

A Home for the Orphan

by Tim Gray

It looked as if no one would tackle Marnie Kaufman's deadly cancer. So she and her husband declared war and started raising an army.

The bright pink scar traces the contours of Marnie Kaufman's slim neck, stretching nearly from her collar to the base of her ear. For months after her surgery in 2004, she covered it with a scarf — one of her sons couldn't stand the sight.

That scar and her numb right ear allow Kaufman to count herself among the lucky. Her surgeon had warned her that, to save her life, he might have to remove part of the web of nerves beneath her face. The operation could leave her with the droopy look of a stroke victim. But missing any of the cancerous cells that were multiplying in her salivary glands would've risked letting the cancer spread into her brain.

Plenty of victims of Kaufman's cancer — adenoidal cystic carcinoma or ACC — end up horribly disfigured, losing an eye or one side of their face. "People are jealous of me" at patient meetings, she jokes. "I'm the hottie."

That she can laugh is a testament to her determination not to be dominated by a terrifying illness. Instead of surrendering, Kaufman and her husband, Jeff — both of the class of 1987 — have chosen to fight back but not in the usual way. They haven't done bake sales and bike rides. They haven't organized survivors' groups or peddled bright rubber bracelets. Instead, they've created their own foundation and become, in effect, the coordinators of an international research effort into a rare disease.

They've not only raised money but also identified leading scientists and persuaded them to help find a cure for ACC. To that end, they've searched around the world to assemble the ingredients that such a push requires. They've arranged for tumor cells grown in petri dishes — called cell lines by



scientists — to be imported from China. They've persuaded pathologists across the country to contribute other people's tumors to enable the creation of more cell lines. They've enlisted the help of a famed



Jeff and Marnie Kaufman

British institute to determine which genes might control ACC's growth. Along the way, Jeff, an investment manager by trade, has steeped himself so deeply in cancer research that scientists with whom he

speaks sometimes think he's one of them.

The Kaufmans have been aided in their efforts by the sweetest sort of serendipity. Their best friend from Carolina, Dr. Ned Sharpless '88, happens to be a leading can-

cer researcher who works at the University's Lineberger Comprehensive Cancer Center. An expert in solid tumors like melanomas, Sharpless serves on the scientific advisory board of the Kaufman's Ade-

noidal Cystic Carcinoma Research Foundation, which is based in their home in Needham, Mass. He has been their closest counselor since Marnie's diagnosis.

"The magic thing [about the foundation] is Jeff and Marnie's commitment," says Sharpless, who also is a 1993 graduate of the medical school. "They'd ask people, 'To get you to work on this disease, what would help you?' And somebody would say, 'I need some cell lines.' So Jeff would find some cell lines. Every scientist says they need a little money because we all do. So Jeff would find money. Whatever the thing was that they needed, he found it."

In the process, Jeff's friends have helped pioneer a new way of organizing biomedical research that he calls "stewarded science." Through a combination of organizational smarts and gentle goading, the Kaufmans have gotten the world's unruly, decentralized scientific community to focus on a disease that, until they happened along, was mostly ignored. Jeff is considering writing a book outlining the steps that they've taken so people interested in unraveling other rare illnesses can follow them. But that'll come later — for now, he just wants to find a cure for Marnie.

A shattered assumption

Adenoidal cystic carcinoma grows slowly but relentlessly. Its sluggish progression means that that five-year survival rate for its victims — the normal benchmark of a "cured" cancer — is high, typically 80 to 85 percent. Trouble is, it can recur 10 years, even 15, after the initial diagnosis, so a victim is never considered cancer-free. "The good news is that you tend to live with it a very long time," says Chris Moskaluk, a pathologist at the University of Virginia and one of the few researchers studying ACC before the Kaufmans' campaign. "The bad news is that it's very difficult to treat. A surgeon may think that he has it all, but recurrences are very common."

An unusual disease doesn't offer much opportunity for researchers to make their reputations or for drug companies to make money. Cure lung cancer, and you might end up with a Nobel Prize or a blockbuster drug. Cure an obscure cancer — known in medicine as an "orphan disease" because the drug industry doesn't see the incentive to adopt it — and you get a

DAN SEARS '74



thank-you note. On top of that, the common cancers, such as breast and lung, have powerful associations that lobby on behalf of their victims. As a result, the National Institutes of Health, the federal agency that disburses money for biomedical research, will give grants for overlapping studies of these illnesses while overlooking lesser-known ailments like ACC.

"You've got 100 to 200 different types of cancer, and only 15 or 20 get funded research projects from the [NIH's] National Cancer Institute," Jeff says. "I just assumed that there was this rational, fair distribution of research money out there. When you've got 60 different comprehensive cancer centers competing to cure breast cancer, that really sets the dynamic for how research gets done nationally."

Without studies, oncologists have little, beyond surgery, to offer ACC patients. They prescribe radiation but can't guarantee that it helps long-term. The cancer strikes too few people to provide a large enough group for meaningful clinical studies. Even worse, no drugs have been discovered to eradicate ACC or slow its growth.

The one you don't read

Marnie Kaufman, 42, had mild pain for

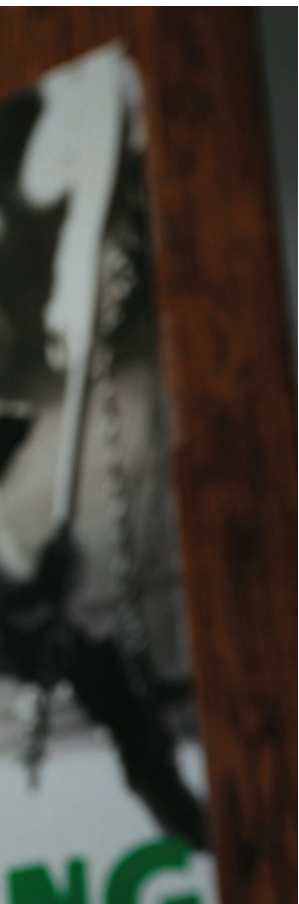
COURTESY OF JEFF KAUFMAN



more than a decade before the telltale lump rose in her neck. By then, she and Jeff, who's also 42, had settled in eastern Massachusetts, where his job as a bond manager with Putnam Investments had taken them.

They'd met at Four Corners, the Chapel Hill eatery, in the last month of their senior year. That summer, Marnie left for a year of teaching in Kenya, while Jeff began a banking career in New York. They wrote back and forth — Jeff even told her of his blind dates — and soon "the letters started to get steamier," says Marnie, who's funny and frank.

When she returned to the U.S., Jeff met her at the airport. They married in 1992



Ned Sharpless '88 in his office in the Lineberger Cancer Center. The Kaufmans turned to their friend for a second opinion. He has been their closest counselor. Jeff and Marnie, he says, have helped pioneer a new way of organizing biomedical research.

At left, Kaufman and Sharpless as Carolina students. The doctor found Marnie to be "just so dignified and strong. You just don't see many patients like that."

and soon moved to Washington, where Jeff had taken another banking job, and Marnie landed one with the National Geographic Society. Jeff's offer from Putnam propelled them to the Boston area in 1994. There, Marnie signed on as a fundraiser for Massachusetts General Hospital. Within a few years, she stopped working to devote herself to raising their four boys, whose ages today range from 5 to 13.

Even before she and Jeff had married, Marnie remembers being nagged by that neck pain. "It was random, like occasional back pain," she says. She'd ask doctors about it, and they'd dismiss it, saying that, without other symptoms, like increasing intensity or a lump, she shouldn't worry.

Then in early 2004, it seemed to worsen just as she caught a cold. A physician diagnosed swollen lymph nodes in her neck, a common cold symptom. But after the illness cleared, her discomfort persisted. So did the lump. She went to see an ear, nose and throat specialist, who told her not to fret because most nodules are benign. But a biopsy brought the bad news — she had ACC.

"You go on the Internet, and that's the one that you don't read because it's so rare, and it's the worst," she said.

Her physician counseled calm, pointing out that biopsies aren't infallible and moving up her surgery a couple of weeks. "We weren't so low-key," she said. "When we got those results, we decided to get a second opinion. We called Ned."

A fortuitous reunion

In his office in Chapel Hill, Ned Sharpless, wearing blue jeans and a button-down, is sitting in front of a poster of The Clash, the famed English punk-rock band. It's an enlarged version of the cover of their *London Calling* album on which one of the group's guitarists smashes his instrument on stage. Sharpless, Jeff's Pi Kappa Alpha fraternity brother at UNC, was no punk or even much of a fan back when the Clash was roaring through rock 'n' roll back in the late '70s and early '80s.

He taped the poster on the back of his door to remind himself and his students that "to do good science, you sometimes have to break a few guitars."

Sharpless combines affability and brashness in a way that's common in physicians. He has a winning candor, volunteering, for

example, his love for the Kaufmans. And his frankness extends to his self-assessment:

He's whip-smart, and he knows it, dismissing the work of "B-plus scientists" who use their "starched white coats" and polite palaver to dupe rich potential donors.

Good scientists — it's a term he uses a lot — let their work, not their clothes or company manners, speak for them, he suggests. You probably have to be self-assured to battle cancer every day, which he does, both as a researcher and a physician. In his lab, he investigates the mysterious ways in which rogue cells divide, and in the clinic, he uses chemotherapy to try to kill them.

He and the Kaufmans had stayed close in the two decades since they'd graduated from UNC. He'd trained in Boston, at Massachusetts General Hospital and the Dana-Farber Cancer Institute. He thus knew many of the physicians whom the Kaufmans might consult. He steered them toward some and away from others. Otherwise, he tried not to sway Marnie's choices.

"There's a saying in medicine that I adhere to for myself and friends and family — 'A doctor who treats himself has a fool for a patient.' I helped them with the foreign language aspects, but I tried not to say that you should do this or that."

Sharpless did tell Marnie that he thought the surgeons at Massachusetts Eye and Ear Infirmary were "a singularly talented group," he says, and she chose them. Her surgery fell during July 2004, as the Democratic National Convention was held in Boston. From her hospital room, she and Jeff watched the fireworks burst above the city and wondered what the future held for them and their sons.

'I'm doing this for me'

Within a few weeks, her radiation treatments began. Oncologists have to pinpoint the photons and electrons that they use to zap a tumor site so they don't sear the surrounding healthy tissue. "They'd bolt me into this mesh mask, and that way, they can draw on it to get the beams lined up," she said. The treatment was painless; the side effects, agonizing. Radiation burns inside her mouth made eating a trial. She choked down Boost and Ensure, high-calorie energy drinks, and still lost 20 pounds. Her face blistered and peeled, as if she had a nasty sunburn.

Sharpless soon visited and, though he

An unusual disease doesn't offer much opportunity for researchers to make their reputations or for drug companies to make money.

Cure lung cancer, and you might end up with a Nobel Prize or a blockbuster drug. Cure an obscure cancer — known in medicine as an "orphan disease" because the drug industry doesn't see the incentive to adopt it — and you get a thank-you note.

routinely sees the ravages of cancer and radiation therapy, was stunned by Marnie's transformation. "She's wearing a scarf, and she didn't look as good as she does now," he recalls. "It really occurred to me that these guys are worried for her life. They're staying up at night, worrying. She's wondering if she's going to see her kids graduate from college. But Marnie, her attitude was, 'We're going to get past this and get on with our life.' She was just so dignified and strong. You just don't see many patients like that. I suspect that that's mostly Marnie and not Jeff. Jeff is a wimp like me."

Jeff was anguished, but he had little time to fret. Even with the help of Marnie's mother, who'd moved in with them temporarily, he faced an exhausting routine. Besides tending to the boys and keeping up with his job, he was logging hours, late into the night, boning up on cancer and ACC. He'd download research papers and puzzle through them. He'd pore over laymen's sites devoted to translating medical knowledge into plain language. He'd fire off e-mails to charities, seeking advice on how best to donate money to finding a cure.

His position at Putnam and the Kaufmans' frugality had given him a larder of cash to contribute, but the lack of attention to the orphan ACC stymied his efforts.

"Jeff was appalled when he realized that there were very few people working on the disease," Sharpless said.

Moskaluk at the University of Virginia was one of the few scientists who'd devoted time to it. His interest had germinated thanks to a mentor who'd pointed out its unusual characteristics. "It even looks different under the microscope," he said. He'd published just three ACC papers, but they'd brought calls and e-mails from patients.

"That's unusual for a behind-the-scenes guy like me." The Kaufmans sent an unsolicited donation, hoping to further his research. Moskaluk's handwritten thank-you note motivated a phone call from Marnie.

"We're talking for awhile," she said. "And I'm realizing that he'd love to do more [on ACC]. I said, 'I can help you raise money. I came from hospital fundraising.' And he was like, 'You would? You'd do that for me. That's so awesome.' And I said, 'Are you kidding? I'm doing this for me. I'm

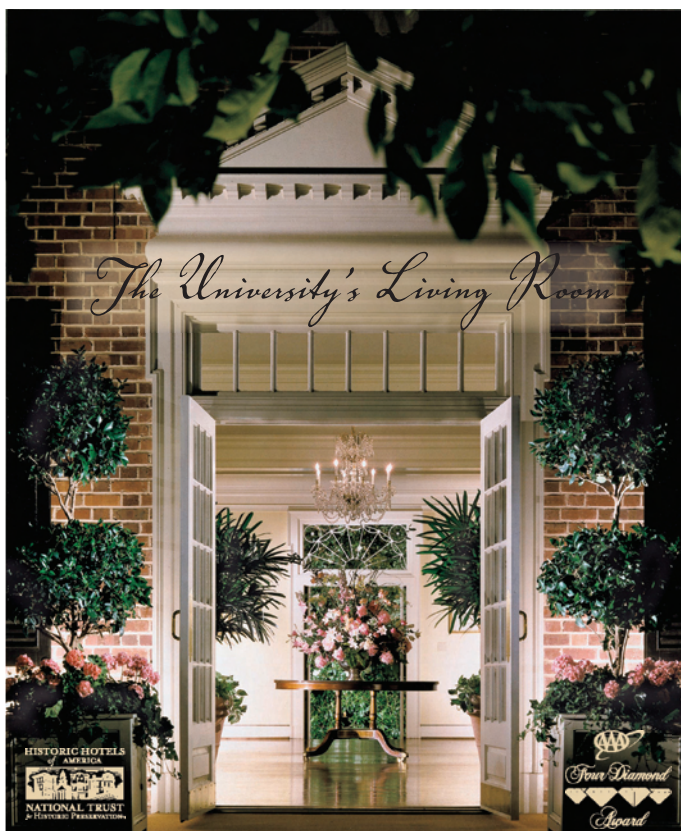
DAN SEARS '74



counting on you. You're going to have to find a way to stop it."

A project approved

One researcher, of course, isn't going to cure a cancer. Science doesn't work that way. Though solo breakthroughs do occur, knowledge of a disease and its treatment typically grows incrementally, as scientists around the world cooperate and compete, with each trying to add some new insight or method. Gradually, a picture of the basic



TRUE BLUE SINCE 1924

What is it that binds us to this place as to no other?

Charles Kuralt - UNC Bicentennial, 1993

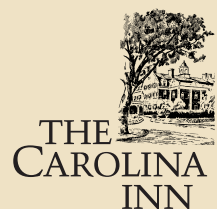
➤ "What binds *you* to this place?" ➤

Alumni Packages Available

MAKING HISTORY

Since 1924

BECOME PART OF A NORTH CAROLINA TRADITION
OWNED BY THE UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL



800.962.8519 | 919.933.2001 | CAROLINAINN.COM | 211 PITTSBORO STREET | CHAPEL HILL, NC



'A lot of scientists don't really care which cancer they work on. They have a system, and they want to use it. They want to discover something with it, and what they work on is just a matter of which cell lines they have in their freezer.'

Dr. Ned Sharpless '88

biology of the cancer emerges, like a mosaic made by a thousand hands. Studies will then commence on chemicals that might cure it, or at least check its growth, without poisoning patients.

Ideally, one of those chemicals will work, and pharmaceutical companies will step in to try to parlay it into a drug.

But too few people cared about ACC for the yeast of creation to ever start bubbling. "In the fall of 2005, we realized that the only way something was going to happen was if we did it," Marnie said. Here, Jeff's background in finance helped them — thanks to it, he saw a novel way to proceed.

A traditional foundation, he decided, would move too slowly. Just raising the money for a self-sustaining endowment — enough cash to throw off sufficient interest to pay administrative bills and fund grants — would take too long. In its place, Jeff conceived an outfit that would operate like a venture capitalist, with a relatively small pool of money that would fund targeted projects designed to produce quick results. "We'd get two to five million that you'd spend over two to five years," Marnie explained.

Like an investor, their little foundation would seek out researchers, as opposed to issuing public invitations for grant proposals, and work closely with its grantees to keep them on track. Small scientific advisory and governing boards would minimize red tape. That'd allow the foundation to rapidly make decisions about grants — an enticement for researchers weary of dealing with elephantine bureaucracies. With the possibility of recurrence chasing Marnie like a hellhound, they didn't want to dawdle.

But would researchers, a famously independent-minded lot, tolerate a foundation telling them what to work on?

Sharpless thought so. "A lot of scientists don't really care which cancer they work on. They have a system, and they want to use it. They want to discover something with it, and what they work on is just a matter of which cell lines they have in their freezer." A new ACC cell line could work as well as the 501st breast-cancer line.

Plus, money would motivate them. Scientists need grants to sustain their labs, just as Starbucks and Wal-Mart need customers queuing up in their stores. The Kaufmans'

"I help prevent child abuse and neglect."

Rachel Foster, doctoral candidate, is one of many dedicated students and faculty at the UNC School of Social Work whose research projects are designed to assist and strengthen North Carolina's communities and families.

As our state's population grows, the number of vulnerable individuals, families and communities grows as well. Now, more than ever, North Carolina needs well-trained social workers.

An internationally renowned faculty, a rigorous master's and doctoral curricula, and a diverse, outstanding student body have established the UNC School of Social Work as a leader in public service, education and research. Year after year, *US News & World Report* ranks our School as one of the nation's top programs.

The UNC School of Social Work: preparing social work leaders for today and tomorrow.



UNC
SCHOOL OF SOCIAL WORK

For information about the School and how you can support our programs, please call (919) 962-6469 or visit our Web site at <http://ssw.unc.edu>



timing, in that regard, turned out to be fortunate. The NIH's research budget has stagnated lately, in inflation-adjusted terms. It had previously grown fast, prompting a big buildup in medical research centers.

"So there's a large group of well-trained biomedical research folks who aren't getting the NIH funding they'd expected," Jeff said. "Eight years ago, they could just go to the NIH and say, 'This is what I want to study' and get funding. Now they can't do that. Now they're more likely to say [to us], 'Oh, I'll do that project.'"

Sharpless says the foundation has another advantage that's just as critical: Jeff. He has the smarts that you'd expect in a guy who makes his living by betting on the bonds of developing countries but also a humility that's uncommon among Wall Street-types. "A lot of rich, smart guys think they can do it all themselves," Sharpless said. "You know, 'I'm an alpha male, and this is how we're going to do it.' But smart guys who don't understand science, those guys are vulnerable." Scientists let them swagger and posture, offer vague assurances, take their money and then keep

doing whatever they were doing before.

"But Jeff listens, and at the end of the day, he decides what he wants to do in a dispassionate way." And he has doggedly sought out researchers who might be able to contribute to his understanding or the foundation's efforts at collecting tumor samples, creating cell lines and producing mouse models — lab mice that grow ACC tumors.

"Jeff visited, I think, every head-and-neck pathologist in the country," Sharpless said. "He'd ask, 'You got anything frozen?' Scientists are usually protective about their stuff. But his passion was contagious. He got people to agree to send stuff."

The foundation's advisory board laid out the research agenda, suggesting the kinds of studies to fund, the order and whom to approach to do them. Sharpless believed that a priority had to be sequencing the gene that mutated to cause ACC. He and the other board members decided to approach Andy Futreal, co-head of the Cancer Genome Project at the Wellcome Trust Sanger Institute in England, to see if his lab would do the work. Sanger is one of the world's leading genomics centers.

"The first time I called him, I thought I'd be talking to some British dude," Sharpless recalled. "It turns out he's got an Andy Griffith accent." Futreal grew up in rural Duplin County, near Warsaw, and earned his doctorate at Carolina in 1993. He agreed to help with the Kaufmans' search.

Sharpless also encouraged Jeff to approach Ed Harlow, chair of the Harvard Medical School's department of biological chemistry and molecular pharmacology. Harlow, whom Sharpless calls a "Nobel-caliber scientist," is an expert in RNA interference, a biochemical process that can turn off individual genes. Jeff phoned Harlow, and their two-hour chat led to a lunch meeting and a proposal from Harlow for a project that the board approved within two days.

As of early summer, Harlow's lab had identified a list of genes that seemed crucial in the development of ACC and was continuing with its investigations.

Someone to tell the story

Though the Kaufmans have chosen to emphasize research, not advocacy or patient support, they do need publicity for their



Friday

Driven to fulfill a promise. When Horace Sewell-El withdrew from community college 27 years ago, the woman behind the desk in the registrar's office made him promise that he would go back to school someday and complete his degree. Year after year, taking one or two Carolina Courses Online classes at a time, Horace has been inching his way towards a degree in anthropology. Soon he will reach his goal and fulfill that long-ago promise.

At the Friday Center for Continuing Education, we understand the courage it takes to return to school after many years, and the commitment it takes to open a textbook after a long day at work. Hard work has its rewards! Let us help you get started as a part-time student. Visit fridaycenter.unc.edu/cp or call 866-441-3683 to schedule an appointment with an advisor.



UNC

THE WILLIAM AND IDA FRIDAY
CENTER FOR CONTINUING EDUCATION

[Credit Programs for Part-time Students](#) | [Conference Center](#) | [Professional Development and Enrichment Programs](#)

efforts. It helps them connect with people who might contribute money, tumor samples or scientific expertise. Marnie, with her background in nonprofit fundraising, has taken the lead there. Though she still devotes much of her time to raising their boys, she writes many of their media materials and fields calls from other patients. She also reaches out when she sees a promising opportunity, as she did in March 2006, when she read a story titled “Cry in the Dark” in *The Wall Street Journal*.

The writer, Amy Marcus, had long covered cancer, particularly patient advocacy, for the newspaper. With this story, she offered a personal account of her own mother’s fight with a rare gall-bladder tumor. Marnie saw an opening to share her story, solicit Marcus’ advice and maybe get coverage of what she and Jeff were doing. “I sent a huge e-mail back to this link on *The Wall Street Journal* Web site. I started out, ‘Dear Amy,’ and Jeff was like, ‘Don’t you mean Ms. Marcus?’ I’m like, ‘Nooo.’ I wrote like five pages. And he was like, ‘She’s never going to read it.’ I wrote about what was going on with us and that we’re start-

ing this foundation. Three days later, I get this e-mail back, and it was, ‘Marnie, I just moved to Needham. Do you want to meet at Starbucks?’ So we did.”

Marcus makes it a practice to answer reader e-mails and was impressed with the amount of time Marnie appeared to have taken with hers. Plus, the Kaufmans’ idea — and the obstacles they faced — did seem like a compelling story.

“I was interested in the idea that she said that when you have a rare cancer it’s hard to get researchers involved even if you come up with money,” Marcus said. “You’d think that anybody would be willing to take money.” After chatting with Marnie and then meeting with Jeff, Marcus decided to follow their efforts and write about them. Her story appeared in May 2007.

Marcus says the Kaufmans have devised an ingenious way to overcome the indifference and inertia that often defeats efforts to study an unusual disease. “The way they’ve gotten around it is by having a scientific advisory board that was very strong and basically contracting and directing what they wanted,” she said.

Last year, Jeff decided to take a leave from his job at Putnam to devote himself to the foundation full time — a downside of inventing a new way of doing business is the hefty investment of time required.

“Instead of nudging two or three projects along every couple of months, I knew that I needed every week to be nudging eight or 10.” Plus, he said, “What else could be a better use of your time than keeping your family together and happy?” He’s pondering the right time to return to his job and believes he has shepherded the research through its critical startup stage. Now the scientists have to be given time to do their work.

“The crucial aspect of what we’ve done that can’t be reversed is that we’ve brought together the building blocks, the things you have to have to do research on any disease — the cell lines and the mouse models. They really didn’t exist before. There are all of these cutting-edge technologies that you can use, but you can’t do that unless you have the building blocks. Researchers globally now have access to these building blocks.”

Does that guarantee a permanent cure

GROWING GREEN... BUILDING GREEN



The North Carolina Botanical Garden is building an environmentally sustainable Visitor Education Center. This building will put Carolina at the forefront of environmental sustainability, and you can be a part of it.

NORTH CAROLINA BOTANICAL GARDEN
THE UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL

To learn about naming opportunities, please call 919-962-9458. For general info about the North Carolina Botanical Garden and our sites such as Coker Arboretum and Battle Park, visit www.ncbg.unc.edu and call 919-962-0522.



COURTESY OF MARNIE KAUFMAN

‘The crucial aspect of what we’ve done that can’t be reversed is that we’ve brought together the building blocks, the things you have to have to do research on any disease — the cell lines and the mouse models. They really didn’t exist before.’

Jeffrey Kaufman
'87

for Marnie, who remains in remission, or anyone suffering from ACC? Of course not. But Bruce Chabner, clinical director of the Massachusetts General Hospital Cancer Center and a member of the Kaufmans’ scientific board, believes it increases the likelihood. As evidence, he points to a rare cancer called GIST — gastrointestinal stromal tumor — and a drug called Gleevec. “No one knew how to treat GIST,” he said. “Then some people created some cell lines and tested an existing compound against them, and it controlled the disease. The drug is Gleevec. It was a drug already used for leukemia.” In theory, now that cell lines exist for ACC, they, too, could be tested against existing drugs and other promising chemical compounds.

No free time to worry

It’s March, and the Kaufmans are sitting in the kitchen of their comfortable Colonial-style house, talking about the emotional toll of the past four years. They’re clad in jeans, and Marnie has baked cookies. Spread across the table are the charts that Jeff, who’s as organized as a card catalog, has created to explain ACC, the foundation and the research process.

A TV murmurs in the adjacent den, as the older boys watch a basketball game, and their younger brothers try to pay attention but mostly bother them, eliciting the occasional visit to the kitchen for a big-brother

consult with mom and dad.

“For me, the cancer is there forever,” Marnie says. “It’s a chronic condition. I was talking with my radiation oncologist, and I know the numbers. The prognosis is bad, so I didn’t want to hear that from him. I wanted to know, ‘What’s the best thing that you can tell me?’ He said, ‘My hope is that you live a long and full life, and you’re not too inconvenienced by this.’ I have to go back and be seen for the rest of my life. I get scanned twice a year forever. So yeah, we’re bringing more of it in than sometimes we can handle. Sometimes it gets really tough for me. Fortunately, with the kids, we don’t have the free time to worry too much.”

“Yeah,” Jeff chimes in, “you’re starting to go down the deep well and one of them ...”

Marnie jumps back in, “... needs you to wipe him.”

“Or he’s just wet his bed.”

“It helps you regulate it all a little bit.”

Just then, commotion in the den prompts Marnie to excuse herself to go in to investigate. A couple of minutes later, she returns to the kitchen, beaming: “State just beat Duke.”

She lifts her hand, palm outward, and offers Jeff a high five. ■

Marnie and Jeff have their hands full with four boys. “Fortunately, with the kids, we don’t have the free time to worry too much,” she says.

TIM GRAY is a freelance writer based in Boston. More about the Kaufmans’ foundation is available online at accrf.org.