumors? Why doesn't all that p16 wipe out the cancer? "When I give talks I get that question every time," Sharpless says.

Let's see if we can explain it. When a carcinogen such as cigarette smoke enters the body, it can damage cells and alter DNA. "Say you have ten cells with equal risk of becoming cancer," Sharpless says. "Eight cells take in a carcinogen, but not enough of it, and spit it out. Nothing happens to those cells; their p16 stays the same. One of the cells takes in the carcinogen, is really damaged, and p16 is activated. P16 stops that cell from dividing. It's in jail, never to be heard from again." The tumor suppressor is working, and p16 increases manyfold. "That tenth cell takes in the carcinogen and DNA is damaged, but p16 is not activated for one of two reasons—the DNA damage is not the kind that activates p16, or the carcinogen mutates the p16 gene so that the protein is not induced. In either event, that cell is significantly damaged and well on its way to becoming cancer."

So that's how carcinogens and p16 interact. And that's why so many cancer researchers, including Sharpless, are interested in p16—it's one of the few proteins that keep cells from becoming cancer. It interacts with kinases called CDK4 and CDK6, which act like gas pedals—they speed up cell division. Many kinds of cancer hijack CDK4 to cause damaged cells to divide like mad. P16 acts like the brakes: it interacts with CDK4 to stifle cell division. Because of this, over the past decade big pharma has created drugs that mimic p16 to target CDK4 and CDK6. The drugs were supposed to act like an emergency brake, but they didn't work nearly as well as everyone had hoped. Sharpless created a mouse cancer model to find out why.

"There are so many things that could go wrong with any drug," Sharpless says. "Maybe it's not hitting the target. Maybe mice can't absorb the pill. Maybe the pill gets metabolized really quickly into something else and is inactivated. Well, we found



"When we tried to get this study off the ground, I pitched the idea to cancer doctors," Sharpless says. "They said, 'This is awful. You gotta do three bone marrows? Who's gonna do that? Why can't you just test the blood?'" Sharpless thought, "Oh, you stupid clinicians. We smart scientists have elegant reasons for why we need to use marrow."

—Ned Sharpless

"If you don't give the mouse the drug, it dies of radiation sickness," he says. "If you give it the drug, it lives; it has nearly complete protection. You never ever get an experiment like this. It worked the first time and it's worked every time since. Young mice, old mice, mice with genetic deficiencies that make them more or less susceptible to radiation. It always works."

—Ned Sharpless

that the p16-like drugs were hitting their target really nicely and just beautifully stopping the proliferation of a few mouse cells that were CDK4 and 6 dependent." But he found that most cells can divide without those kinases. "A lot of cancer cells use any kinase available to them; they're promiscuous," he says. "They have ways of turning on other kinases, such as CDK2." Scientists have developed drugs that target all three CDKs, but they're miserably toxic, Sharpless says, because shutting down all three kinases means stopping all cell division. And humans need for some kinds of cells to divide. Blood and gut cells, for instance. "Every week you make a whole new intestinal lining with new cells," Sharpless says. "If you can't do that, it's really unpleasant."

P16 drugs—several companies have slightly different versions—are not the panacea researchers had hoped. But many scientists are still searching for cancers that would respond to p16 compounds. Sharpless, though, took a different tack. He wanted to know whether the p16 drugs he had been working with shut down cell division in normal tissues. They did, and in a big way.

"The big kahuna cells we could make stop dividing were the hematopoietic stem cells," Sharpless says. They're in bone marrow. They're like blood cell matriarchs, he says, and their progeny include white blood cells, which get whacked during chemotherapy. "Protecting white blood cells is a twenty-billion-dollar-a-year business in oncology."

But it wasn't such a big deal to use the p16-like drugs to protect hematopoietic stem cells, because most of them are out of the division cycle at any given time. Radiation and chemo, for example, hurt cells that replicate a lot. The cells responsible for forming hair are some of the fastest-growing cells in the human body; that's why chemo and radiation often cause hair to fall out. Sharpless knew that the big kahuna cell's immediate progeny—multipotent progenitor and common myeloid progenitor cells—divide fast. But he thought they would use a different kinase to proliferate, not CDK4. If he was right, then p16-like drugs would not protect those progeny cells from chemo or radiation.

"I was wrong," Sharpless says. "And that's good. Turns out, the first couple progeny cells depend on the CDK4 kinase, too."

In his experiment Sharpless gave mice the drug, gave them radiation treatment, and watched what happened. The result astounded even Sharpless.

"If you don't give the mouse the drug, it dies of radiation sickness," he says. "If you give it the drug, it lives; it has nearly complete protection. You never ever get an experiment like this. It worked the first time and it's worked every time since. Young mice, old mice, mice with genetic deficiencies that make them more or less susceptible to radiation. It always works."

It also worked up to twenty hours *after* the mice had been exposed to radiation.

Sharpless's lab put the drug up against many common chemotherapies, and the drug protected mice against all of them. The idea is that doctors could give the drug to cancer patients. Chemo or radiation would attack the cancer cells while the p16 drug protected bone marrow.

Sharpless started a company called G-Zero Therapeutics that's developing a class of p16 compounds for human use. The company has received more than one million dollars in funding, mostly from the federal government, which is interested in drugs that protect against radiation poisoning. And G-Zero is also developing a p16 diagnostic test to pinpoint people's molecular age. One day, Sharpless thinks, you'll be able to go to your doctor, consult on why it might be good to test for your real age, and find out what exactly is going on in your T cells.

After analyzing two hundred blood samples, Sharpless's lab found that twenty-year-olds have an average p16 level of 4.5, as measured by using an RNA analysis technique and fancy math. Of the study participants—all of whom had no preexisting diseases or conditions and were not on medication—a twenty-one-year-old had the lowest p16; it was 3. The highest was 9—a fifty-eight-year-old smoker who didn't exercise. That numerical difference of 6 doesn't seem like much, but on this scale an increase from 5 to 6, for instance, means that the amount of p16 has doubled. So that number 9 represents a real age much higher than the participant's birth certificate age of fifty-eight. That person's real age is probably in the eighties.

Sharpless's blood test is simple; he could tap your arm and give you results within a week. UNC patented the process and is working with G-Zero to commercialize it. But would you really want to know your molecular age? If you already know that smoking isn't so good for you, do you really need to know that, as a longtime smoker, you're really sixty instead of fifty? Maybe, maybe not. But doctors would love to know.

Two different groups of European scientists cited Sharpless's research in their papers on p16 in human kidneys and transplantation. They used a slightly different method, but their test accurately predicted which donors had provided kidneys with the best graft-survival rates. Measuring p16 was better than knowing chronological age when it came to predicting which grafts would be most successful.

A p16 test could predict how patients would handle surgery or how well wounds would heal. Doctors could use Sharpless's test to see if his p16 drug protects bone marrow in cancer patients who receive chemotherapy or radiation. "P16 goes up when hematopoietic stem cells are damaged," Sharpless says. "You would be able to see how much older, in molecular terms, someone is after chemotherapy."

But Sharpless warns that seeking to know your p16 should not be for kicks and giggles. The test could give you really bad news; you'd need to be prepared. Still, Sharpless says, if patients really want to know their molecular age, doctors should let them know.

"You could use your p16 level as evidence that your healthy lifestyle is paying off or not," he says. "Maybe you'd change behaviors. I think that's a good reason to do it. A bad reason would be using it as a means for employment or insurance discrimination. Someone could say, 'Well, you no longer can get health insurance because you're molecularly old.'"

During Sharpless's study, the white coats who drew my blood also took a sample from Sharpless and his dad. Both Sharpless men had low p16 for their age. Ned's was 5; Dad's was 7. That meant Sharpless was really twenty-eight instead of forty-one. (He's now forty-three.) His dad was sixty-five instead of eighty-one. "I was very proud about that," he says. "I was going around the lab, all sanctimonious, telling everyone, 'That's the jogging and the nonsmoking. The Sharpless lifestyle is paying off!'"

Unfortunately for the Sharplesses, the lab was not done studying the blood samples. They found a common single-nucleotide polymorphism in the genome that affects p16 levels. Depending on your DNA, you could simply make less p16 than other people. And it turns out that the Sharpless men have the genotype with less p16 in T cells. "I had no right to brag," he admits. When accounting for genotype, Sharpless was really thirty-six. Still, he gets to relive part of his thirties, and that's not so bad.

Sharpless is not sure how important p16 genotyping is with regard to aging. "That's a question we're trying to figure out now," he says. "Should you be interested in your total p16 or your p16 normalized for your genotype?" Probably both.

Having a low p16 level in tissues aside from blood is not always a good thing. For one, it means you're more likely to get atherosclerosis—hardening of the arteries.

But Sharpless isn't sure whether his own p16 levels are low everywhere. Logic tells him that having a low p16 level in T cells is a good thing. "I think you'd have better immune function because your lymphocytes would work better," he says. "But that's pure speculation. We have no data to back that up." To figure that out, Sharpless says he'd have to test T cells in a lot of people—say, a thousand—and follow them for years to see how they age. "I predict high p16 will show bad outcomes," he says, no matter the genotypes.

The Sharpless lab is still honing the blood test, collecting more samples from volunteers, and measuring p16 in other tissues. He says he could expand his research to figure out whether other behaviors such as sunbathing or inhaling secondhand smoke are linked to p16 and aging. He could study eating habits. Do blueberries and tomatoes *really* keep us young? What about red wine or salmon? Bee pollen? Green tea? Dark chocolate donuts filled with grape jelly?

"The best I can tell, lycopene and antioxidants don't do anything," he says. Not as antiaging agents, anyway. Resveratrol, the stuff in red grapes that gives red wine such a good reputation, might have beneficial antidiabetes properties. But Sharpless says other research questioned the antiaging properties of resveratrol compounds.

"You know, one day I want to write *Ned Sharpless's Guide to Healthy Aging*," he says. "It will be one page—don't smoke, avoid carcinogens like tobacco, stay thin, and exercise is probably good. That's it. Everything else is controversial."

Ned Sharpless is an associate professor of medicine and genetics in the School of Medicine and associate director for translational research at Lineberger Comprehensive Cancer Center. Sharpless was one of four professors to win the 2009 Phillip and Ruth Hettleman Prize for Artistic and Scholarly Achievement by Young Faculty at Carolina. His research was funded by the National Institutes of Health, the Ellison Medical Foundation, and the Burroughs Wellcome Fund.

Sharpless's blood test is simple; he could tap your arm and give you results within a week. But would you really want to know your molecular age? If you already know that smoking isn't so good for you, do you really need to know that, as a longtime smoker, you're really sixty instead of fifty? Maybe, maybe not. But doctors would love to know.

Aging and body mass

Sharpless thought that obesity would accelerate molecular aging, but his lab found only a weak correlation between body mass index (BMI) and p16. "That surprised us because you'd think people who exercise more would have lower BMI, and that's generally true," he says. "Also, we knew that eating less is a good way to retard aging in mammals. But as we thought about it, our results made sense because BMI is not a good measure of caloric intake or exercise." One study volunteer was a football player, very young and fit. But he had a high BMI. "We'll have to do more studies, but it might be that exercise is good for you even if you don't become thin by doing it. In other words, you don't have to exercise to the point that you're skinny. Just exercise, per se, is a good thing to do."

Clinical p16

"He's a zealot," Sharpless says of oncologist Hyman Muss. "He's a preacher for geriatric oncology." So it's not surprising that Muss was one of the first oncologists to push Sharpless's p16 findings into clinical trials. He's running several trials to figure out whether chemotherapy and radiation cause p16 expression to increase in white blood cells. If p16 doesn't go up substantially, no big deal. If it does go up—as Muss suspects—then that means those treatments accelerate the natural aging process. The implications would be far-reaching.

In one trial, Muss will measure patients' p16 before they get chemotherapy or radiation or both. He wants to know whether people with higher p16 are the same patients who get severe side effects such as white cell depletion, infections, nerve damage, and heart problems. If he can figure that out, then someday doctors could use p16 tests to help minimize side effects. "If a patient has a high p16 level, we could start them on a lower dose of chemo or radiation," he says. "If we're worried about low blood counts, we could give patients growth factors."

Muss says that chronologically older people with higher p16 levels may be more susceptible to severe fatigue or frailty after getting cancer treatments. A p16 test could help doctors predict which patients would need assistance at home. "We could show that a group of patients needs a geriatric social worker to visit them weekly," Muss says. "We could predict which patients would need physical therapy; we could know that before their health declines and they have to go to a nursing home." It would be monumental, Muss says, to limit the most severe side effects he sees his patients deal with every day. "It's not like we'd learn their p16 and not do anything about it," he says. "This test has a very practical aspect."

—Mark Derewicz

Hyman Muss is a professor in the School of Medicine and associate director for clinical research at the Lineberger Comprehensive Cancer Center.

Man, in a mouse

This little rodent has a human immune system. Can it help us cure AIDS?

by Mark Derewicz

This mouse looks like any other, but it has a human thymus and human T and B cells. It is part of the first animal model that researchers have used to study how HIV is transmitted and how transmission of the virus can be stopped. Photo by Courtney Potter, UNC Medical Center News Office.

A humanized mouse. That's what the laboratory of J. Victor Garcia-Martinez created: a mouse with a fully functioning human immune system. It's the first animal model of its kind and has opened new doors to research possibilities, especially for HIV. And the Garcia lab has used the model to find that an existing drug can prevent HIV transmission.

For the past decade, scientists have been able to transplant human cells into mice to study diseases particular to humans. That's what Garcia-Martinez and his lab set out to do—create a mouse with human T cells in its blood and other lymphoid tissues. But they wound up making something much better.

First they surgically implanted tiny pieces of human liver and thymus tissue under the kidneys of mice that were genetically immune deficient—the mice didn't have B cells and were missing thymuses, the organ that produces T cells. Then the team transplanted human hematopoietic stem cells into the mice's bone marrow. In a few days, each mouse started generating an entirely new thymus. Garcia-Martinez and his lab call their animals bone marrow/liver/thymus, or BLT, mice.

"The thymus is not *like* human," Garcia-Martinez says. "It *is* human. It looks exactly like a human thymus." Just smaller.

Because HIV researchers know that HIV destroys a significant part of the immune system that is housed in the gastrointestinal tract, Paul Denton in Garcia-Martinez's lab checked the mice after the transplants to see if human lymphoid cells—including T cells and B cells—had populated the large and small intestines. And there they were. "This was a huge surprise to us and everyone in the field," Garcia-Martinez says. "We found human T cells in places where nobody would even have looked for them. Nobody anticipated that the distribution of human cells in a completely different species would be almost exactly the same as in humans."

His lab then checked for human cells in the rectums and female reproductive tracts of the mice. Human cells were there too, which meant that for the first time researchers could study HIV transmission in an animal model.

Scientists from around the world have since come to Garcia-Martinez's lab to learn the technique firsthand, because the mice can't be bred. If you want a BLT mouse, you must surgically implant human tissue and perform a bone marrow transplant into each mouse. It's a laborious process, but one that Garcia-Martinez says is well worth it.

Once they mastered the procedure, Garcia-Martinez decided to up the ante. "We wondered if we could *prevent* HIV transmission in these mice using the same drugs we use for treating patients."

After HIV enters the body it uses an enzyme called reverse transcriptase to copy itself backward from RNA to DNA. If that first step of the virus life cycle is completed, then the virus is on its way to spreading and eventually infecting T cells, leading to full-blown AIDS. Right now, some of the drugs doctors use to treat HIV—including a common therapy called Truvada—inhibit reverse transcriptase and stop the virus from destroying T cells. Garcia-Martinez's team wondered if Truvada could block reverse transcriptase *before* HIV took hold inside the humanized mice.

In one experiment, the lab gave Truvada to one group of mice but not another. Then both groups were exposed to HIV vaginally. All the mice that were given Truvada were protected from infection. Most of the mice in the other group got HIV and developed symptoms similar to those found in humans.

The lab then found that Truvada provided 100 percent protection against rectal HIV transmission, the most common way HIV is transmitted in the United States. Still, Garcia-Martinez was concerned that the drug might not have been distributed throughout the entire body, which is what has to happen in HIV patients. To quell that concern his lab gave mice a dose of Truvada and then injected them with HIV intravenously so that the virus could theoretically go anywhere in the body. Even though the dose of HIV was hundreds of times greater than is typical during human transmission, the mice were protected 90 percent of the time.

These findings have added weight to the idea that HIV treatments could help prevent HIV transmission in humans—something that previous clinical trials had been unable to substantiate.

But while Garcia-Martinez's team was proving that Truvada protects mice from HIV, researchers from around the world were conducting a large clinical trial in South Africa to see if a topical gel made with small amounts of tenofovir—one of two compounds found in Truvada—could prevent HIV transmission in women who face a higher-than-normal risk of contracting HIV.

It's difficult to get accurate results from such trials, Garcia-Martinez says. First you have to enroll a large number of people—889 women, in this case. Then researchers have to make sure the women use the gel properly, use correct amounts, and apply it at the right time (up to twelve hours before having sex). Researchers educate the women on risk-prevention behaviors. Also, Garcia-Martinez says, it's impossible to know whether all participants follow proper trial protocol.

Still, researchers announced in July 2010 that the tenofovir microbicide was 39 percent effective in reducing a woman's risk of contracting HIV. At that rate, the gel would protect more than half a million South African women from getting HIV over the next decade. The researchers also found that there was a 54 percent reduction in HIV infections when women used the gel more than 80 percent of the time.

"These are great and highly encouraging results," Garcia-Martinez says. Still, he admits that big questions loom. If a lot of people use a tenofovir gel, could the virus mutate and become drug-resistant? If so, would that mutated virus be strong enough to be transmitted from person to person? Would a pill work better than a gel? Would a combination therapy such as Truvada be better than a single compound such as tenofovir? These are questions that the humanized mouse model could help answer, Garcia-Martinez says.

"For the first time we are one step ahead of the virus," he says. In the past, researchers would create a drug, introduce it to humans, watch as HIV mutated into a drug-resistant strain, and then try to come up with better drugs. "Now we can use humanized mice to anticipate the problems. Are those new strains transmissible? Are they really going to be a health problem? We don't know. But because of the humanized mice we can test it."

And Garcia-Martinez is not shying away from the biggest question of all: can people with HIV and AIDS be cured?

Right now antivirals such as Truvada can drive down a patient's viral load to nearly undetectable levels. But HIV is there in a state scientists call latency, which means that the virus has infected some cells but hasn't damaged or killed them yet. It just sits there. No known drug can get at those latent cells. But if a patient stops taking medication, the virus *will* damage or kill those cells, and HIV will spread throughout the body.

It's not easy to study latency in humans. "How do you go into a human and find the virus in the liver or the lung or the lymph nodes?" Garcia-Martinez says. But by using humanized mice, scientists can search for ways to drive the virus out of latency in a living organism.

"We are only limited by our own imaginations," Garcia-Martinez says. "This is our charter: to cure a mouse under any circumstances and then translate that into humans."

J. Victor Garcia-Martinez is a professor of medicine, and Paul Denton is a research instructor, both in the School of Medicine. *They received funding from the National Institutes of Health and the Foundation for AIDS Research.*

An AIDS vaccine? Still a long way off.

"We are not going to treat our way out of the AIDS epidemic," Garcia-Martinez says. We need a cure or better ways to prevent transmission.

Most research dollars have gone toward creating a vaccine. So far, scientists have been unsuccessful because the virus can change its surface proteins that bind to human cells. Those changes result in different strains of HIV that the immune system can't recognize. But scientists have found a few areas on HIV's surface that don't change, and in July 2010 researchers found antibodies in human blood that can prevent those areas from latching onto T cells. In lab tests, those antibodies stopped transmission of known HIV strains into human cells 91 percent of the time. This was some of the best news in vaccine research in years. But scientists still have to figure out how to use those unchanging surface proteins to train the body to produce antibodies in amounts capable of killing the virus. A vaccine based on this work is still a long way off, if it'll work at all. Meanwhile, global rates of HIV transmission continue to increase each year, especially in Africa.

A story for Chase

Doctors didn't know what he had or how to treat him. The state mental health system had no place for him. But Randi Davenport never stopped fighting for her son.

by Margarite Nathe

When Randi Davenport was a little girl, she set up shop in the attic with her father's Royal typewriter and churned out books of poems and short stories. She typed title pages and copyright pages and wrapped each volume in a handmade cover. And for decades she kept writing, even after she'd had her first baby, a son she named Chase. A few years later, though, Davenport had to stop. There was no way to keep at it once everyone realized there was something wrong with Chase.

The diagnoses started rolling in just a year or so after he was born. His symptoms were all over the place, the doctors said. He missed his developmental milestones; he didn't wave bye-bye or reach for the ball or say *kitty* when shown a picture of a cat. His doctors called it global developmental delay and watched him closely. As Chase got older and things got worse, Davenport saw new words appear on the doctors' reports: *Tourette syndrome*, *severe ADHD*, *seizure disorder*, *psychotic symptoms*, *atypical autism*. But none of them exactly fit for Chase. A Yale specialist later said Chase's disorder had "a population of one."

When Chase started school, he complained that the other kids bothered him at recess, tried to take his toys, hit him, control his thoughts, make him do things. But his teachers never saw him play with anyone. After school, he sat—and sometimes thrashed and screamed—through MRIs and EEGs, trips to the pediatrician and the neurologist. Everyone agreed that something was wrong, but no one could put a name to it. If she had just known what to call his disease, Davenport says, it would have been some comfort.

When the family was still living in the Midwest and Chase was six, one of his doctors, a pediatric psychiatrist, came up with what may have been the most accurate diagnosis. But it was also the rarest and the most dismal, so he decided not to burden Chase's parents with it. Privately, he'd written down the words *true childhood schizophrenia*.

Davenport says there were bright moments and flashes of normalcy in her son's childhood, and these gave her hope. Chase won the science fair's blue ribbon with his soda-bottle model of a tornado, complete with a tiny plastic cow that swirled through the twisting water. He loved music (when he reached his teens, Korn and Rage Against the Machine were his favorites). He rode his bike and swam for the swim team. He was sweet, funny, and endlessly curious. But from year to year, his symptoms only intensified.

In 1999, Davenport moved her family to Chapel Hill to find better services and treatment for Chase. The TEACHH program in UNC's School of Medicine helped for a while, although there was only so much they could do for a kid like Chase.

As he approached his fifteenth birthday, Chase got scared. He thought his peers were plotting against him, following him, were gang members who planned to kill him. The gang members morphed into other enemies—an executioner, the Nailers (a roving squad whose objective was to nail people to chairs before killing them), FBI profilers, people trying to poison him, talking to him, hovering outside his bedroom

DONN YOUNG

window at night. The thread holding Chase to reality finally broke, and he sank into a deep psychosis.

Chase stayed in the psychiatric intensive care unit for adolescents at UNC Hospitals for more than seven months; he held the record for their longest stay. None of the medications prescribed by Dr. B.—the name Davenport gives the attending psychiatrist during Chase's stay at UNC Hospitals—could pull Chase out of it, not even the most powerful antipsychotics on the market. In his most lucid moments, Chase believed he was being held in a concentration camp and that Davenport was an imposter, his real mother having been kidnapped by terrorists.

"I remember Chase's case pretty clearly—it was unique," Dr. B. says today. There was no way to diagnose him, Dr. B. says, "because there were no other patients like Chase." For doctors, a diagnosis means having a group of patients with whom to compare the person being treated. Doctors can then treat the patient based on what's worked for others in the same group. It also means having a concrete label to satisfy impatient insurance companies. But without a diagnosis, Dr. B. and his staff could only treat Chase's symptoms by trying one drug after another. And they had to be quick about it—the longer a period of psychosis lasts, he says, the slimmer the chance of coming out of it.

But seven months after he was admitted to UNC Hospitals, Chase was skidding further and further out of reach. He still did not recognize his mother. Some days he believed he was the lead singer for Rage Against the Machine, other days the grim reaper or Jesus Christ. And his physical health was deteriorating. That's when officials from the North Carolina State Health Plan decided that Chase no longer needed acute care and refused to pay for any more of his services.

Jarrett Barnhill, a UNC neuropsychiatrist, has been one of Chase's doctors for the past twelve years, since Chase was ten. One of Barnhill's specialties is treating people with autism, and he has some patients now in their sixties who've been under his care for over thirty years. He's dedicated most of his career to treating patients who, like Chase, have a dual diagnosis—that is, both a developmental disability (such as autism spectrum disorder, cerebral palsy, or Down syndrome) and a mental disorder (such as schizophrenia, major depression, or obsessive-compulsive disorder). Chase had some of the most complicated symptoms Barnhill had ever seen.

"I often wonder if what kept me fighting was the fact that **I never lost hope.** If I had been told when Chase was two, 'This is what's about to happen,' I imagine I would have been emptied of all hope."

—Randi Davenport

Treating a patient with a dual diagnosis is tough, Barnhill says. Getting an accurate psychiatric diagnosis is tricky because these are usually based on self-report, which calls for a degree of self-perception that many patients with developmental disabilities don't have. People with autism are also very sensitive to side effects and sometimes have unusual responses to medications, he says, so their doctors have to make careful treatment decisions.

But one of the hardest parts of treating a dual diagnosis: "These folks take a lot of time," Barnhill says. "And the way the system operates, you've got seven or eight minutes you're allowed to see a patient. You can't take a lot of time. So in training for twenty-first-century psychiatry, you approach things as a medication problem."

This sometimes leads to rampant overuse of medication. When one medication doesn't work, Barnhill says, psychiatrists often add others without eliminating the previous, ineffective drugs. The drugs interact and sometimes interfere with one another and cause unexpected side effects. "You can end up on five, six, seven drugs, and no one knows what the drugs are doing at that point," he says.

Barnhill worked with Chase to sort out the effects of his seizure disorder and the anti-seizure and psychiatric medications, and to understand his underlying metabolic problems. He says that it's possible the combination of medications Chase was taking had something to do with his psychotic symptoms, although no one really knows what causes psychosis (or what can end it). There's an old saying, Barnhill says: "'All medicines are poisons with positive side effects.' Some side effects can act like symptoms, and some actually produce psychosis themselves. Some can increase aggression, self injury, all the very things you put people in hospitals to try to correct."

At UNC Hospitals, after every medication prescribed for Chase had failed, Dr. B. began to draw the same conclusions that Chase's pediatric psychiatrist had come to years before. Most people with schizophrenia begin to show symptoms during their teen years, Dr. B. says. But childhood schizophrenia begins to show itself in early childhood. It's resistant

Chase was almost two years old when this photo was taken in his classroom at day care. "When Chase was a baby, I was still writing a lot," Davenport says. "You can look at my vita and see his deterioration. You can see publications happening all the way up to 1995 or 1996, and then, there is nothing." Photo courtesy of Randi Davenport.

"I remember how difficult it was to understand the road we were walking on," Davenport says. "It was right there under our feet and we were experiencing it every day, but we didn't know what that road was." Photo by Donn Young.

to almost all treatments. It's often a hopeless prognosis. It was Dr. B.'s best guess for Chase, but it didn't give him any better ideas about where to send the boy when Davenport lost insurance coverage.

Almost every facility in the state took one look at Chase's file and concluded that he was too complicated, too expensive to take in. While North Carolina offers state services and treatment options for people who are mentally ill and for people who are developmentally disabled, there's almost nowhere for patients who are both, Davenport says. The one place in North Carolina that had the services Chase needed and that had agreed to treat him—the BART unit of the Murdoch Developmental Center in Butner—had only twelve beds to serve the entire state, and no one was sure when a space would open up.

So Chase was moved instead to John Umstead Hospital in Butner. It was supposed to be temporary. State law stipulates that psychiatric hospitals aren't allowed to care for people with developmental disabilities for any extended time. The doctors and staff at Umstead did the best they could, Davenport says, but their only real option was to ratchet up Chase's medication. After five months, he was almost comatose. He'd lost too much weight and he spent the days drooling and nodding off, she says.

Friends suggested a lawsuit. But Davenport was terrified that Chase would waste away and die while the lawyers and hospitals and state officials battled things out. She'd called and written letters to everyone she could think of, asked for help from every official in the state's Department of Health and Human Services (DHHS) that she could get on the phone. But eventually, when it became clear there was no easy fix for Chase, Davenport's calls were stonewalled. One DHHS official even wrote to another in an email that Davenport "did not seem litigious, and so all was well."

When Davenport had run out of options, she went to the only person in the state she thought could give her some advice. He happened to have an office right on UNC's campus, not far from Davenport's own. In her book *The Boy Who Loved Tornadoes*, she writes, "I knew that everyone said he was the most powerful man in the state, that three governors were indebted to him, that John Edwards had had to get his okay before he got into politics . . . I could not imagine that

he would take an interest in me or in Chase." But Bill Friday did take an interest.

"Randi came to me and told me what had happened," says Friday, who served as UNC system president for over thirty years. "When I saw that I could do something about it, it was my duty then to respond. I made a few phone calls to help her get her boy the right kind of attention."

After Friday made his phone calls, Chase suddenly had a room at the Murdoch Center. And, the staff assured Davenport, no one had had to lose services there for it to happen.

When Chase was ten years old, he and his family visited North Carolina just before moving permanently to Chapel Hill. Before they moved, Davenport and her family lived in the Midwest for several years. But there were almost no services for kids like Chase there, she says. The state they were living in sent checks for two hundred dollars a month to parents of kids with complicated disorders to pay for special treatments. It didn't pay for much, Davenport says, and some people suggested they spend the money instead on a padlock for Chase's room or a fence to keep him in the back yard. Photo courtesy of Randi Davenport.

STATE DOLLARS FOR mental health care in North Carolina have been dwindling for years, and funding for many services has already dried up completely. In 1998 the state government put into place the Community Assisted Care Program (CAP), a Medicaid-funded system that was supposed to ease the burden on state mental hospitals. In theory, CAP would allow hundreds of patients who lived in residential facilities to go home and live with their families, where experts would come to help care for them and administer treatments.

"But there are a small number of patients who are extraordinarily difficult to manage in the home setting," Dr. B. says. "There are patients who need to be supervised twenty-four hours a day. Single parents can't do that. Even for a large extended family, that's an incredible burden." So under the CAP program, the most severely disabled North Carolinians who cannot be treated at home must turn to expensive private facilities, which have the option to turn away complicated, unprofitable patients. When this happens, the patients are often left with nowhere to go. Many have ended up on the streets.

The CAP program helped Davenport's family, at first. But the year before Chase's psychotic break, the CAP worker assigned to care for him forgot to give him his anti-seizure medication. Chase had a seizure while brushing his teeth, fell, and broke his neck. He underwent four painful surgeries on his cervical spine before it healed. Barnhill says the trauma of these surgeries may have been the final insult that spurred Chase's psychosis.

"Community-based care has failed in this state," Davenport says. "Untrained, ill-prepared care providers are sent into homes to provide services, and we call that community-based care."

Barnhill says, "I think community-based care *could* work. But the system has to be funded appropriately and you have to have enough people to provide the care. That's one of the big struggles, trying to find enough people who can provide those services in the community."

The Murdoch Center creates detailed treatment plans for each patient, including tailored drug regimens and rigorous behavioral therapy. Every hour of every day is meticulously planned, and the staff work one-to-one with each patient. Residents on Chase's unit all live together, and when they're ready, they start school there, go on outings, assume chores, shop for food, and cook meals. The goal is to teach the residents skills that will help them move toward independent living. And the system works. Little by little, as the staff worked with Chase and Barnhill adjusted his medication, he began to grasp who and where he was. It took time, but he eventually recognized his mom and his sister again.

Today, Chase delivers messages and balloon-o-grams around the Murdoch Center campus. He's a six-foot-eight twenty-two-year-old who still loves music (new favorites include the Beatles, Pearl Jam, and U2). He visits home and watches movies with his family. His memories of that awful year are only of being jailed in a concentration camp, Davenport says, so they don't talk about it much.

"We say that people with really severe mental illnesses are irretrievable, that the illness takes them and we can never get them back," Davenport says. "We may never get the person they were before back, but with the right kinds of services and approaches, it's astonishing what the individual is able to achieve. Chase has come a long way since he first came to Murdoch."

Now Davenport is working with state officials to draft policy changes that will help people like Chase. North Carolina's system is broken, she says. And although Chapel Hill has offered more help for her son than some other regions could, the stigma attached to mental illness is very much alive here.

"I've seen my share of letters to the editor of the *Chapel Hill News* written by people here in town," Davenport says. "They're outraged by the homeless people downtown

Communication is still tough for Chase. He can't always get his thoughts out in words. But she told him what she'd been doing and asked, **"Is it okay for me to tell your story?** So it'll help other people?"

and outraged by the fact that the mentally ill are among them. You can see the way in which people still view those who are sick, as if they're somehow responsible for their own misery. I don't know of any other disease where we take the sufferers and throw them out on the street and say, 'It's all your fault.'"

Friday says, "When the state made that decision to put people back out on the street some years ago, that was just wrong. And we're now harvesting that decision. But the important thing now is to move ahead, and Randi's son proves that it can happen. The state of North Carolina has got to regroup and pay attention to people like Randi Davenport."

Chase's story, *The Boy Who Loved Tornadoes*, is what brought Davenport back to writing, she says. It's the first thing she's written in more than ten years.

The first sentence had floated fully formed through her mind for some time: *In my dreams, we are whole again.* "So I sat down and I wrote it," she says. "And I thought, 'Okay, now what happens?'" The result is staggeringly beautiful, sometimes stark, never sentimental or self-pitying. Critics from the *Los Angeles Times* and *Publishers Weekly* gave it rave reviews, as have many readers who are parents and have lived through similar nightmares with their own children. The story is told entirely based on Davenport's memories. "I didn't keep notes when Chase was in the hospital," she says. "I didn't have a journal. I didn't run around with a little pad of paper in my purse. It was the furthest thing from my mind."

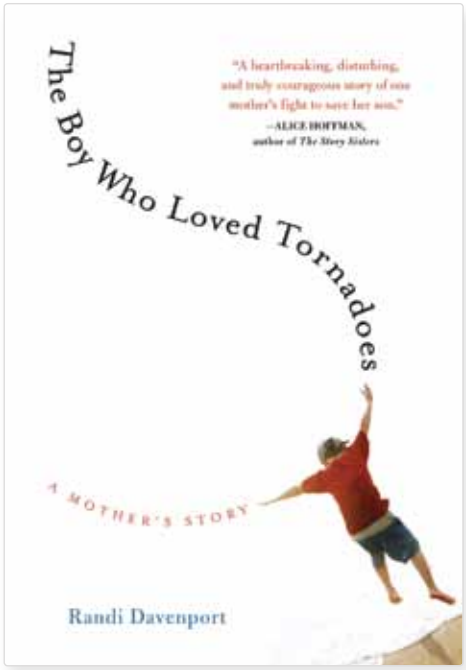
She intended at first to write a short op-ed piece about mental health care for a local paper, the *Independent Weekly*. After so many years in "survival mode," Davenport says, she worried her writing was rusty and she didn't know if she still had the skill to do it. But instead of writing a few paragraphs, she wrote a hundred pages. Then she cried a lot. The writing was excruciating, she says, and not just because she was reliving terrible memories; she was worried she wouldn't do Chase's story justice. After she had six hundred pages, she went to talk to her son.

Communication is still tough for Chase. He can't always get his thoughts out in words. But she told him what she'd been doing and asked, "Is it okay for me to tell your story? So it'll help other people?"

"Yes," Chase said.

"I never planned to write this book," Davenport says. "I never had any intention of writing a book about my son. But after I began, I felt very much called to do it. I think writers avoid those kinds of calls at their own peril. You don't want to set aside a story that's asking you to write it. You have to go where it takes you, no matter how terrifying."

When *The Boy Who Loved Tornadoes* first came out in bound galleys, Davenport says, Chase held them in his hands "and he was just radiant." The hardcover appeared in his Easter basket, and he still carries it around with him. "Above and beyond the diagnoses and the battle and the struggle," she says, "*The Boy Who Loved Tornadoes* is a love story. I think it's a book for anyone who's ever loved anyone else, and wanted to do the best they could for them."



Randi Davenport is the executive director of the Johnston Center for Undergraduate Excellence and an adjunct assistant professor in the Department of English and Comparative Literature in the College of Arts and Sciences. She received support for her book from the Residency Program at Wildacres Retreat. Jarrett Barnhill is the consulting physician/psychiatrist for the BART unit at the Murdoch Center and director of the UNC Developmental Neuropharmacology Clinic. Barnhill won the 2010 Frank J. Menolascino Award for Excellence from the National Association for the Dually Diagnosed. Division TEACHH, based in UNC's School of Medicine, is an evidence-based service, training, and research program for individuals of all ages and skill levels with autism spectrum disorders. For more about Randi Davenport as well as excerpts from The Boy Who Loved Tornadoes, *visit www.randidavenport.com.*

Spotting schizophrenia sooner

Eighteen years ago, the pediatric psychiatrist who suspected that Chase had childhood schizophrenia should have told her about his conclusion rather than keeping silent, Randi Davenport says. Now a UNC study shows that scientists may be able to detect the brain abnormalities associated with schizophrenia in babies as young as a few weeks old.

John Gilmore, author of the study, says that by the time symptoms such as delusion and hallucinations are detectable, the disease has progressed to a stage that's difficult to treat. Gilmore and his colleagues used ultrasound and MRI to examine brain development in babies of mothers with schizophrenia. They found that baby boys with larger brains and larger lateral ventricles (signs that are also associated with autism) were at higher risk than babies whose mothers had no psychiatric illnesses. Gilmore's team will track the children in the study to monitor their motor skills, memory development, and language skills.

—Margarite Nathe

John Gilmore is a professor of psychiatry in the School of Medicine and director of the UNC Schizophrenia Research Center.

FOR THE RECORD

A group of undergrads start a label to help campus musicians find their groove.

by Alex Raines

Right: Colby Ramsay of My Boy Rascal. On working with Vinyl Records, Ramsay says, "It's amazing how far my music has come. It's just worlds better." Photo by Alex Raines.


FRAGIL
AGILE

In high school Tripp Gobble would drive an hour from Louisburg, North Carolina, to hear his favorite bands at Cat's Cradle in Carrboro. When he arrived at Carolina in 2006, Gobble immersed himself in the local music scene, where he befriended some musicians. One was Al Mask, a pianist minoring in music, and after returning from a summer spent playing and recording and performing at the Berklee College of Music, he had an idea for Gobble. Mask wanted to start an organization to help students produce their own music, because he knew firsthand just how hard it was. Gobble was in.

Tripp Gobble, cofounder of Vinyl Records: "Once we got going, we realized how hard it really is for student bands." Photo by Alex Raines.

Gobble admits he isn't much of a musician. "I've never been incredibly skilled at any instrument, outside of the trombone in middle school," he jokes. But he had always wanted to be more than just a music fan. Gobble took Mask's idea—to help student bands financially—and thought, "What if we started a label with an entire network of support around these musicians and helped them build a professional portfolio?"

Of course, neither Gobble nor Mask knew anything about starting a record label. They turned to mentors in the music department and the Kenan Institute of Private Enterprise for guidance, developing a business plan that they entered in the Carolina Challenge, UNC's venture capital competition. They didn't win that competition, but they revised their proposal and won a $25,000 grant from the Carolina Entrepreneurial Institute's Innovations Fund in the spring of 2008. Vinyl Records was born.

Gobble and Mask set about finding a staff. They posted fliers, flooded inboxes, held informational meetings. The morning after the first meeting, a job application appeared under the door of their tiny office in Hill Hall. "It was in this nice manila envelope and it was very professional and I thought, 'Okay, this guy is serious,'" Gobble remembers. The application was from Andrew Hamlet, a first-year student from Atlanta who had experience recording with his own bands. "It was obvious that he had diverse but also pretty refined tastes in music and artistry," Gobble says. "So we put him in artistic development and repertoire, where he would be scouting new talent but also trying to help them find their sound."

Gobble and Hamlet took a democratic approach to finding new artists. They hoped that letting the campus community choose the artists would generate grassroots support that would translate into album sales. The staff narrowed down thirty applicants to ten bands, who auditioned live. From those they selected six bands to battle it out in a free concert on campus they dubbed the September Showdown. After the show, more than twenty-five hundred students voted for their favorite bands, and the top three won that coveted record deal. Step one was done, and Vinyl Records had its first artists: indie pop band Lake Inferior, folk rock act Lafcadio Shot Back, and hip-hop artist Apollo. Next step: record and promote the artists.

That turned out to be more work than anyone expected. "Off the bat we approached it as a three-hundred-sixty-degree deal for artists," Gobble says. "Then we realized how overwhelming and consuming that can be, and we started recognizing why Warner Brothers can't make money and EMI is in debt." Vinyl Records was trying to do everything: on top of recording and producing albums, it was acting as manager and agent for the bands, as well as booking shows and tours and marketing them on campus and around town.

Merge Records, one of the most successful independent labels in the United States, is just down the road from Chapel Hill in Durham, so Gobble and Hamlet paid them a visit. They were surprised to find how streamlined Merge was. A staff of about fifteen people represents dozens of artists, including major names such as Arcade Fire and M. Ward. Merge has focused on producing

and selling good albums, letting the musicians take more responsibility for advancing their own careers. It takes more work from the artists but also gives them more creative freedom. Gobble and Hamlet decided to take the same approach with Vinyl Records. They would record and produce the albums, but each band would have to make sure it was playing enough to get its name out there and generate a following of people who would want to buy the album.

The new plan worked. Vinyl Records released its first three albums in January 2009 to a sold-out crowd at Local 506, a rock club on Franklin Street in Chapel Hill.

In March, Vinyl Records released *The Study of Animal Magicality* by My Boy Rascal. It's a great example of what Vinyl Records can do for an up-and-coming musician. Singer-songwriter Colby Ramsay (the band name is an anagram of his name) came to Carolina from the mountains of British Columbia. Ramsay had worked for Vinyl Records as a graphic designer and videographer in the label's first year, but he resigned his position so that he could try to be signed as an artist. (Vinyl Records does not sign any of its own staff, though many are musicians.) He won the most votes with his performance in the February Faceoff in 2009. As soon as he was signed, Ramsay felt the effect of the heightened publicity. "It opened up a lot of performing opportunities for campus events," he says. "People knew about me." But the biggest impact came when Ramsay stepped into the recording studio.

The Study of Animal Magicality was the first album recorded in Vinyl Records' new studio space in the basement of Hill Hall. The studio allows artists to record for free whenever and for however long they like. For My Boy Rascal, it took the entire fall semester, working at least five days a week—some days until four in the morning. "We made the basement of Hill Hall our home," says Hamlet, who produced the album. "I think if we had known what we were doing, it wouldn't have taken as long. But we were really trying to feel the songs out."

That process is critical for most new artists, but it takes more time than a bigger label or studio is willing to spend on an untested band. "When you listen to what Colby came in with," Gobble says, "it was good. But Andrew and Colby worked a lot of hours on putting that record together and bringing it to the best that it could be in terms of all the different musical elements working together. I think it became a lot bigger and bolder and made a much stronger statement."

Ramsay agrees. "You can't really even compare—it's amazing how far my music has come." That's mostly thanks to Hamlet, who helped push Ramsay's music beyond its one-guy-and-his-guitar character. Hamlet played electric guitar on the album and brought in drummers, bass players, and other musicians. Ramsay did lead vocals, guitar, and keyboards; filled out his arrangements with his friends in Tar Heel Voices on backup vocals; and even brought in a string quartet for three of the tracks. All of these resources are well beyond the means of the typical student band, and the difference in the end product is huge. "People don't understand the work that goes into an album," Hamlet says. "A song is a three-minute experience for them." But it can take months or even years to record.

When recording was finished, the process wasn't over. Hamlet and Ramsay sent off the album to be mastered and manufactured. This is the other major financial hurdle for emerging artists, and accounts for most of the ongoing expenses at Vinyl Records. Despite the label's name, most albums from Vinyl Records are released as CDs and are also available on iTunes. Lake Inferior was the one exception when it decided to release its second album as a ten-inch vinyl record (though it does come with digital downloads for those without a record player).

"These days, music is almost becoming public domain," Hamlet says. Labels will have to change their business models to survive. It's easier than ever for artists to self-produce: bands can record on their laptops and post the songs on the internet for anyone to hear, and fans can decide for themselves which artists to support. But with a lower threshold for producing music, artists can have a hard time being heard above the noise.

That's where Vinyl Records comes in. It raises the profile of the artists, helps them develop their sound, and produces a professional, refined album that stands out in a crowded field. "I see the current major label model as something that can't work," Gobble says. "But the small label will always exist, and so will the idea of branding, legitimizing, and helping define an artist."

Gobble graduated in May, after passing the presidency of Vinyl Records to Hamlet in January to give him time to settle into the role. "Andrew's been one of the most dedicated people in the organization since he came in," Gobble says, "so it made sense

Vinyl Records put on a party at the Student Union Cabaret for the release of My Boy Rascal's *The Study of Animal Magicality* in February 2010. My Boy Rascal's Colby Ramsay told the *Daily Tar Heel* why the group chose the Student Union rather than a bar or rock club: "It can be a more focused event at the Cabaret where people can sit there and really listen to the music and feel something." Photo by Tang Yi.

Left: The album cover for Lake Inferior's *Pegasaur.* **Center, top to bottom:** Covers for albums by Lafcadio Shot Back, My Boy Rascal, and Apollo. **Right:** My Boy Rascal performs at the release of its album *The Study of Animal Magicality.* Photo by Tang Yi.

that he would take the reins of the organization. People trusted him." In turn, Hamlet will hand over the reins in January 2011 to Reed Turchi, the current vice president. They've already signed two new artists for the fall: hip-hop artist Sikz Pointz and indie-folk-jazz band Group Mentality.

Gobble is somewhat amazed by the success Vinyl Records has achieved so far. It's sold over a thousand records, and its last showcase drew yet another capacity crowd and nearly two thousand votes. "People actually know the name of the label behind the artist," Gobble says, "which in the broader world rarely happens." Lake Inferior is playing up and down the East Coast, and Lafcadio Shot Back has also enjoyed post-graduation success. Ramsay of My Boy Rascal is hoping to build off of *The Study of Animal Magicality* to launch a career in music, possibly combined with producing video and multimedia projects.

Many of the staff also want their experience with Vinyl Records to lead to a career playing or producing music. Hamlet interned with Merge Records last year and this summer worked with the National Academy of Recording Arts and Sciences, which puts on the Grammy Awards. Gobble has founded a record label in Raleigh called Denmark Records. He's not sure how long he will stay with this new label—but he thinks Vinyl Records has the potential for longevity. "It creates a sense of community that is probably more direct than any label outside of a university setting could do. It becomes a gateway, a music incubator helping the artists grow as musicians. But it's also helping those who are involved in the business side or the production side to build their portfolio with experience in the music industry." e

Alex Raines is an MD/PhD student studying neurobiology.

Vinyl Records is funded by a grant from the Carolina Entrepreneurial Initiative, which is managed by the Frank Hawkins Kenan Institute of Private Enterprise, and by ongoing support from Student Government. *Clarence "Tripp" Gobble graduated in May 2010 with a degree in environmental studies. Andrew Hamlet is a senior psychology major and a music minor. Colby Ramsay graduated in May 2010 with a degree in journalism and mass communication.*

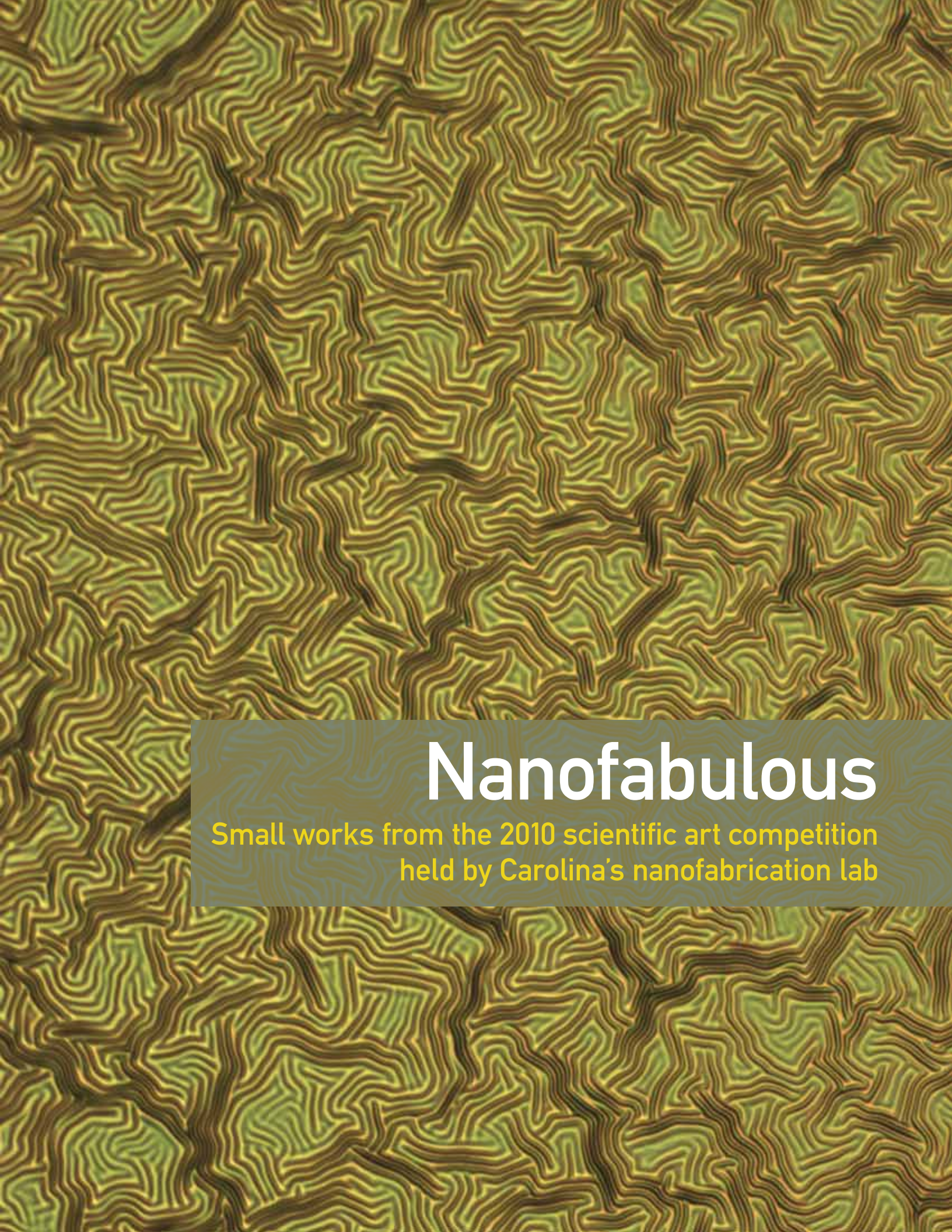
The Life Cycle of Vinyl Records

Or, 12 Simple Steps for Running Your Own Label

1: Get funding
2: Hire a staff
3: Invite artist applications
4: Put on concert; let students choose new artists
5: Book performances around campus and town
6: Help artists define musical sound and style
7: Record and mix album
8: Create album art
9: Send album to be mastered and manufactured
10: Put on album-release concert
11: Sell and promote album
12: Go back to step 3

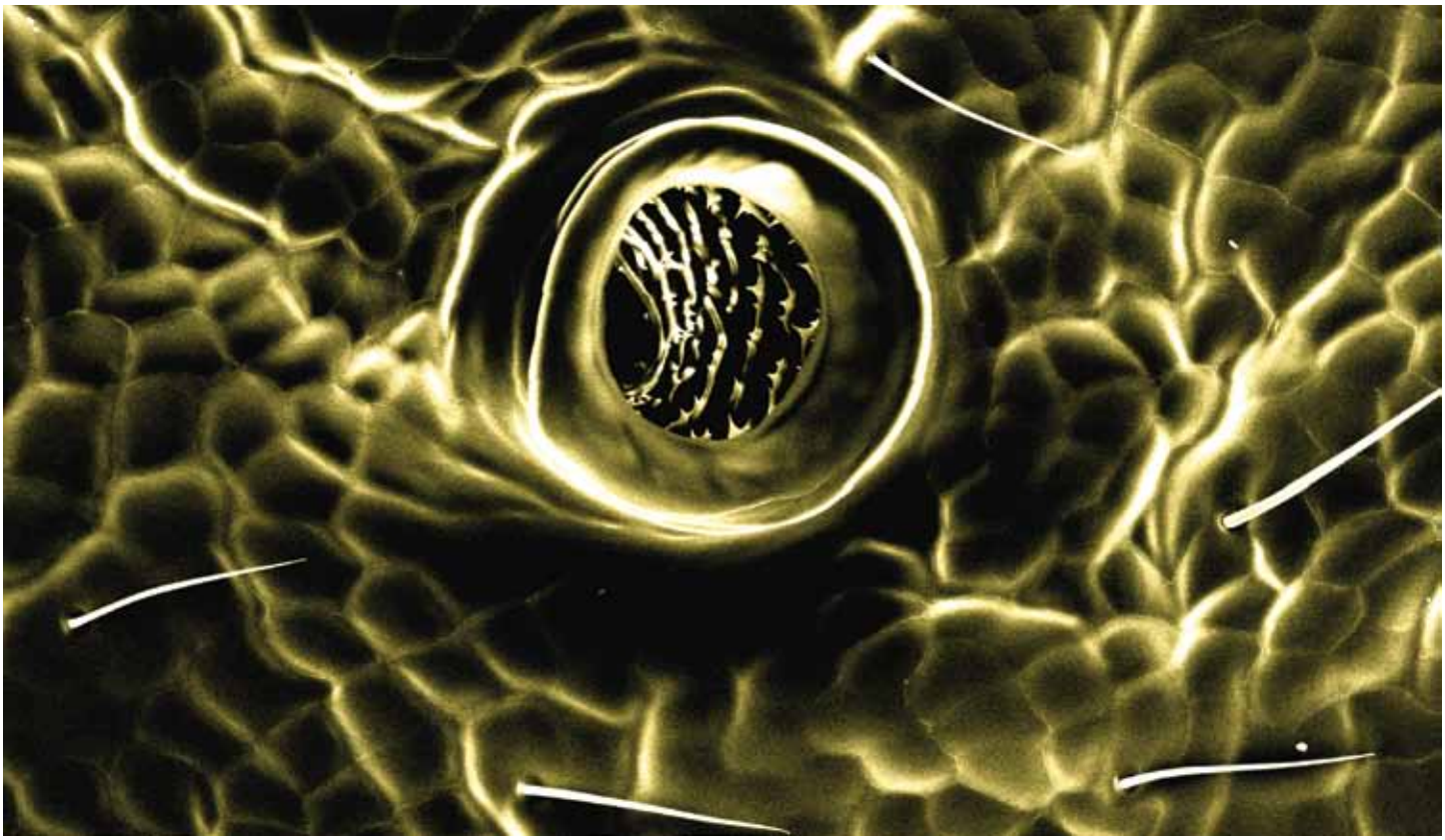
Because people access music in so many different ways, the success of Vinyl Records depends on getting music into as many outlets as possible:

- music available on iTunes, Amazon, etc.
- videos of concerts on YouTube
- streaming music on website
- VR Presents, a monthly series producing free demos of local nonstudent bands
- podcast on iTunesU
- "Vinyl Press" blog



Nanofabulous

Small works from the 2010 scientific art competition held by Carolina's nanofabrication lab



***The Sarlacc* by Adam Shields.** This ant's spiracle, or air hole, is thirty-five microns wide—smaller than the width of a human hair. The opening leads to the ant's respiratory system, a network of hollow tubes that runs throughout its body. "To a nerdy physicist," Shields says, "this image was reminiscent of the Sarlacc, the tentacled desert monster in *Star Wars* that Jabba the Hutt tries to use to execute Luke Skywalker, by slow digestion over a thousand years." *Shields is a doctoral student in the Department of Physics and Astronomy in the College of Arts and Sciences. Equipment: Scanning electron microscope*

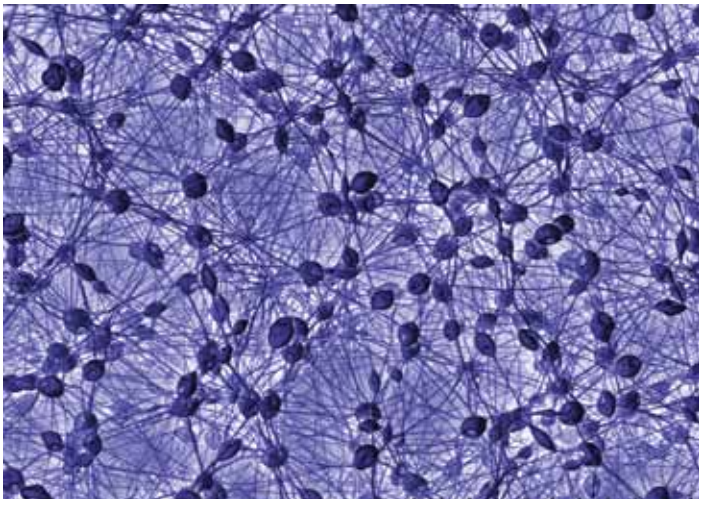
These images are from the second annual scientific art competition held by the Chapel Hill Analytical and Nanofabrication Laboratory (CHANL). CHANL is home to a series of electron microscopes, an x-ray photoelectron spectrometer, a cleanroom with photolithography, deposition, and etching systems, and many other powerful imaging tools and equipment. The scientific art competition takes place in the spring and is open to anyone on campus. Entries this year came from students and faculty across the university, including many in pharmacy, biomedical engineering, medicine, computer science, studio art, physics and astronomy, and chemistry.

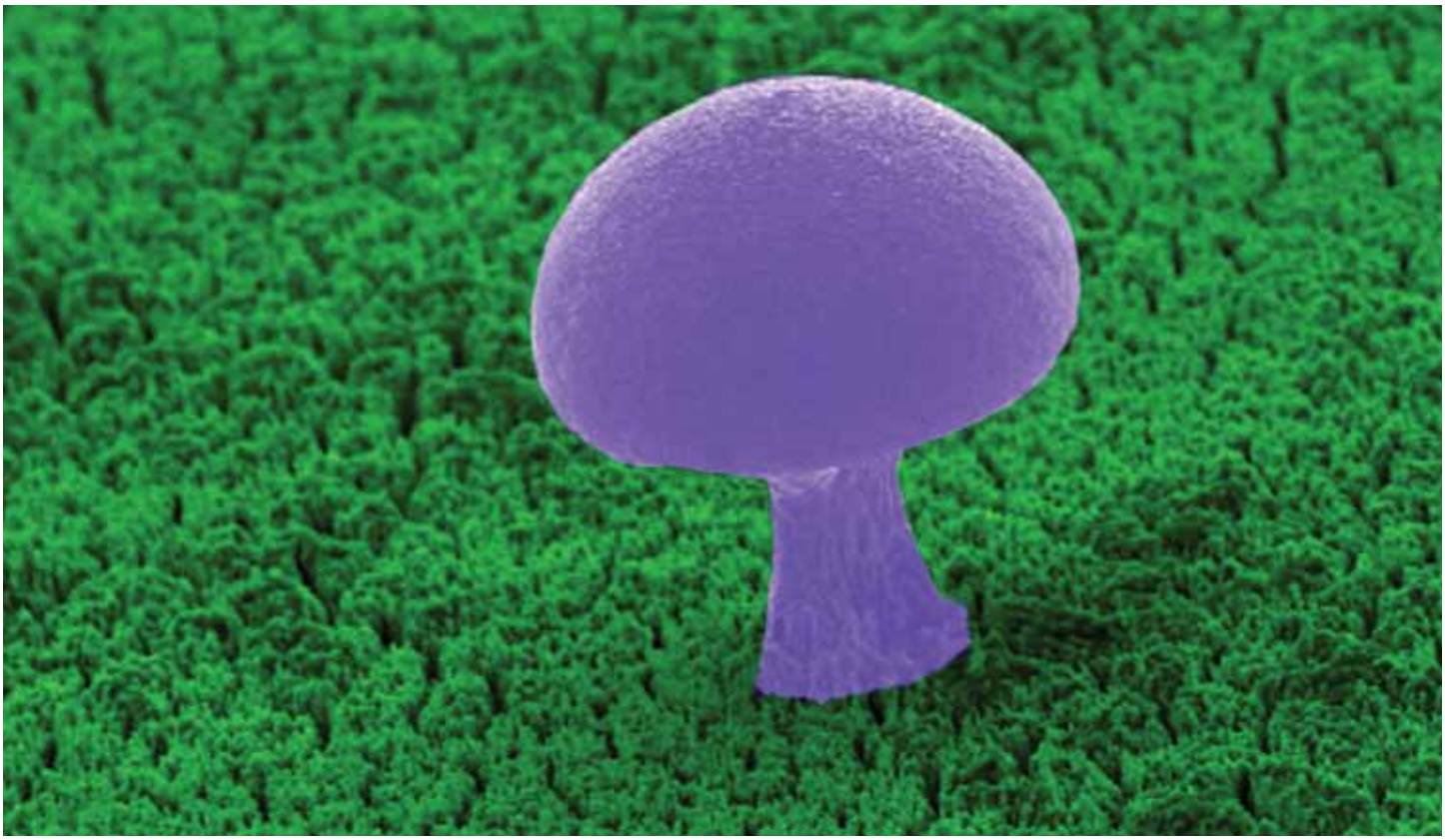
—Margarite Nathe

Carrie Donley is the director of the CHANL Instrumentation Facility in the Institute for Advanced Materials, Nanoscience, and Technology at Carolina. For more information, visit chanl.unc.edu.

Previous page:
***Chrome Labyrinth* by Michael Woodson.** Millions of tiny wrinkles formed when Woodson layered a sheet of chromium (0.1 micrometers thick) over a layer of acrylic polymer and heated the two together. "The formation of these patterns was totally accidental," he says, "and actually caused a fair amount of trouble for me." The wrinkles tend to be parallel and spaced almost equally, and the distance between them varies—higher temperatures make larger wrinkles that are spaced farther apart. The reason the wrinkles form is a mystery, he says, but it could be because the different materials expand in different ways when heated, or because the way the chromium layer is deposited puts some stress on it. *Woodson is a postdoctoral researcher in the Department of Chemistry in the College of Arts and Sciences. Equipment: Motic PSM-1000 microscope*

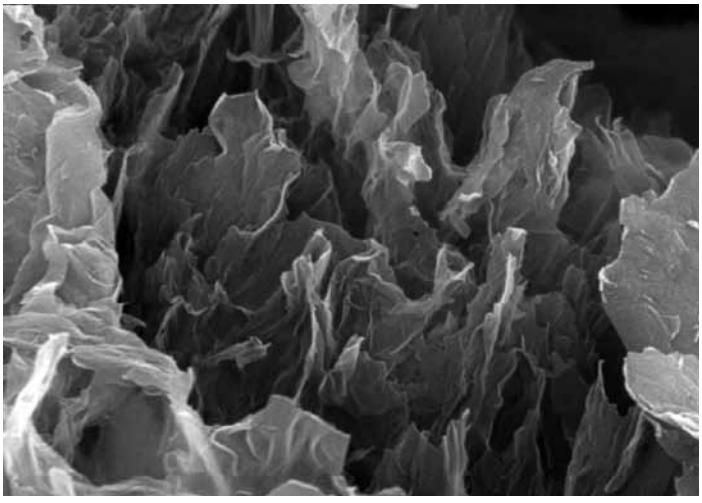
***String Theory* by Peter Coneski, Jessica Nash, and Mark Schoenfisch.** These electrospun polymer microfibers were prepared in chemist Mark Schoenfisch's lab, where Coneski and his colleagues are looking for ways to make antibacterial and antithrombotic medical device coatings from polymer microfibers that are capable of controlled release of nitric oxide. *Coneski is a doctoral student, Nash is an undergraduate, and Schoenfisch is a professor of chemistry, all in the Department of Chemistry in the College of Arts and Sciences. Equipment: Scanning electron microscope*



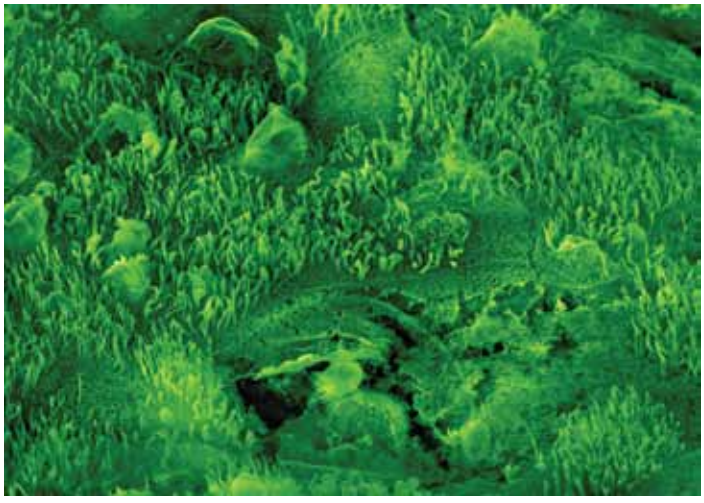


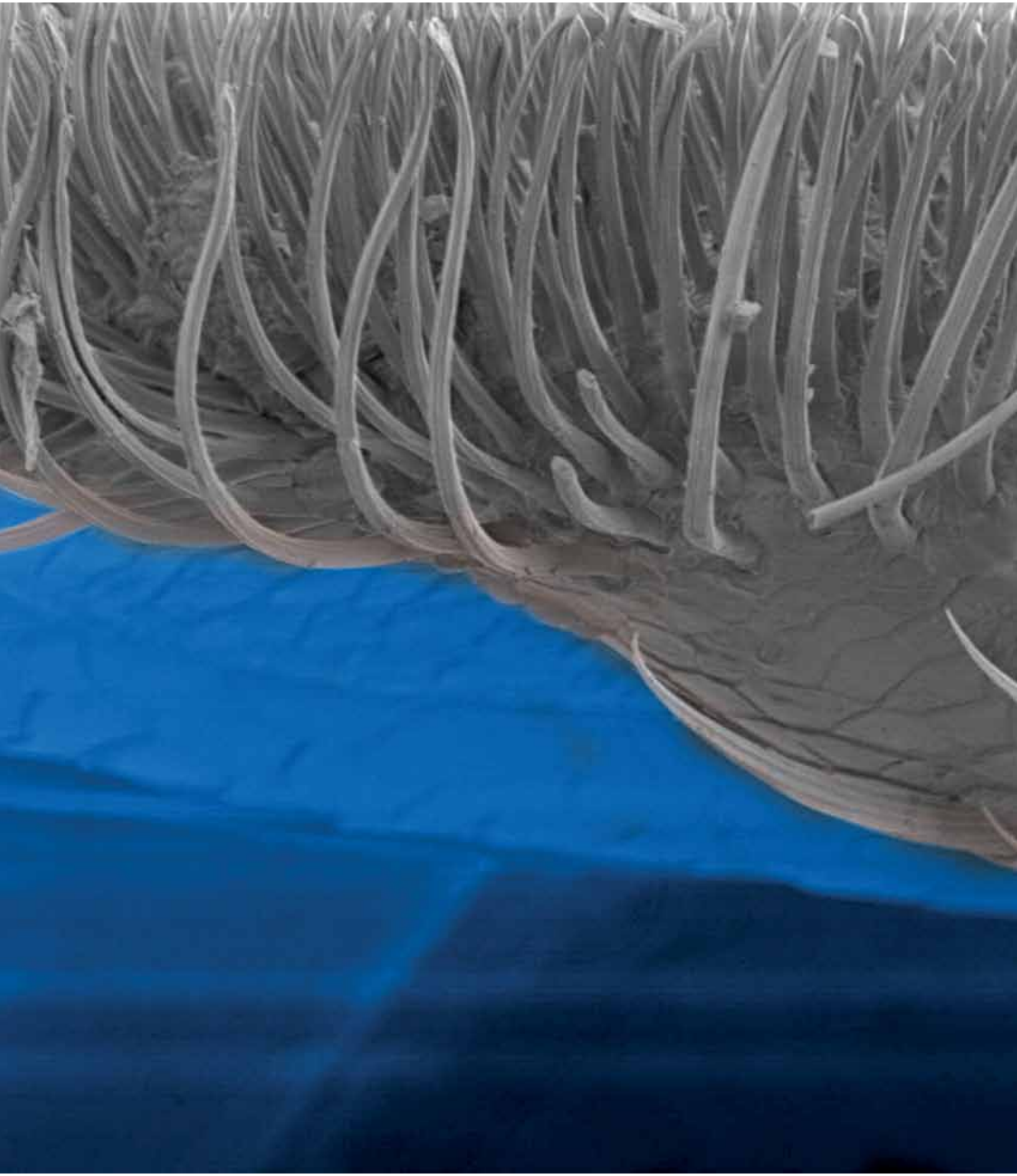
***Nanomushroom* by Pavel Takmakov and Sergei Smirnov.** Takmakov and Smirnov make gold nanowires by depositing metals into tiny holes in a membrane made of aluminum oxide. They use a strong base to dissolve the membrane and release the gold nanowires. But sometimes, when the metals deposited don't spread uniformly, metal blooms on the outside of the membrane, creating mushroom-like growths like this one. *Takmakov is a doctoral student in the Department of Chemistry in the College of Arts and Sciences. Smirnov is a professor in the Department of Chemistry and Biochemistry at New Mexico State University. Equipment: Hitachi S-3400 scanning electron microscope*

***Frozen Fire* by Craig Cavanaugh and Yongchao Si**
This is graphene, a 1-atom-thick sheet of carbon, magnified 35,000 times its actual size. The crinkled, tissue-like sheets resemble a high-speed photograph of an inferno, Yongchao Si says. *Cavanaugh is a lab technician at UNC. Si is a scientist at Allotropica Technologies, a UNC spin-off company. Equipment: Scanning electron microscope*

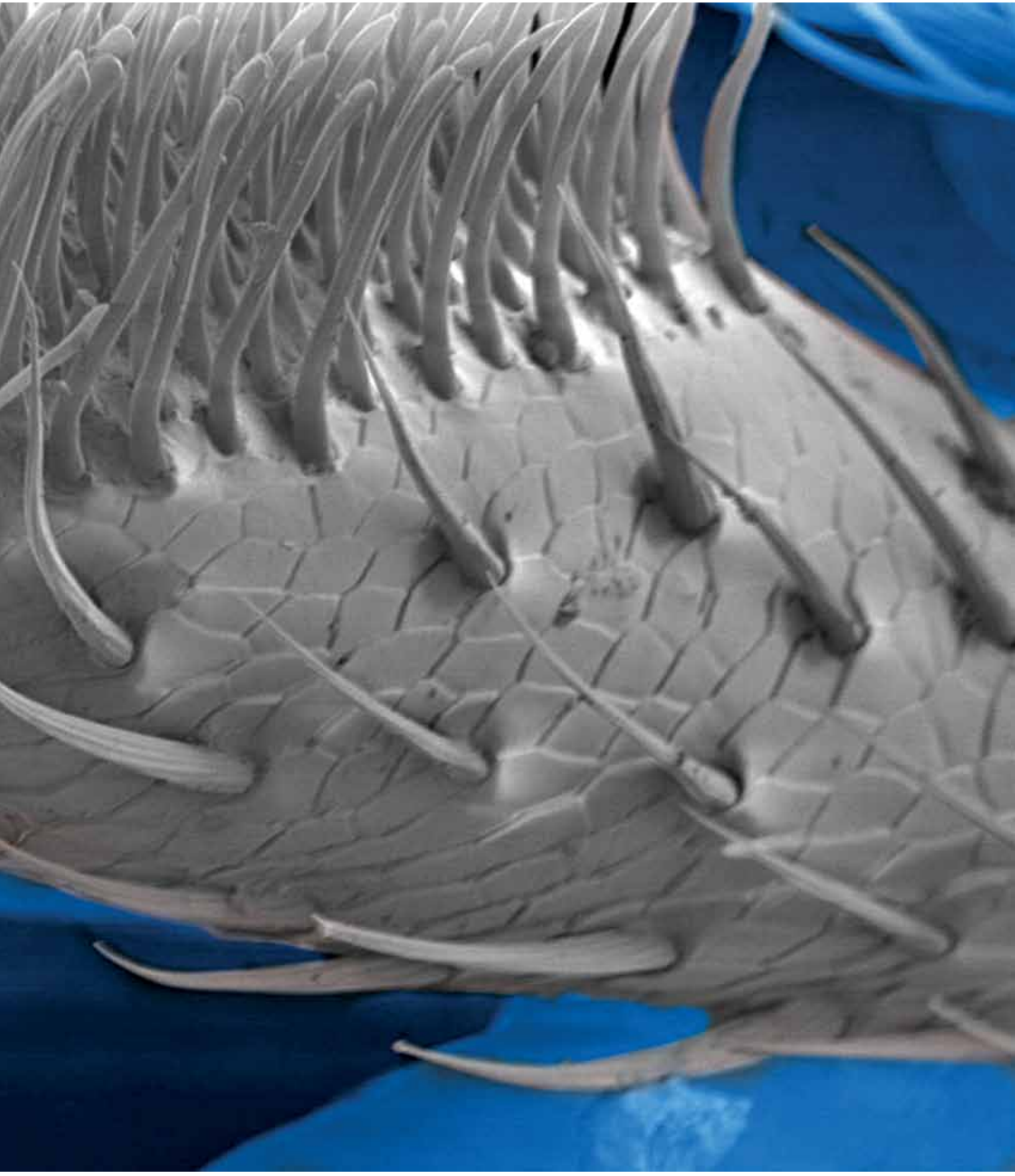


***Pulmonary Plains* by Jerome Carpenter.** A breath of air sweeps over these human epithelial cells, which line the human airway and keep our lungs clean and germ-free. The cells secrete mucins (the boulder-like formations in this image) that trap germs and contaminants. The grass-like cilia push any contaminated mucus out of the lungs. *Carpenter is a doctoral student in the Department of Physics and Astronomy in the College of Arts and Sciences. Equipment: Scanning electron microscope*





***Aquatic Antenna* by Daniel Torelli.** A ladybug antenna, pictured upside down. Torelli's goal when he created this image, he says, "was to show the public what the world around them looks like on a microscale." *Torelli is an undergraduate in the Department of Chemistry in the College of Arts and Sciences. Equipment: Environmental scanning electron microscope*



BLACK-SIX MOUSE BRAIN
STRANGE LITTLE VESSELS
ALBINO MOUSE BRAIN

Most of the time, you don't need them. But your ability to recover from a stroke, heart attack, or major wound may depend on how many collateral blood vessels you have.

by Meagen Voss

James Faber works on blood vessels that are as useful as the appendix is for everyday life. But when the cardiovascular system malfunctions, these vessels—called collaterals—form a backup system that can mean the difference between life and death.

Collaterals are just plain weird. They're rare: there may be only one collateral vessel for every thousand arteries, capillaries, and veins in the human circulatory system. And they're tiny—nearly a hundred times smaller than an average artery. Instead of following the standard artery-to-capillary-to-vein route, they connect groups of arteries called artery trees. There's also little, if any, net blood flow through collaterals under normal circumstances. And an even more bizarre feature is that in collaterals blood can flow in *both* directions. According to Faber, people could survive perfectly well under normal circumstances without any collaterals at all. Yet people with more collaterals have a better chance of surviving a heart attack or stroke. And Faber wanted to know why.

During World War II, cardiac surgeon Michael Debakey noticed that some soldiers who had received wounds that obstructed major arteries in their arms or legs had to have amputations, but others didn't despite having similar injuries. Debakey thought that blood was bypassing the blocked arteries by traveling through collaterals, and that the soldiers who could still use their arms and legs simply had more collaterals. Faber and other scientists thought that something similar could be happening when a clot or a cholesterol plaque cuts off blood flow.

Still, the idea that some healthy people have more collaterals than others has been difficult to prove. The only direct method for determining the number is to count them—postmortem. Even then, finding collaterals isn't easy. And to estimate the number of collaterals in a living person, researchers have to insert a device into a person's heart, a risky procedure. "Right now, we can't tell whether the difference in the number of collaterals comes from genetics or the environment," Faber says. "You don't know how many of those people were exercisers or ate too many cheese nachos."

So Faber decided to use mice. Other scientists had identified two strains of mice that recovered very differently after an artery was blocked in their legs. Blood flow in the BALB/c strain, an albino strain, recovered more slowly and had more tissue damage compared to another strain called C57BL/6, also known as the black-six strain. The scientists noticed that the collaterals expanded more in the black-six strain than in the albino strain after an artery was blocked, and concluded that that was why the black-six strain healed faster. That conclusion bothered Faber. When he examined the data, he was convinced that the difference in expansion couldn't explain the faster recovery of the black-six mice unless they had more collaterals to begin with.

Faber wanted to repeat the study and improve it. But he needed to find a better method for counting collaterals. The earlier study had examined the thigh muscle, but there are only ten to twenty collaterals in a mouse's thigh. The methods to find these rare vessels in muscle were not easy or very reliable. There had to be a better way.

"We were driving back from a meeting in Washington, D.C.," Faber says. "I was sitting in the back seat of the car and I was thinking: What tissue has its circulation laid out in two dimensions where you can really see everything? I thought of the retina, but it doesn't have collaterals. Then it hit me—the cerebral cortex."

The cerebral cortex requires a constant supply of blood. But the major blood vessels for the brain don't enter the brain itself: instead, they sit on its surface and send tiny branches inside so that valuable brain space isn't taken up by larger blood vessels. Faber realized by using the mouse cortex as a model, they could take pictures of the vessels without having to dig through brain tissue.

When Faber and his students returned from their meeting, they injected the albino and black-six mice with fluorescent barium sulfate. They used barium sulfate crystals that were small enough to pass through larger blood vessels, including collaterals, but that were too big to pass through the smaller blood vessels that traveled into the brain and into the capillaries and veins. The result was a set of clear images that showed that the black-six mice had lots of collaterals while the albino mice had very few. Faber's group also found similar differences in the thighs and intestines. But why did the black-six mice have more collaterals than the albino mice?

"They live in the same environment," Faber says, "eat the same food, drink the same water and have the same bedding. The environment was controlled, so we concluded that the difference must come from their genetic background."

The hunt was on for the genes that controlled collateral formation. To narrow down their search, Faber selected fifteen mouse strains, including the albino and the black-six strains, to represent genetic diversity. His lab members counted the collaterals in the cerebral cortex. The number of collaterals varied widely among the fifteen strains. But they also found a new pattern: the mice that were genetically similar to the albino mice had fewer collaterals, and the mice that were genetically similar to the black-six mice had more. There was a physical trend, too: Faber and his team noticed that the mice with a small number of collaterals had more severe strokes than the mice that had a high number of collaterals.

To figure out which genes are associated with the number of collaterals, Faber's group bred the albino mice with the black-six mice. Then they interbred the hybrid mice once more to create a new generation with more genetic variety. They counted collaterals

Left: The left brain hemisphere of a black-six mouse and the right brain hemisphere of an albino mouse. The black-six mouse has lots of collateral vessels interconnecting the cerebral artery trees (marked with red stars), but the albino mouse has hardly any collaterals. Image courtesy of James Faber.

A black-six mouse and an albino mouse from Faber's lab. The albino mouse strain, which has fewer collateral arteries than the black-six strain, suffers more severe strokes. Photo by Meagen Voss.

in each mouse and then searched for genes linked to the number of collaterals. Out of the thousands of genes they investigated, Faber's group found four that were connected to the number of collaterals. They decided to focus on the one that showed the strongest connection in both mouse strains. This allowed them to narrow down their search from more than thirty thousand genes to only nine.

The nine genes that Faber's team uncovered have no known connection to blood vessel formation. The next step will be to test whether these genes are involved in building collaterals. But Faber is also hoping that their findings will eventually translate to humans. Knowing the genetics behind collateral formation could lead to better treatments for vascular diseases.

"We could genetically screen people inexpensively and see how many collaterals people have to determine their risk for vascular diseases," Faber says. Having a screen could also improve tests for new drugs that target collaterals. Some scientists are attempting to make drugs that cause collaterals to expand and let more blood flow. But, Faber says, if these types of drugs were tested on people who have few collaterals in the first place, then researchers wouldn't be able to tell whether the drugs were effective.

According to Faber, another way to tackle the problem would be to create drugs that form more collaterals and redirect blood around blocked vessels. Faber's lab has found that collaterals form late in gestation, well after the general circulatory system has already been established in the fetal mouse. And once the collaterals are there, no new ones form. Faber's still working out the details, but he says that his team has identified two genes that trigger collateral formation, and they are searching for more.

There is also the question of how collaterals escape the process that normally prunes away unnecessary or malfunctioning blood vessels that have little or no net flow. Faber thinks that the cells that line the inside of the collaterals—called endothelial cells—are different from those in other blood vessels, which could mean that collateral endothelial cells somehow defy the signals that mark redundant blood vessels for elimination.

There's still a lot to learn about these tiny, bizarre vessels. Faber says he and his lab aim to pursue this vascular puzzle until it's finished. He is continually fascinated by collaterals and amazed that vessels that are normally useless in healthy individuals can actually save lives. "That's a big deal for accessory vessels that you ordinarily don't need," he says.

Meagen Voss received a master's degree in neurobiology in spring 2010.

James Faber is a professor in the Department of Cell and Molecular Physiology in the School of Medicine. This work has been published in Physiological Genomics, Circulation Research, *and* Journal of Cerebral Blood Flow and Metabolism. *Funding came from the National Institutes of Health.*

(Net)work wonders

Currency exchange rates and Congress, the Bowl Championship Series and Facebook: Peter Mucha's math can tell us why they work the way they do.

by Susan Hardy

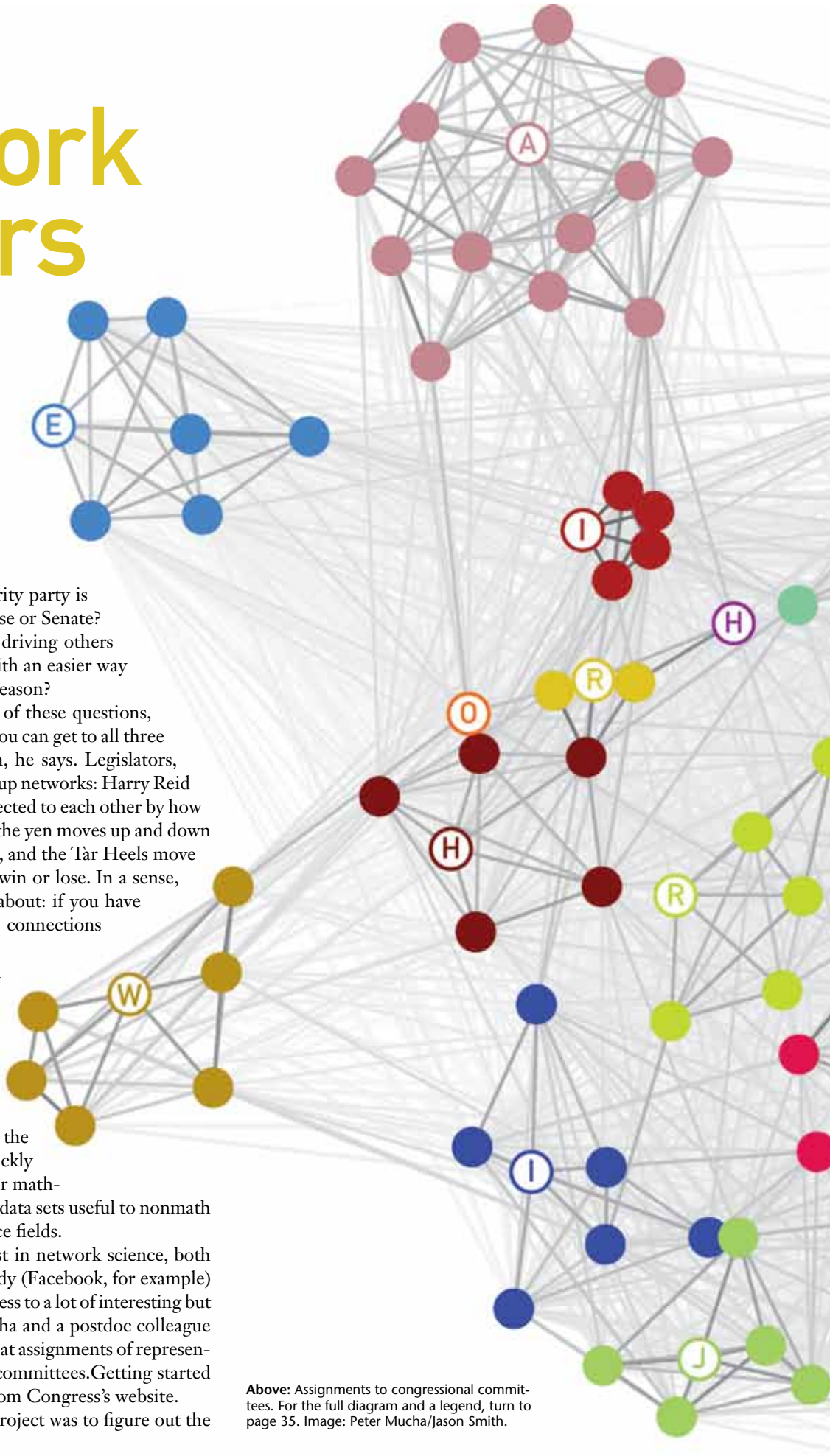
Want to predict whether the majority party is going to change soon in the House or Senate? Or find out which exchange rates are driving others up or down? How about coming up with an easier way to rank Division I football teams this season?

Peter Mucha isn't an expert on any of these questions, but he can help out with all of them—you can get to all three answers using the same kind of math, he says. Legislators, exchange rates, and sports teams make up networks: Harry Reid is a node in a network of senators connected to each other by how they vote, the dollar's strength against the yen moves up and down as other currencies gain and lose value, and the Tar Heels move around in a network of teams as they win or lose. In a sense, it doesn't matter what you're talking about: if you have nodes and some kind of data to make connections between them, you have a network.

Mathematicians have always been interested in networks, Mucha says, but computers have allowed them to start working with much more complicated systems. When a network has just a few nodes connected by a few pieces of data, it's pretty easy to see how they're all connected to each other. As the number of nodes increases, things quickly get more complicated. Mucha looks for mathematical strategies to make these large data sets useful to nonmath researchers in science and social science fields.

The internet has also driven interest in network science, both because it creates new networks to study (Facebook, for example) and because it gives researchers easy access to a lot of interesting but more traditional data sets. When Mucha and a postdoc colleague decided to study networks, they looked at assignments of representatives to House committees and subcommittees. Getting started was as easy as pulling the data from Congress's website.

The idea behind that first project was to figure out the



Above: Assignments to congressional committees. For the full diagram and a legend, turn to page 35. Image: Peter Mucha/Jason Smith.

math that would help them quantify relationships between nodes in a network, dividing them into groups of higher connectedness. "If I tried to draw a picture of every one of the nodes in the network," Mucha says, "that would be 435 representatives, plus delegates, plus midterm replacements and so on, connected by their memberships in 115 committees and subcommittees. It's a mess; you can't make any sense of that picture. What the algorithm does is group the dots."

The way this happens is written in notations that don't give you much to grab onto if you're not mathematical, but it's easy enough to get the idea in words. The connections between nodes in a network aren't all the same—they can carry different weights. In this case, some representatives might have one committee or subcommittee assignment in common, while others might have two or three. The community detection math uses these weighted connections to cluster nodes and describe exactly how closely they're connected to each other and to other groups of nodes. The strength of this clustering result is called modularity.

Mucha used roll-call voting data in Congress to define how modular (or not) congressional voting has been throughout U.S. history. This puts a number on a phenomenon most people just sense in a general way: there are years when senators and representatives vote in fairly stable blocks, usually along party lines, and years when they vote less predictably. The researchers found that modularity in Congress has gone up and down many times: it was high in 2004, the year George W. Bush was reelected, but it was just as high at the end of the eighteenth century, not long after George Washington gave his farewell address cautioning Congress not to become too partisan.

They also found that when Congress is medium in modularity—a state somewhere between the very polarized voting in the Senate today and the lower polarization of forty or fifty years ago—there's a higher chance that the majority party will change. When voting modularity in Congress is low, the researchers say, party membership doesn't mean as much and there's less drive for one party to try to gain control. When modularity's high, it's hard for the minority party to overcome the majority's cohesion.

In congressional networks, the nodes are connected by simple information: counts of committee memberships or common votes. But there are lots of other ways to link nodes in a network. For example, two nodes that correlate 70 percent with each other can be clustered more tightly than nodes that correlate 50 percent. That's how Mucha and economics colleagues organized networks of currency exchange rates. When two exchange rates correlate closely with each other, they show up in a cluster.

Before the Asian currency crisis of 1997, the Australian dollar dominated a large cluster of exchange rates. But after the crisis began, the Australian cluster broke up and a new cluster of rates emerged based on the value of the British pound. This is the kind of result that isn't visible in a data set until you build the network—economists wouldn't have guessed that the Thai bhat, the currency that began the crisis when its value suddenly dropped, had so much influence on the value of a major European currency.

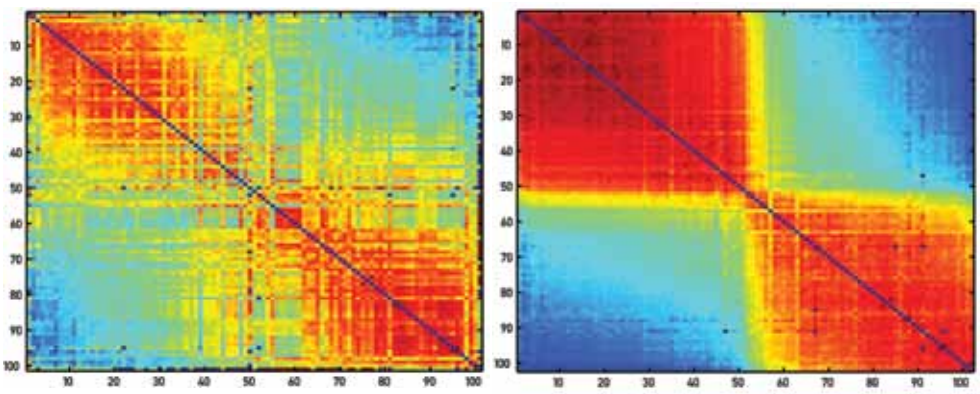
Right now, Mucha is in the early stages of collaborating with other UNC faculty in areas from population demographics to materials science to international studies. But in his spare time, he plays around with network analysis in some less academic ways.

Mucha wasn't impressed with the Bowl Championship Series (BCS), the mysterious matching system that decides which top Division I football teams will play each other. "We've all experienced befuddlement upon perusing the BCS standings, because of the seemingly divine inspiration that must have been incorporated into the determination," he wrote to other college football fans on his blog, *Random Walker Rankings*.

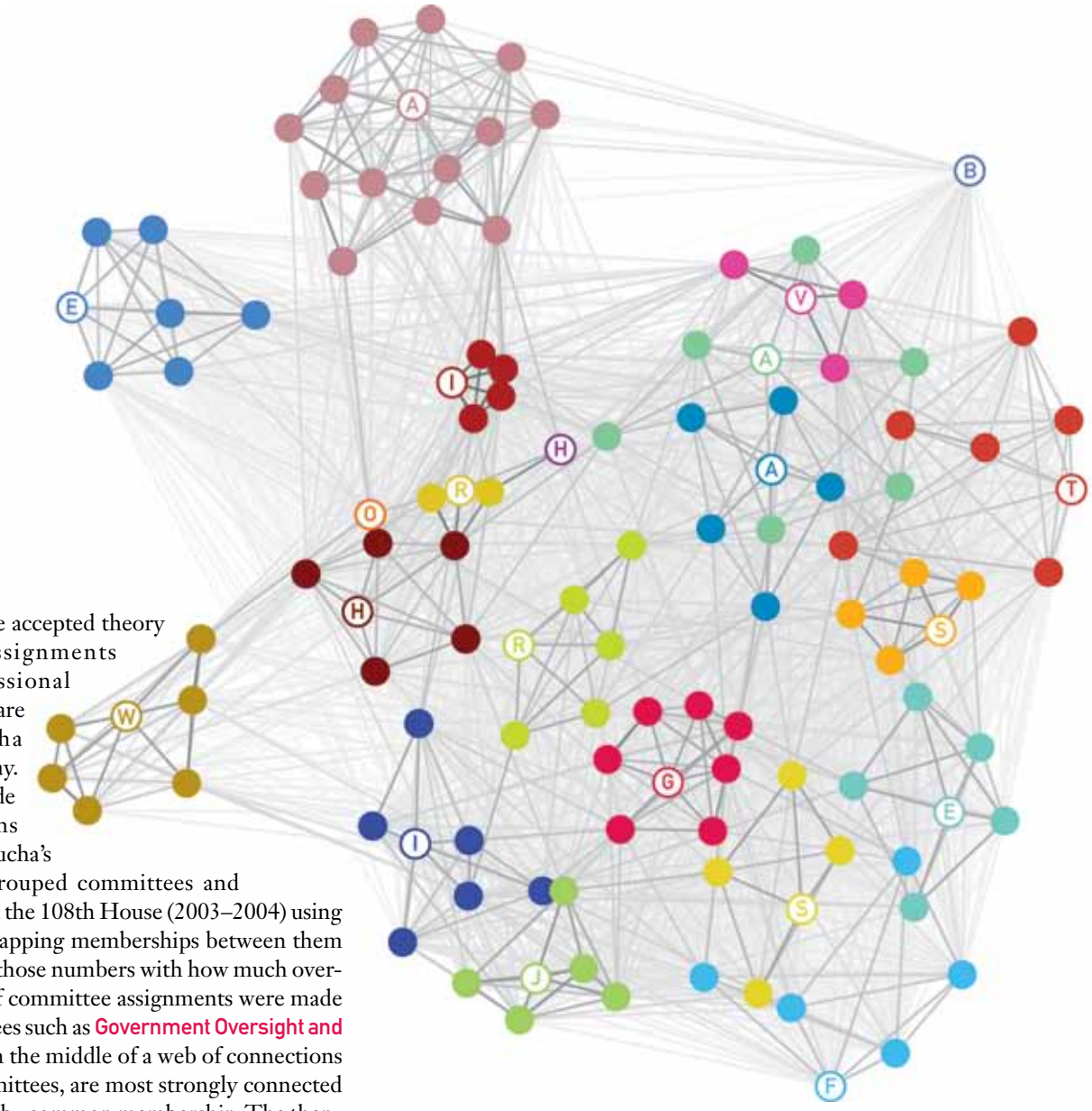
So he decided to come up with a simpler ranking system using an algorithm that randomly "walks" around the network. On each walk, it acts like a football fan with no loyalty strolling through the network, changing allegiances based on teams' records of wins and losses. Collectively, the walking fans make up a ranking of the teams. The system guarantees that strong teams will play other strong teams, and it's easier to understand than the BCS method. Each season, Mucha blogs about the system's rankings, and he's published about the system twice in math journals. He's no football expert, he says—it's just another way to play with the mathematical concepts he works with every day.

"There are focused people in the world whose life's mission is to study X," he says. "My path has been more that I've met people who have introduced me to some interesting problems. I'm a tools guy."

Peter Mucha is chair of the Department of Mathematics in the Colleges of Arts and Sciences, and an associate professor in Carolina's Institute for Advanced Materials, Nanoscience, and Technology. Much of his network analysis research was done in collaboration with Mason Porter, now a lecturer at Oxford University. James Fowler, a professor of political science at the University of California, San Diego, coauthored the study of polarization in Congress.



Left: Mucha's network analysis puts a number on how polarized Senate voting was during each Congress. On the left, the 85th Congress (1957, in the middle of Eisenhower's presidency), and on the right, the 110th Congress (2007, during George W. Bush's second term). Two senators with very similar voting records are toward the red end of the spectrum; opposite voting records are in blue.



There's no one accepted theory of how assignments to congressional committees are made, Mucha and his colleagues say. Are assignments made for partisan reasons or other factors? Mucha's network analysis grouped committees and subcommittees from the 108th House (2003–2004) using the number of overlapping memberships between them and comparisons of those numbers with how much overlap there would be if committee assignments were made randomly. Committees such as **Government Oversight and Reform (G)**, sitting in the middle of a web of connections to many other committees, are most strongly connected to other committees by common membership. The then-new **Committee on Homeland Security (H)** was closely tied to **Intelligence (I)**. But it was also closely linked to the powerful **Rules Committee (R)**, which determines for how long and under what rules the House will debate bills, and to **Official Conduct (O)**, which sets the standards for ethical conduct by representatives. In fact, Homeland Security was more closely tied to these committees than to **Armed Services (A)**. Image: Peter Mucha/Jason Smith

When THE *End* WAS *Nigh*

How medieval thinkers used reform and the apocalypse to change the world.

BY *Mark Derewicz*

Christ turned to his disciples and said, "Other sheep I have, which are not of this fold: them also I must bring, and they shall hear my voice; and there shall be one fold, and one shepherd."

For centuries, Christians have used this passage from the Gospel of John as motivation to spread the word of Christ. But historian Brett Whalen found that medieval theologians also used it to foment a movement they hoped would spur on the End Times, an era of peace after Christ's defeat of the Antichrist, when all peoples would accept Jesus or face the wrath of God.

But a funny thing happened on the way to the apocalypse. Several medieval popes and thinkers did usher in a sort of end time. Just not the one they had envisioned.

Created between 1200 and 1250, this map of the world features Jerusalem in the center and what the map's creators considered to be representations of monstrous races on the outer edges. Jesus is at the top. The map is held at the British Library in London.

Whalen has a fascination with the Middle Ages. To him they weren't that dark—only a bit gloomy. A pall was cast over Christian Europe in the eleventh century, Whalen says, when the one fold of believers turned into two: the Latin Church in Rome and the Eastern Church in Constantinople.

Whalen was researching the schism when he found that theologians seemed very concerned with the apocalypse. They said that Rome must reunite with Constantinople, and that Christians must become one community of believers before Christ would return. Some of these apocalyptic thinkers had the ear of the pope. But some were average clergymen, simply giving voice to thoughts commonly held during the High Middle Ages.

While researching rare documents at the Bibliothèque Nationale in Paris, Whalen noticed an early-eleventh-century manuscript titled *Letter from A Humble priest to the Rulers of the Saracens* (that is, Muslims). As far as Whalen could tell, it had never been published or even referenced by another researcher. "Everything in it was apocalyptic, trying to make sense of how God could allow Muslims to control the Holy Land," Whalen says. The anonymous author wrote that God must have allowed Muslim control of Jerusalem so that the sultan would learn about Christ and convert to the one true faith. Conversion of Jews and Muslims is another end-time prophecy, Whalen says.

Little did that priest know that his kind of understanding of events would inspire great battles aimed at bringing forth the end of days.

Brett Whalen traces the troublesome cycle of apocalyptic thinking during the High Middle Ages in his book *Dominion of God.* Photo by Mark Derewicz.

Here's how all this

got started. Before the Last Supper, Jesus said to his disciple Simon, "Thou art Peter. And upon this rock I will build my church." Peter brought Christ's message to Rome, and he was martyred. Later, Roman bishops thought of themselves as Peter's heirs and appointed a pope as God's viceroy on Earth. But in the fourth century, Constantine—the first Roman emperor to convert to Christianity—moved the imperial capital to Constantinople, where bishops didn't always bow to papal authority.

That wasn't too big a deal back then. "Papal authority existed only on paper," Whalen says. "For vast stretches of time, the pope was just another bishop who had a theoretical grandeur."

Until the eleventh century. That's when European cities grew and commerce prospered. And so did the Church. Christians gave the Vatican more money, which it used to exert direct control over individual churches and communities. As the Church grew stronger, some monks and abbots conjured ideas of what the Church's larger role in society should be. Well-known theological reformers, such as Peter Damian and Humbert of Silva Candida, urged the Church to separate itself from society. They said clergy should not marry or have children or own property. That separation, they thought, would give the Church more moral authority and greater influence in the day-to-day lives of Christians, including secular rulers.

"There's this grassroots movement in the eleventh century with all these reformers," Whalen says. "And then one of them became pope—Leo IX—and a whole cadre of reformers went to Rome. They had a vision for what the world should look like and *would* look like."

And as Whalen writes in his book, *Dominion of God*, that vision included when the apocalypse would come.

In 1054, with reformers now in the Vatican, the Latin Church demanded that Eastern Christians conform to Western rites and sacraments, such as using unleavened bread for the Eucharist. The Eastern Church refused; it preferred leavened bread. And so the two wings of Christendom officially split. Looking into this era, Whalen found that many theologians displayed an apocalyptic zeal; they thought it a travesty that Christendom had been rent asunder.

In the late eleventh century, the Church gained even more power, seizing from the German emperor the right to appoint bishops and abbots in an episode historians have written about extensively.

"What fascinated me about this time was how the reformist papacy started looking outward toward the Islamic world, the Greek Church, and the Jews," Whalen says. In particular, reformers started talking about the Peace of God—peace among Christians.

In 1095, Pope Urban II received a letter from the patriarch of the Eastern Church, who needed help repelling Muslim Turks. Later that year, at a large gathering of church leaders and laymen, Urban II addressed violence among European Christians. "Why fight each other?" he said. "Why not turn our swords toward the infidels who are plaguing the church in the East and defiling the Holy Land?"

Historians have long known about Pope

Pope Urban II addressed violence among European Christians. "Why fight each other?" he said. "Why not turn our swords toward the infidels who are plaguing the church in the East and defiling the Holy Land?" Urban II felt that Christianity should be thriving in Jerusalem; only then would the Antichrist appear and persecute the faithful—a necessary evil—before his final defeat at the end of time.

Urban II's speech. But Whalen emphasizes the pope's motive: little-known historian Guibert of Nogent quoted Urban II saying that Christianity should be thriving in Jerusalem; only then would the Antichrist appear and persecute the faithful—a necessary evil—before his final defeat at the end of time. Urban II then called for the First Crusade, which began in 1096. Three years later, Christian knights seized Jerusalem, its surrounding provinces, and several other Mediterranean counties and cities.

It was a stunning victory, and apocalyptic-minded reformers considered it the will of God. The prophecies were being fulfilled, they thought.

"It's easy to see that

God is on your side when things go well," Whalen says. "But what happens when things go wrong? Well, reformers had an answer for that, too." God was angry. And between the eleventh and fourteenth centuries, historians say, reformers found explanations for God's wrath. Reports had reached Rome of crusaders raping Christian women, killing children, and plundering cities. Clergy were upset and made sure the pope knew how they felt. But according to Whalen's findings, some texts reveal what the reformers were thinking. They said the End Times would come only when the Church was made pure. But as time went on, Whalen says, reformers saw the Church more and more as an intractable part of the problem.

In his book, Whalen writes that twelfth- and thirteenth-century apocalyptic thinkers began looking toward a glorious future when the Church would be hardly recognizable—no clergy, no sacraments, no church institutions at all.

"Reformers still believed in spreading the gospels around the world to bring people into one fold," Whalen says. But they thought the Church had become too corrupt to shepherd the flock. "They thought there'd be a new spiritual leadership of monks in the future," he says.

Joachim of Fiore, the best-known proponent of that kind of thinking, divided time into three stages—the age of the Father (from Adam to Christ), the age of the Son (from Christ to Joachim's day), and a future age of the Holy Spirit, which would be, according to Joachim, "without war, without scandal, without worry or terror, since God shall bless it and he shall sanctify it."

According to Whalen's research, kings and popes found inspiration in Joachim's description of the Greeks as the "lost sheep" who would be brought into the one true fold before the end of days. Jews would recognize Christ, Joachim wrote, and some Muslims would convert.

In 1204, Pope Innocent III quoted Joachim in a letter to Constantinople. The pope said that the successful siege of that Christian city during the Fourth Crusade was a sign of God's hand in history because the Latin Church needed to become one with the Eastern Church.

But Joachim's followers wrote books about how the sins and decadence of Rome would be exposed before the End Times and that the Antichrist would purge the Church of its shortcomings. "One such book was burned by papal order," Whalen says. "But the idea didn't go away." Reformers more radical than Joachim took up his mantle. Peter John Olivi, for instance, called Rome "the carnal church" and advocated for major reform, Whalen says.

Whalen traced the lineage of Joachite thinkers through the fourteenth century. Most of them were more radical than Joachim and each was critical of Rome's decadence. Yet, Whalen says that the strong papacy was able to contain rebellion among radical monks, abbots, and priests or purge them from the Church.

Until the fourteenth and fifteenth centuries. That's when the Vatican weakened politically and European monarchs gained power, opening the door for a sort of end time the Church did not foresee.

Whalen ends his book

at the dawn of the fifteenth century, by which time the influence of the apocalyptic thinkers on the papacy had waned. But reformers are forever.

In 1517 a Dominican friar named Johann Tetzel knocked on Martin Luther's door in Wittenberg, Germany, to sell indulgences—payments to the Vatican for blessings and penance. The encounter with Tetzel inspired Luther to post ninety-five theses critical of the papacy. Number eighty-six read: "Why does the pope, whose wealth today is greater than the wealth of the richest Crassus, build the basilica of St. Peter with the money of poor believers rather than with his own money?"

Indulgences were nothing new: the Vatican had granted them to the earliest crusaders. Later, popes granted indulgences to women and others who couldn't fight. Over time indulgences became big business, Whalen says, and the Vatican grew rich while many believers stayed poor. This did not sit well with many ordinary Christians and reformers.

"People in the Middle Ages were just as aware of hypocrisy as we are today," Whalen says. "They knew Christ and the apostles lived lives of poverty." Pope Leo X excommunicated Luther, but German princes and other clergy came to Luther's aid, sparking the Protestant Reformation. Christendom would never be the same.

Whalen points out that Luther, like previous reformers, had never wanted to break from the Church. But also like his predecessors, Luther became more radical when the Vatican, in his eyes, did not respond well to calls for reform.

"Luther even called the pope the Antichrist," Whalen says—a sure sign that the apocalypse was at hand.

Brett Whalen is an assistant professor of history in the College of Arts and Sciences.

DETECT, DETAIN, DEPORT

287(g) is a controversial immigration program. Does it work?

by Mark Derewicz

In August 2008, at dusk on the banks of the Haw River, a North Carolina Wildlife Resources officer found five Hispanic men fishing without licenses. The officer asked the men for other forms of identification. Two produced IDs from other countries, and a third handed him an expired California license that the officer thought looked fake. According to press reports, the officer said that he could have issued citations, but he arrested the men instead because he couldn't establish their identities and none of them had a license to drive the car they used to get to the river. Using a federal immigration program called 287(g), the Alamance County Sheriff's Office detained the five men. Soon after, U.S. Immigration and Customs Enforcement (ICE) established that the men were in the country illegally and deported them.

Some find no fault with this story: the men were here illegally and got what they deserved. Others say that the officer racially profiled the men, and that's illegal.

Still others, including two UNC researchers, say that 287(g) was designed to help police get rid of the worst criminal elements—thugs and terrorists—not a bunch of guys fishing the Haw.

That's true. But police say there's more to it.

Pluses and minuses

According to the ICE website, 287(g) is supposed to give resources and latitude to local and state police while they pursue investigations related to violent crimes, human smuggling, gang or organized crime activity, sexual-related offenses, narcotics smuggling, and money laundering. The ICE standard memo of agreement with local jurisdictions states that 287(g) is for "identifying and processing for the removal of criminal aliens who pose a threat to public safety or a danger to the community."

William Riley, acting director of ICE's Office of State and Local Coordination, said at a congressional hearing in March 2009 that 287(g) jail space should be used "to detain the aliens who pose the greatest risk to the public." According to anthropologist Hannah Gill and urban planner Mai Nguyen, most Hispanics detained through 287(g) are not major threats. The two researchers analyzed crime data from five North Carolina counties and found that 86.7 percent of people detained and then processed through 287(g) between 2007 and 2009 had been charged with misdemeanors, usually traffic violations. The Durham City Police Department was the lone jurisdiction that applied 287(g) solely to the more serious crimes listed on the ICE website.

Because of the way 287(g) has been designed and used, Gill and Nguyen say, the program has cost millions of dollars while having no measurable effect on crime rates. Instead, it might have negative long-term consequences on crime fighting and local economies. "On paper, it looks unobjectionable," Gill says. "If the program were carried out the way it was intended, you'd be getting rid of the worst offenders in our society. Who could argue with that? But in practice you have to ask: What's this program really about?"

Here's how 287(g) works. When police arrest and book suspects, officers can access the ICE database to determine whether the suspects are in the United States illegally. They can detain suspects or send them to a federal detention center while ICE starts the deportation process. Alamance County, one of eight North Carolina jurisdictions that use the 287(g) program, built a jail to federal standards to house detainees, including some sent to Alamance from surrounding counties.

The specifics of 287(g)

In 1996, Congress passed the Illegal Immigration Reform and Immigrant Responsibility Act. In section 287(g), the act authorizes the Department of Homeland Security to work with local and state law enforcement agencies to enforce immigration law. Federal immigration and customs agents train local police to detect, detain, and deport undocumented people. Each jurisdiction contracts with Immigration and Customs Enforcement through a signed memorandum of agreement, which describes the role and authority of each party. Until 2009, each memo had been tailored to each jurisdiction. All memos are now standardized.

Left: Federal Immigration and Customs Enforcement (ICE) agents can work with local police and sheriff's departments to identify and deport illegal aliens. But the 287(g) program that allows this partnership has come under fire across the country, including in North Carolina. Photo: Associated Press

Alamance County is one of the few counties in North Carolina with a detention center that meets federal standards for holding inmates before and during federal court hearings as well as prior to the completion of federal deportation proceedings. Other jurisdictions send suspected illegal aliens to the center. Photo by Donn Young.

Randy Jones, spokesman for the Alamance County Sheriff's Office, says, "The vast majority of illegal aliens we have criminal contact with use false names. It's hard to have a successful criminal justice system if you don't know who you're dealing with." Many suspects don't have driver's licenses. Jones says they often give false addresses, too, which makes issuing citations ineffective. "There was no integrity to the system," he says. "It was almost a joke. So now, we use ICE databases to screen everybody we arrest. That's the only way to be fair."

Jones also says that most serious criminals, no matter their race or nationality, are often arrested while committing a lesser offense, such as a traffic violation. "We've been successful in eliminating thirteen or fourteen gang members," he says. "But they had been picked up for minor violations."

Gill says that 287(g) is a legal way to deport illegal immigrants, no matter their crimes. But she and Nguyen interviewed more than one hundred people—including police officers—some of whom said that police officers have profiled suspected aliens based on race. Some of Gill's informants within the Hispanic community told her that police have asked them for immigration documentation in the field, before they were arrested. According to 287(g), suspects can only be asked for documentation back at the station after they have been arrested.

"In some counties, we found that Hispanics are pulled over for a lot of questionable reasons—what they look like, what sort of car they drive," Gill says. "This is where the issue becomes tricky. This is why so many people are upset about the new law in Arizona."

Because of the way 287(g) is set up, Gill says, the program helps ICE deport low-level offenders instead of violent felons. This costs taxpayers a lot of money that Gill and Nguyen say would be better spent on crime-fighting measures and outreach programs that have already been proven effective, such as Gang Resistance Education and Outreach Training.

Costs and consequences

Some proponents of 287(g) have said the program should be used because the influx of illegal immigrants has caused crime rates to soar. But that's not what Gill and Nguyen found. In Mecklenburg County, the immigrant population—not just Hispanics—was estimated at 6,000 in 1990. It climbed to 80,000 by 2006. But during that span, violent crime decreased in Mecklenburg County from 10,300 incidents to 7,450, according to statistics from the North Carolina Uniform Crime Report.

Since 2006, when 287(g) was first adopted in North Carolina, crime rates have remained steady in jurisdictions that use the program. Yet 287(g) isn't cheap.

Nguyen's analysis shows that first-year costs in Mecklenburg County for implementing 287(g) in 2006 were an estimated $5.5 million. Alamance started the program a year later at an estimated cost of $4.8 million. These costs included ICE training of local police and salaries for officers dedicated to enforcing 287(g). But the vast majority—$4.8 million in Mecklenburg County—went toward the detention of prisoners. The federal government covers costs once ICE determines that a suspect is an illegal alien.

"But taxpayers pay for all of it, whether at the federal, state, or local level," Gill says.

Julia Rush, Mecklenburg County Sheriff's Office spokeswoman, says it costs a little over a hundred dollars to jail one inmate for one day. But she says the Mecklenburg Sheriff's Office, like Alamance's, does not go out of its way to arrest undocumented residents. Both offices arrest people who commit crimes; *then* they use 287(g).

"We told this to the media and the Latin American community: If you don't want to encounter the 287(g) program, don't commit a crime," she says. "You might say we're identifying low-level offenders, but if a person is driving without a license and has no insurance and doesn't know the rules of how to drive in North Carolina and runs into your family, should it be considered a low-level offense?"

Such tragic incidents are rare, but they've happened in highly publicized cases across the country, including in Graham and Gastonia, North Carolina.

Nguyen and Gill say it's much more difficult to estimate other costs of the 287(g) program, such as jail expansion or retrofitting, medical and social services for prisoners, transportation costs to federal detention centers, court costs, new computer equipment for accessing ICE databases, and litigation fees. Indirect costs were even harder to measure. Communities lose business and tax revenue when thousands of people are deported each year. Counties save money when immigrants are deported and no longer use resources, such as health-care clinics. According to a report from UNC's business school, Hispanic immigrants contributed more than $9 billion to North Carolina's economy through purchases, taxes, and labor in 2004. They cost the state less than $1 billion in health-care, education, and imprisonment costs.

There might be more dire consequences of 287(g). During Gill and Nguyen's research, many Hispanics said they no longer report serious crimes to police and don't come forward as witnesses for fear that they and their families will be deported. This common refrain makes Gill and Nguyen wonder if 287(g) is having a negative effect on police work.

Jones says Alamance still receives many calls from Hispanics reporting crimes. Rush and Jones also say that Mecklenburg and Alamance officers have no interest in questioning victims or witnesses about their immigration status, and that both counties have reached out to Hispanic communities. "We're constantly on Latino radio, we work with Latino reporters, attend Latino events, and invite people from the community to come and talk to us," Rush says. "They should not be afraid to come forward with information. *And* we've also told them to make sure they come to court

In Alamance County, inmates at the county detention center are separated into groups. One group is composed of federal inmates, many of whom await deportation as a result of the 287(g) program. Photo by Donn Young.

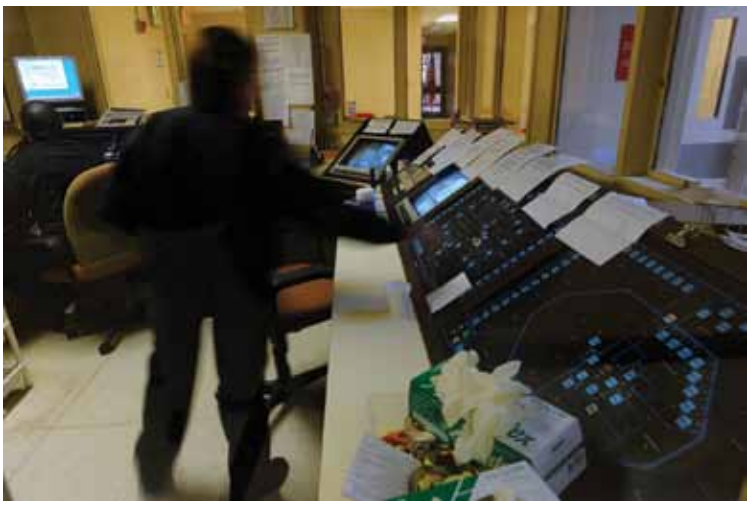
"If the program were carried out the way it was intended, you'd be getting rid of the worst offenders in our society. Who could argue with that? But in practice you have to ask: What's this program really about?"

—Hannah Gill, anthropologist

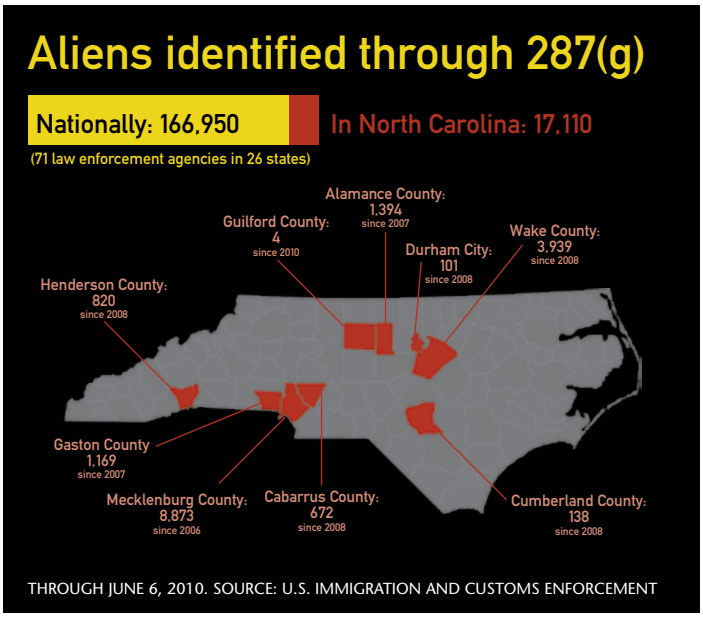
"You might say we're identifying low-level offenders, but if a person is driving without a license and has no insurance and doesn't know the rules of how to drive in North Carolina and runs into your family, should it be considered a low-level offense?"

—Julia Rush, Mecklenburg County Sheriff's Office

The command center at the Alamance County detention facility, where illegal immigrants are held before being deported. Photo by Donn Young.



so that they don't have orders for their arrest issued. Their immigration status will not be checked in the courtroom." But it will be if they are arrested—for any reason.



JASON SMITH

No line on the horizon

In 2008, in a highly publicized case in Alamance County, a Graham librarian named Marxavi Angel Martinez was arrested and eventually deported, though not through 287(g). Alamance County Sheriff Terry Johnson told the *Burlington Times-News* that police learned about her immigration status during an investigation of Hispanic patients using aliases at the county's health department, where Martinez had received prenatal care. Some Alamance residents, including Marilyn Tyler, a friend of Martinez's, wondered if police had been trolling through confidential health records trying to find undocumented workers. That's against the law. Later, Johnson told reporters that his office had been tipped off about Martinez's immigration status—that she used a fraudulent Social Security number to get her job—and his office relayed the information to state investigators, who contacted ICE.

Tyler and Gill say that Martinez's case is a good example of the complexity of the immigration issue. "Yes, she broke the law," Tyler says. "That wasn't good. But she did that to get a good job and go to college. Isn't that what America is about? She was adding to the American community. And we lock her up and send her away. I can't think of any goodness that came from this. This case is emblematic of the system that is so broken in our country."

No one has disputed that Martinez was a hard worker who contributed to society. She paid taxes and also paid into a social security system that would never have benefitted her. Jones acknowledges the unfortunate personal stories of cases like Martinez's. But he also says that police are not to blame for these situations. In Martinez's case, he says, the parents were responsible for their daughter; they brought her to the United States when she was three years old and didn't return to Mexico when their work visas expired.

Gill says that stories like Martinez's are common among Hispanic immigrants. Gill spoke to a teenager who had been deported to El Salvador even though his mother had brought him to the United States as a baby. He had never learned to speak proper Spanish. Had he been born a few months later, he'd be a U.S. citizen.

But proponents of 287(g) say that the law is the law; illegal aliens must be deported whether they've committed minor or major offenses, or no offense at all.

On paper, the 287(g) program tries to focus on the worst criminal elements within the community of undocumented residents. In reality, though, the program is putting law enforcement officers right in the middle of a sociopolitical situation that the federal government has yet to fully address.

So what's the solution?

"True immigration reform will be tricky," Nguyen says, and not just because it's a hot-button issue for politicians. "Reform has to be thoughtful and comprehensive. The government will have to secure the borders while giving people who are already here a path toward citizenship. Otherwise we're just using people for their labor without giving them any rights." (*See* Endeavors, *Spring 2009*, *"A Good, Swift Kick."*)

Gill says, "There has to be a shift in the way visas are granted. Right now we prioritize high-skilled labor when our demand is for low-skilled jobs."

As for the eleven to twelve million undocumented residents in the United States, Gill says the U.S. government could start an amnesty program similar to the one George W. Bush proposed in 2006, or one similar to more-recent bipartisan bills.

"The idea is to have immigrants show that they've been paying taxes for, say, five years," Gill says. If they proved that, then they could be granted legal residency and put on a path toward citizenship. That would not completely solve the problem. "What about people who've not been here for five years?" Nguyen says. Should the U.S. government grant the reward of citizenship to anyone who crosses the border? Nguyen and Gill say that, at the very least, a basic amnesty program would help the millions of people like Marxavi Martinez.

Marilyn Tyler says she's heard that Martinez is trying to use legal means to come back to Alamance. But getting a visa is nearly impossible. Her four-year-old son could come back any time. He was born in the United States; he's a citizen.

"The Marxavi case was appalling," Tyler says. "I've known her since she was twelve. I'd see her all the time at the library where I worked. She went to the same school as my kids. I can't tell you how horrible this was, watching my government toss her in with federal felons. It was sickening to me. It was a nightmare that didn't have to happen." e

Hannah Gill, the assistant director of UNC's Institute for the Study of the Americas, will publish a book through UNC Press in November 2010 titled The Latino Migration Experience in North Carolina. *Mai Nguyen is an assistant professor in the Department of City and Regional Planning in the College of Arts and Sciences. Their report is available here: http://isa.unc.edu/migration/287g_report_final.pdf.*

They received funding from the Z. Smith Reynolds Foundation and four UNC units: the Institute for the Study of the Americas, the Office of the Vice Chancellor for Research and Economic Development, the Center for Global Initiatives, and the Department of City and Regional Planning.

SEND IN THE CELLS

Klaus Hahn's guiding light can make cells move. Some day we may be able to use it to repair nerve injuries, assemble cells into new muscle and bone, or figure out how an embryo develops.

by Susan Hardy

Living cells twitch. They crawl, vibrate, expand, contract. They rush off to fight infections, heal wounds, or grow organs in developing embryos. How do they know how and where and when to move?

Each cell has an internal network of proteins that signal it to move or change shape in response to what's going on inside and outside the cell, pharmacologist Klaus Hahn says. Hahn's spent his career trying to figure out how that complicated network does its job—and how to use it to let scientists control where cells are going in a living organism. That means working on ways to reach inside the cell and turn the signaling proteins on and off.

Researchers figured out a way to turn proteins on with light years ago, Hahn says. "You take a protein and bind a photocleavable molecule to it—when you shine light on it, the group falls off and the protein turns on." That technique had a lot of problems. Once the protein-silencing molecule fell off and the protein was turned on, it couldn't be turned off again. The ultraviolet light used to break the bond with the amino acids was so strong that it hurt other parts of the cell. And getting these modified proteins into a cell without damaging it was hard to do.

There's a different kind of protein that's better at responding to light, called LOV (Light, Oxygen, or Voltage). Plants use it to sense light and turn their leaves toward the sun, Hahn says. Last year a postdoc in his lab, Yi Wu, changed the genetic code of a signaling protein to include instructions for making the LOV protein. They chose this signaling protein, Rac1, because it controls the first step in cell movement, in which the edge of a cell protrudes. Then that edge attaches to whatever it's moving on, and the other end follows behind.

The resulting protein comes out wound up sort of like a yo-yo string, Hahn says: "When you shine light on the side of it, the string unwinds and the protein can do what it wants. When you turn the light off, it winds back up. The LOV protein blocks it from activating just by covering it up."

Shine a blue light on one of these modified proteins near the edge of the cell, and it signals the cell to head for the light. In video clips from Hahn's lab spliced together by the National Institutes of Health, a cell chases a circle of light across the screen ("like a horse trotting after a carrot on a stick," the narrator says). In another video, a protrusion emerges from the side of a cell, ending in a sharp point where a beam of light shines: the cell gets bigger in response to the light.

The cells Hahn's lab works with are fibroblasts: large connective tissue cells that help heal wounds and "like to move anyway," Hahn says. Last fall, after he and Wu published a paper on moving cells with light, other researchers started using the technique in living organisms: first zebrafish, then fruit fly embryos.

At Johns Hopkins, Denise Montell found that activating the signaling protein in one cell in the fly embryo made nearby cells fall into line with it. "As if all the other cells said, 'Aha! You've got more activity so we're heading your way,'" she says. Developmental biologists study how a small number of cells in an embryo differentiate into brain and blood and other types of cells. They'll be able to move groups of undifferentiated stem cells in a fruit fly embryo, for example, and figure out what those cells do by watching to see whether the embryo develops differently from how it normally does, Hahn says.

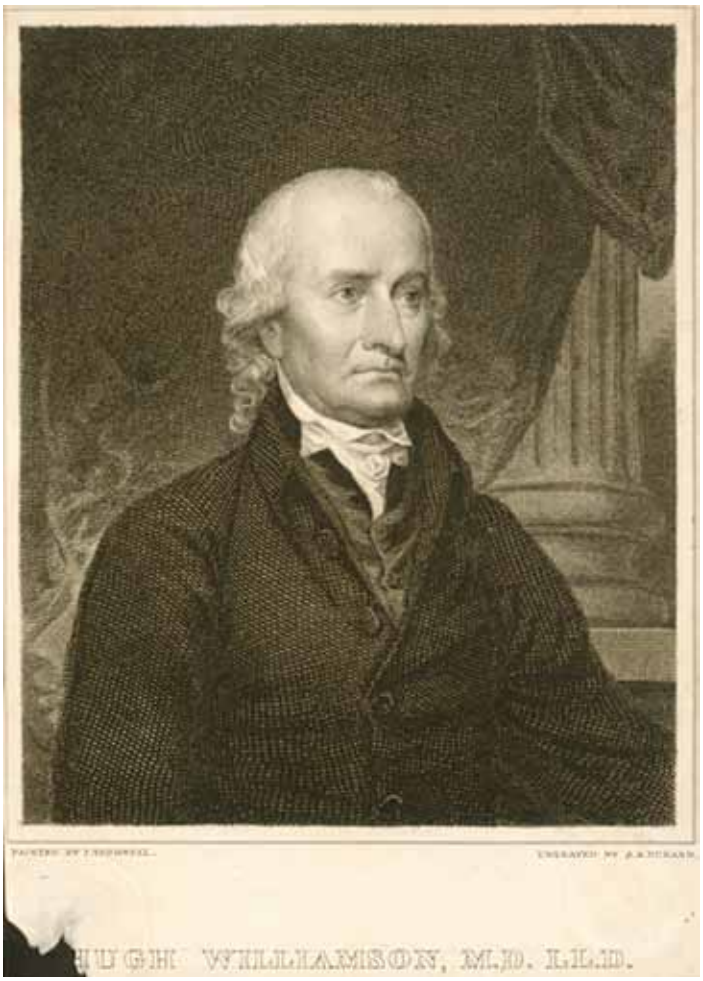
Cell movement is also a central part of many illnesses—cancer is usually the first one mentioned, because it's most deadly when cells break away from a tumor and travel to other organs. Moving metastasized cells with light may be a possibility, Hahn says, but that could turn out to be impractical because the cells are so scattered. He's more excited about the technique's potential to help with nerve regeneration: surgeons may someday fix a severed spinal cord by guiding the cells back together with light. And then there's the young field of tissue engineering, which still lacks good ways to assemble cells into muscle and bone and other kinds of tissue. "Imagine paint pots with different cell types," Hahn says. "We can take some from one pot, some from another, and paint them into the right places using light."

Could the technique work on other proteins, or use multiple colors of light to change different proteins in one cell? Yes, Hahn says: stay tuned. A more complete version of his answer is in UNC's Office of Technology Development, somewhere in the patenting process.

Meanwhile, his lab is using the LOV protein technique to study the movement of immune cells from the bloodstream into other tissues. "The immune cells travel through the bloodstream," Hahn says, "and when they have to leave the blood, they attach to the endothelial cells lining the wall of the blood vessel. The walls somehow sense the cells are there and open up a porthole—not between the vessels, but right in the middle of one—to allow the immune cells to pass." His lab will look at what triggers the immune cells to stop in the right place and what lets the endothelial cells know to let them out. They picked this type of cell movement to study because immune cells are part of the body's inflammation response, which plays a role in all kinds of diseases from Alzheimer's to diabetes to heart disease. Hahn also wants to make the LOV protein technique available commercially to other researchers. "I've found that that's the best route to get something you make into a lot of people's hands," he says. "It's a simple tool, and we made it that way so that people will be able to use it for a lot of different things."

Klaus Hahn is the Ronald Thurman Distinguished Professor of Pharmacology in the School of Medicine. This fall, Yi Wu began an assistant professorship at the University of Connecticut. The work by Anna Huttenlocher's lab using the Hahn lab technique in zebrafish was published in February 2010 in Developmental Cell. *The work by Denise Montell's lab with* Drosophila *embryos was published in May 2010 in the journal* Nature Cell Biology.

in print



Hugh Williamson, painted by J. Trumbull and engraved by A.B. Durand. Image: University of Pennsylvania Archives

HISTORY OF THE REPUBLIC

The forgotten father

by Mark Derewicz

Hugh Williamson: Physician, Patriot, and Founding Father. By George Sheldon. Prometheus Books, 361 pages, $25.00.

Founding father. Scientist. Doctor. Revolutionary War veteran. Writer, educator, state representative. Entrepreneur. U.S. congressman. Mathematician, UNC Trustee, philanthropist. Friend to Thomas Jefferson.

Sounds like the kind of fellow you would have heard of. But few people know the name Hugh Williamson. UNC surgeon George Sheldon hadn't heard of him until he found Williamson's name in a 250-year-old London registry. A little research revealed a telling character. And lot of research convinced Sheldon that there was no other North Carolinian more influential than Hugh Williamson in the founding of the American democracy. In fact, it was Hugh Williamson who first said that the Constitution would become the supreme law of the land—a fact obvious now, but not in 1787.

Sheldon tells Williamson's story in *Hugh Williamson: Physician, Patriot, and Founding Father*.

"'Involved' is a good word to describe Hugh Williamson," Sheldon says. And one reason for Williamson's relative anonymity, is that the man was involved in a lot of different areas. His first love was education. His second, medicine. But his greatest accomplishments came in service to a new nation.

Sheldon, who teaches a course at Carolina called The History of Medicine, came across Williamson's name while researching the former students of John Hunter, a British scientist who trained most American professors of medicine during Colonial times. Williamson was one of them.

Williamson taught English, math, and Latin when the University of Pennsylvania was called the College of Philadelphia. But he left the colonies before the Revolutionary War to study medicine at the University of Edinburgh. Williamson then went to London to study under Hunter, the leading biologist-surgeon of the Enlightenment.

Williamson was later elected to the American Philosophical Society, an exclusive group founded by Benjamin Franklin, and wrote astronomy papers for the society.

It seemed as though Williamson would focus on science and medicine, but his attention was split among many fields, Sheldon says. Williamson attended planning sessions for the Boston Tea Party in 1773, after which he traveled to Europe to raise funds for the Newark Academy, where he was a trustee. While in London he studied the electric eel with Franklin and Hunter in 1775.

During the Revolutionary War, Williamson returned to Philadelphia to deliver dispatches from Franklin. But Williamson didn't stay there.

"To my surprise, he wound up in North Carolina in 1777," Sheldon says.

Sheldon enlisted the help of Mary Jane Kagarise, a registered nurse at UNC, to check North Carolina sources for mention of Williamson, including the state archives in Raleigh. Turned out, Williamson started a shipbuilding and trade company with his brother in Edenton, a vital Colonial port. At the same time, Williamson established a medical practice.

When the Revolutionary War came south, Governor Abner Nash appointed Williamson as surgeon general for the North Carolina militia. Sheldon and Kagarise found letters showing that Williamson used his own money to buy supplies to treat the wounded. He organized medical camps in ways unique for the eighteenth century, such as using sewage systems and isolating

Scene at the Signing of the Constitution of the United States, by Howard Chandler Christy, oil on canvas, 1940. Even in this iconic painting, Williamson, a central figure, is overshadowed by the well-known men who surround him. On the dais, George Washington looks out over the assembled delegates. In the foreground, Alexander Hamilton leans over to speak to Ben Franklin. James Madison is seated just to the right and slightly behind Franklin. Hugh Williamson, standing in profile, is just to the right of the center of the painting, wearing a brown coat with his foot on the step of the dais. The painting, which is twenty feet tall and thirty feet wide, hangs in the east stairway of the House of Representatives wing in the U.S. Capitol Building. Image courtesy of the Architect of the Capitol.

the sick in tents. "He carefully attended to the soldiers' sanitation, diet, food, clothing, shelter, and sleeping quarters," Sheldon says. "The result was a remarkable record of health among the troops." In six months, with five hundred to twelve hundred men in camp at any given time, only two died from disease and none were sent home. Williamson was also one of the first doctors to inoculate soldiers against smallpox. Historians agree that such vaccinations helped the Colonists win the war.

Williamson's service led to his reputation as a patriot, Sheldon says, and he got back into politics. After a stint in the North Carolina House of Commons, Williamson was appointed as a delegate to the Continental Congress in Philadelphia, where he argued for a Southern site for the new national capital, preferably on the Potomac River. Williamson wanted to limit slavery in territories north of Ohio. He never owned slaves and thought that slavery was "an incumberance to society."

Hugh Williamson was one of three North Carolina delegates to sign the U.S. Constitution, but there's no monument to him in the Tar Heel state. There are no towns or boulevards or buildings named after him.

Williamson was then appointed as a delegate to the Constitutional Convention, where state representatives wrangled over issues while drafting the U.S. Constitution. "He was by far the most active, valuable, and influential North Carolina delegate," Sheldon says.

Adept at the art of compromise, Williamson worked hard to defeat legislation that would alienate Southern states, which he desperately wanted to keep in the Union, Sheldon says. Williamson helped forge the three-fifths compromise—each slave would be counted as three-fifths of one person. That compromise meant that North Carolina had one of the largest state populations, which translated into more representatives in Congress than most states.

It was Williamson's idea to pay senators so that men who weren't wealthy could afford to hold high office. He pitched the idea of a national census to determine how many representatives each state should have in Congress.

"He was on five committees, including the one that dealt with

all the issues that the framers couldn't agree on." That committee, which included James Madison, rewrote the Constitution's preamble to read the way it does today.

A second reason many people haven't heard of Williamson is that he was often overshadowed by the giants of his day. Williamson worked with George Washington on a few occasions—a proposed canal project in the Great Dismal Swamp of North Carolina, for instance. He worked closely with Thomas Jefferson to develop a system to survey land. The Ordinance of 1785 included Williamson's grid design for the settlement of 1.3 billion acres west of the original thirteen Colonies. Jefferson, rarely forthcoming with compliments, spoke highly of Williamson, including this account from Sheldon's book: "We served together in Congress during the winter of 1783-84; there I found him a very useful member, of an acute mind, attentive to business, and of a high degree of erudition."

A third reason for Williamson's anonymity, Sheldon says, is that Williamson left public life and the national stage in the 1790s. But the man still used his notoriety for good.

He was an original trustee of UNC and served as secretary of its board of trustees for seven years. In the North Carolina State Archives, Sheldon found a letter in which Williamson asked Governor Alexander Martin to grant land to the Davidson family as payment for General William Lee Davidson's service during the Revolutionary War. Martin responded positively to Williamson's letter, Sheldon says. The state donated the land and the family later used it to establish Davidson College.

A fourth reason why many people haven't heard of Williamson, Sheldon says, is that he moved around a lot. He spent his early years in Philadelphia, several years abroad, and sixteen years in North Carolina. Then he married a rich twenty-one-year-old Manhattanite and spent the last twenty-six years of his life in New York, where he wrote a history of North Carolina and more scientific papers, founded the Literary and Philosophical Society of New York, and became deeply involved in charity work mostly on behalf of New York's poor. Williamson also cared for his new family's vast estate, a plantation called Bloomingdale, which today would cover fifty city blocks on Manhattan's Upper West Side.

Sheldon also points out that Williamson had no direct descendents, another possible reason why the man's legacy seems to have slipped through the cracks. His two sons died young—as did his wife—before Williamson passed away in 1819 at the age of eighty-three.

"There's no monument to Williamson in North Carolina," Sheldon says. No towns or boulevards or buildings named after him. "His name is on the obelisk near South Building. And there's a historical road marker in Edenton. And that's it."

The marker reads: "Dr. Hugh Williamson. Signer of the Federal Constitution, member of Congress, historian. His home was 4 blocks SE."

George Sheldon is the Zack D. Owens Distinguished Professor of Surgery and Social Medicine in the School of Medicine. His book is the only biography of Hugh Williamson. Mary Jane Kagarise is associate chair of the School of Medicine's surgery department. Sheldon's assistant, Sidney Holdege, conducted research on Williamson's New York years.

Katie Bowler. Photo by Donn Young.

SALVAGE POETRY

Out of the wreckage, a verse

by Mark Derewicz

State Street. By Katie Bowler. Bull City Press, 23 pages, $10.00.

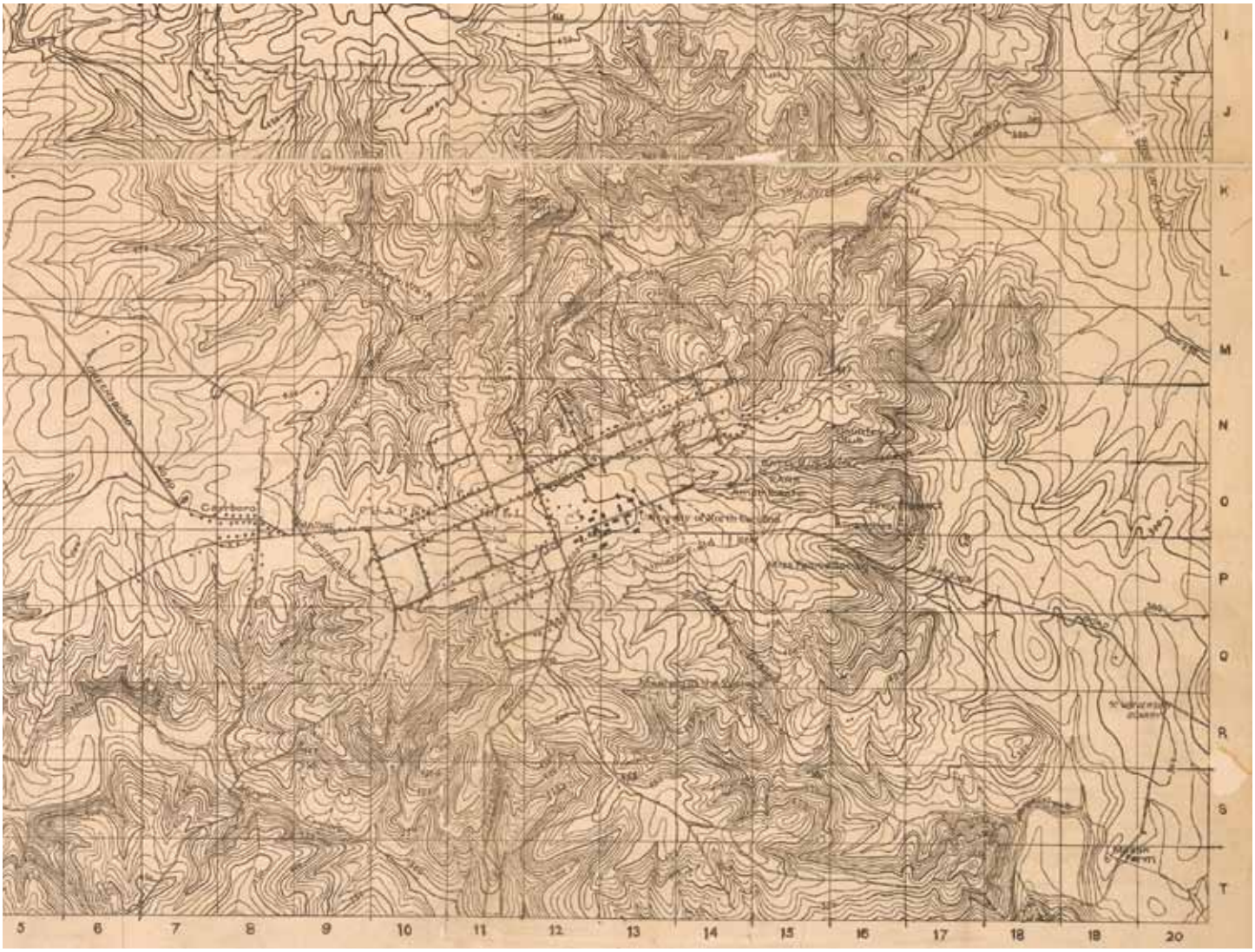
Did you know that even in the twenty-first century
In the United States of America,
There was a time when nobody could buy a plastic bag?
But I've got some garbage bags.
This really is too bad, Donn.
Nobody wants to put their life's work in a garbage bag.

Katie Bowler wrote that passage while helping photographer Donn Young scavenge for what was left of his life's work. Hurricane Katrina had just flooded his studio, and an NBC television news team was following Young through the wreckage. Young had pleaded with his friend Bowler to come along, and so she did, documenting the day as she rummaged for salvageable photos.

Bowler wore a Hazmat suit in ungodly heat and humidity and heaped "armloads of negatives" onto a truck, trying not to succumb to the putrid smell of things rotting. When finished, Bowler cleansed herself by writing a long poem called *State Street*, in which she wove the day's events and her own thoughts of loss into a sort of dialogue with friends and family. Sometimes humorous, sometimes angry, the poem is also about relationships. It's about the fact that nothing is permanent and the only thing we've really got for sure, right now, is us.

Katie Bowler is the assistant dean for communications in UNC's School of Law.

endview



Topography of Chapel Hill and vicinity, Orange County, North Carolina, circa 1918 (detail). On this map you can see the University of North Carolina, Battle Park, Raleigh Road, Mason Farm, University Quarry, too many creeks to mention, and the train station that lay between campus and Carrboro along the Chapel Hill branch of the Southern Railway. The map was surveyed by the U.S. Geological Survey in 1896; T. F. Hickerson and W. F. Morrison made additions to it in 1918. Image: North Carolina Collection, University of North Carolina at Chapel Hill University Libraries

DIGITAL CARTOGRAPHY

A 1584 map of the Southeast. Nineteenth-century survey maps showing details of the North Carolina coastline. Full-color maps documenting 116 towns in 67 counties, down to individual buildings. You can find all this and a lot more at the North Carolina Maps website, a three-year collaborative project to identify and scan nearly every original map of the state published from 1584 to 1923. The collection also contains maps of every North Carolina county and maps published by the state through the year 2000. You can even lay selected historic maps over current street maps and satellite images. "The interactive maps have been a lot of fun," says Nick Graham, coordinator of the North Carolina Digital Heritage Center. "We've even heard from people who have used these to find the location of their homes on hundred-year-old maps."

The North Carolina Collection of the University of North Carolina at Chapel Hill University Libraries produced the site in collaboration with the North Carolina State Archives and the Outer Banks History Center in Manteo. The UNC University Libraries and the State Archives scanned the maps, and the library hosts and administers the site.

www.lib.unc.edu/dc/ncmaps/

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endeavors

Inmate uniforms in storage at the Alamance County Jail. Story on page 40. Photo by Donn Young.