Phi Kappa Phi FORUM
A QUARTERLY PUBLICATION

Cancer Research

Winter 2003

NATIONAL CANCER INSTITUTE
Extraordinary Opportunities in Cancer Research

JOHN WAYNE CANCER INSTITUTE
Combating Cancer Drug Resistance: The Ceramide Connection

JOHNS HOPKINS UNIVERSITY
News from the Sidney Kimmel Cancer Center

DUKE UNIVERSITY MEDICAL CENTER
Stem Cells: Working to Improve Nature's Miracle

Phi Kappa Phi FORUM

Phi Kappa Phi Forum Mission Statement

The purpose of the *Phi Kappa Phi Forum* is to enhance the image of The Honor Society of Phi Kappa Phi and promote the pursuit of academic excellence in all fields through a quality, intellectually stimulating publication for its membership.

The views expressed in this publication are not necessarily those of the staff of *Phi Kappa Phi Forum* or the Board of Directors of The Honor Society of Phi Kappa Phi.

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The Honor Society of Phi Kappa Phi was founded in 1897 and became a national organization through the efforts of the presidents of three state universities. Its primary objective has been from the first the recognition and encouragement of superior scholarship in all fields of study. Good character is an essential supporting attribute for those elected to membership. The motto of the Society is *philosophia krateitō phōtōn,* which is freely translated as "Let the love of learning rule humanity."

Phi Kappa Phi encourages and recognizes academic excellence through several national programs. Its flagship National Fellowship Program now awards more than $460,000 each year to student members for the first year of graduate study. In addition, the Society funds Study Abroad Support Grants and Internship Support Grants, awarded to deserving undergraduates, as well as Promotion of Excellence Grants awarded to faculty projects that research and promote academic excellence. For more information about how to contribute to the Phi Kappa Phi Foundation and support these programs, please write Perry A. Snyder, PhD, Executive Director, The Honor Society of Phi Kappa Phi, Box 16000, Louisiana State University, Baton Rouge, LA 70893 or go to the Phi Kappa Phi web page at www.phikappaphi.org.

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The Honor Society of Phi Kappa Phi Mission Statement:

Recognizing and Promoting Academic Excellence in All Fields of Higher Education and Engaging the Community of Scholars in Service to Others

The cover photo of a pathologist at a microscope, by Bill Branson, was obtained from the National Cancer Institute's NewsCenter website and was digitally enhanced by Laura J. Kloberg.

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Letters to the Editor

Phi Kappa Phi Forum publishes appropriately written letters to the editor every issue when submitted. Such letters should be 150-300 words in length.

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A Note from the Editor

James P. Kaetz

AN UNWELCOME PHONE CALL: MY OWN CANCER STORY

In July of 1997, I had what was supposed to be routine surgery to have what everyone assumed to be a fatty cyst removed from underneath the skin on the back of my head. It was outpatient surgery and was performed by a highly recommended plastic surgeon, Dr. Robert Brown. My greatest fear at the time was that the hair around the incision would have to be shaved, and that when it grew back it would be some odd color. As it turned out, the surgeon did not have to shave anything at all.

About a week after the surgery, I was sitting here in my office doing some task that I don't even remember when I got a phone call. It was Dr. Brown. He said that he was afraid he had some bad news; my "fatty cyst" was instead a malignant tumor. It had tested strongly for melanoma, skin cancer, a form of cancer that is being increasingly diagnosed among baby-boom sun-worshippers (yet a sun-worshipper I definitely had never been).

It is hard to describe the reaction I had to the doctor's words. Stunned disbelief probably would sum it up best, followed by a gut-dropping terror and depression. You see, I had just watched a good friend die of lung cancer, and not a year before another friend had died of the same thing. One was a smoker; one had never touched a cigarette. My wife's mother had also recently died of breast cancer, and we were pretty sick of hearing about this disease. At the time of the call, I was forty years old. I had never smoked (other than a very brief period of pretentious grad-school pipe-puffing), exercised regularly, and could count on the fingers of one hand the times in my life I had been badly sunburned. The news that I received that day was totally unexpected.

The next few days were a blur — having to make all the "calls," especially the one to my wife, was the worst part, along with the nightly terror and the tremendous sense of the unfairness of it all. The visit to the surgeon to talk about what was next certainly did not help us feel any better, and in fact only added to the puzzlement. He informed me that this lump, because it was under the skin, had to be considered metastatic melanoma, because it generally only gets under the skin after it has first begun on the surface. The thing was, after a thorough examination of every square inch of my body, he could find no originating site. Dr. Brown said that melanoma was one of the oddest forms of cancer in some ways, and that in about 5 percent of cases, an origin is never found, as proved to be the case with mine. But that still did not change his opinion that its being under the skin was very bad.

The next step was the surgery. I was to have a wide patch of skin removed from the area surrounding the now-excised lump, and a skin graft from my hip placed there. That meant that I would never have any hair on the back of my head again — so much for my worry that it would come back some odd color. In addition, I was to have what is known as a radical neck dissection, where the lymph nodes in the left side of my neck and left shoulder would be removed and sent off for testing. Needless to say, none of this news made me or my wife happy at all.

Thus it was that in the summer of 1997, instead of enjoying the Phi Kappa Phi Centennial Celebration in New Orleans, I was lying on a hospital bed in a drugged stupor, literally unable to lift my head except by picking it up with my right arm, with my back cramping severely from lying in the same position, catheterized, and pretty much unhappy with everything. The only positive thing was that the surgery was over. During the neck dissection, three nerves had to be cut and moved, as well as a muscle removed completely; to this day, I have no feeling in much of the left side of my head and neck, as well as on the top of my left shoulder. The shoulder itself fatigues more easily because of the missing muscle.

About the third day in the hospital, when I was feeling much better, most of the tubes had been removed from various parts of my anatomy, I was finally able to go to the bathroom, and friends were even beginning to make cautious jokes about the tales I could make up to explain the mess that was the back of my head, we received the first good news that we had had in the whole process: No other melanoma had been found in the surrounding tissue or in any of the lymph nodes that had been removed. None of my earlier X-rays or an MRI had shown any internal involvement at all. Technically, I was cancer-free. The lump being right up against my skull actually had been a fortunate thing — as my surgeon put it, bone is a great barrier.

On the advice of Dr. Brown, over the next seven months I went to Duke University Medical Center's Melanoma Clinic, where I received a course of immune-system therapy that consisted of injections of dead and treated melanoma cells designed to stimulate my body's T-cells to fight any new melanoma cells that it found — a cancer-vaccine clinical trial. We

tried to make these trips, about an eight-hour drive from our home in Auburn, Alabama, into adventures. We visited a number of friends whom we had not seen in several years, and I got to show my wife the campus at UNC-Chapel Hill, where I had spent five years getting a PhD. The fun was tempered, of course, by the reason for going in the first place, but at least some good came from it.

In the ensuing five years, which is considered the critical period for recurrence and after which one is considered indeed cured — of that particular incident, at least — there were scares: a shadow on an x-ray that proved to be nothing, a lump on my neck that turned out to be a nerve bundle caused by cutting the nerves during surgery. Most recently, in July 2002, I had surgery to remove another lump from my neck that everyone seemed to think was a problematic lymph node but turned out to be still another nerve bundle. And now I am officially past my five years and considered cured.

In the meantime, cancer has visited us again. My wife's friend and colleague died just last year from lung cancer so advanced before they found it that it was already in her brain. Chemotherapy and an iron will brought her an extra year of life, but ultimately her body simply wore out.

My doctor kept telling me, after he found out that I edited a magazine and was an English PhD, that I should write about my experience. But I never really wanted to do so, and if it were not for us doing this issue, I might never have. I keep thinking that somehow writing about it will jinx it. But I know that is superstitious and absurd.

So how has this experience changed me? Well, I would like to say that it has made me more aware of each moment in life and has made me a better person all around. But I cannot truly say that. It certainly has made me aware of how precious time can be, and every now and again I am stopped short by the realization that even if I am lucky enough to have another fifty years to live with my wife, it still will not be enough. But fundamentally the experience has not changed me; maybe I was a pretty good person before.

The one thing I have discovered is that the fear never entirely leaves you. Every time I go for my now-yearly chest x-ray, I fear that this time something might show up. Every time I go to the dermatologist for my extremely thorough visual examination (How thorough? A strip search could not be much more intrusive), I worry that I will hear a sudden intake of breath and a dreaded pronouncement. Maybe in ten years, if all remains clear, I can lose some of that fear. And I can only hope that continued strides in research, like those described in the articles in this issue, will some day make it so that no one will ever have to fear cancer again.

IN THIS ISSUE

To lead off, Peggy Vaughn of the National Cancer Institute discusses some of the many initiatives that are being conducted and supported by the NCI. These initiatives include work at the genetic and molecular levels, new imaging techniques, further research on the tobacco/cancer link, and so on.

Next, Gregory Vogel, writing for the John Wayne Cancer Institute, explains the work being done on solving the problem of cancer cells developing resistance to chemotherapy drugs. A drug that is effective the first time around in battling a patient's cancer often loses its effectiveness if the cancer recurs because the cells that survived the first round are the ones with natural resistance to the drug. John Wayne researchers are targeting ceramide, a naturally occurring substance that seems to play a large role in cancer cells developing resistance, with the intention of neutralizing it so that cancer-fighting drugs remain effective.

Vanessa Wasta then delivers news from the Sidney Kimmel Cancer Center at Johns Hopkins. She tells us of research that has pinpointed the gene that may trigger one particularly aggressive form of cancer, the establishment of a cancer education and prevention center, and work on detecting a virus linked to about a quarter of all head and neck cancers.

Finally, Becky Levine of the Duke University Medical Center tells us of the work of Dr. Joanne Kurtzberg on stem cells and their possible therapeutic use in a number of diseases in children, including immune-system deficiencies and blood-borne cancers. One of the areas Dr. Kurtzberg is focusing on is coaxing stem cells to develop into T-cells that the patient's body will not reject; T-cells, of course, are the primary fighters of infections of all kinds in our immune systems.

And in a very special "Lagniappe," associate editor Stephanie Bond shares with us the story of losing her husband, Gordon, to lung cancer, and wonders where lung cancer's celebrity spokesperson might be.

APPRECIATIONS

In addition to the people who actually wrote for this issue, we want to thank Deborah Shore of the John Wayne Cancer Institute, Caroline McNeil of the NCI, and Vanessa Wasta of the Sidney Kimmel Cancer Center for making sure that their institutions were represented. We also want to thank the people at all four institutions who took the time to talk about their work and review the articles sent to us. We know that their time is precious as they lead the fight against cancer.

And we bid adieu to the second half of our current columnists: Terry Palardy, Charles Davis, Daniel Berger, and Robert Burns. We are so appreciative of their wonderful work during the past three years; it is hard to believe that their time is up.

Also, thank you to all the people who volunteered to replace our outgoing columnists. As usual, the choices were difficult, and we hated to turn away any offer of help at all. Introduce yourself to our new columnists on pages 12 and 13. They will begin writing with the Spring 2003 issue.

In addition, this marks the first issue of the *Forum* to carry outside advertising. We plan to carry ads that forward our mission in some way, and we welcome member institutions to place ads to let all members know of their excellent programs and publications.

Enjoy the issue! Schedule that complete physical, which you have been meaning to get, soon. And always wear sunscreen.

Forum on

Education & Academics

Terry Palardy with Floyd McManus

Questions Worth Asking

In the dim morning light of late winter, the sun barely over the horizon, the day begins with a line of cars competing with the foot traffic and buses in the middle school parking lot. Inside the cafeteria window, the principal sits at a table watching the arrivals, his pen lightly tapping a notepad, his brow furrowed. As he watches, some parents share quick hugs with their children; others seem to be giving words of advice or reminders of after-school plans.

The teacher watches from the same window as the edge of last night's storm slips eastward, and faint rays of light begin to crown the tree branches on the hill. She walks toward the table and glances at the principal's notes.

"What are you writing?" she asks, sliding into the opposite bench.

He turns back from the window. "An article for the parent newsletter," he answers, moving the notepad toward her. "I had a thought in mind when I began, but I'm not sure it's coming across. Take a look."

She begins to read:

> A middle student leads a very complex life, for early adolescence marks the beginning of a child's quest for independence and all that this implies. Not only is this the age of the onset of puberty but also a time of new social and intellectual demands. Every decision, every reaction is colored by a need to show at least a modicum of self-reliance, which, in turn, often creates an unwelcome feeling of vulnerability. The events of this crucially formative phase can shape an individual's life course.
>
> It is one of the most fascinating and complex transitions in our life span: a time of accelerated growth and change, second only to the first year of life; a time of expanding horizons, self-discovery, and emerging independence; a time of transformation from childhood to adulthood. Its beginning is associated with biological, physical, behavioral, and social transformations.

"They really are very important years, pivotal in so many ways — and what we do, and what the parents do, are critical parts of the experience. Is that what you're going for here?" she asks.

"Yes, but more than that — read on."

> Barely out of childhood, young people ages ten to fourteen attempt to experience more freedom, autonomy, and choice than ever, but it is also a time in their lives when they still need special nurturing, protection, and guidance. Without the sustained involvement of parents and other caring adults in safeguarding their welfare, young adolescents are at risk, at the very least, of not achieving to their full potential.

"You're reminding parents here that the job is far from finished — that these are not the years that allow parents to step back and admire the job?" She looks back at the parking lot, watching the attentive parents and their children.

"No — I don't think they would step back," he says thoughtfully. "The parents remain invested in their children's education. The community does as well. They pay a great deal of attention to academic achievement, to musical accomplishment, to athletic skills, to community spirit. I'm sure that many of those parents outside are asking their children whether they have the materials for the day, whether they are ready for a quiz, whether they are going to score points on the basketball court. I don't doubt their interest in motivating the children to do their best in those areas.

"The point I want to make is that the affective development of the students is just as important and is due as much recognition and support as the other areas of growth." He turns back to the window.

She slides the notes back across the table toward him. "You're right. Our world is witnessing enormous growth in the number of students who go on to higher education, and those students often go to college with multiple pages of extracurricular skills and talents developed over years of scheduled, structured, and supported activities. However, those impressive résumés don't often list the qualities of kindness, of generosity, of friendship, of the sharing with and caring for others that we see in our students. These are also skills and values waiting to be cultivated, developed, and recognized in our communities. Social creatures that they are, adolescents are well-tuned to each other's emotions and needs, and often display great care. They are approaching the ability to experience and act on true empathy, and this is something to be celebrated, here at school and out in the community."

They both watch as another stream of children exits a bus and hurries along the slushy path, laughing, sliding, juggling backpacks and musical-instrument cases and poster boards in mittened hands, holding the door for each other. As they watch, the sunlight reaches beyond the trees and brightens the colorful caps and smiling faces of their students.

"You might add a section that speaks to the type of morning conver-

sations parents have out here with their children," she says, nodding toward the scene that they are sharing. "You could suggest that if parents included questions in their repertoire that highlight these affective qualities, the children themselves would recognize that the development of kindness, of generosity, of goodness, of friendliness and helpfulness, is as valuable as the development of other skills and talents."

"I was just thinking of those questions," he answers. "If the children were asked by their parents each evening, 'Did you help anyone today? Was someone kind to you today? Did you befriend anyone today? Was there anything that you did or could have done to make this a great day for someone else?' I think these are questions worth asking."

The sun reaches the long cafeteria windows just as the last wave of students floods into the school. The principal gathers his notepad and pen, and the teacher collects her jacket and bag, and they turn to walk toward the corridor door.

"Did you tell me that you are writing one more column for your journal?" he asks her as they cross the cafeteria.

"Yes — the last one. Do you have any ideas you'd like to share?"

They continue to talk as they walk. A student holding the door for them seems to be listening in. The bell rings.

Terry Palardy is currently a middle school teacher in Massachusetts. Mrs. Palardy has taught elementary, special education, and graduate school classes. Her e-mail address is tepalardy@aol.com. Floyd McManus is the principal of Doherty Middle School in Andover, Massachusetts.

BIRCH GRAVE

I saw the birches where they fell for good,
striving uphill, as if to assault the sun.
Logs don't last very long in the ravenous wood.
And still, they mark where something once begun

has ended. The look of an animal euthanized —
or a man who's tripped on the stairs — immense surprise,
and all the gestures of normalcy preserved,
only their lithe, white forms are unnerved

by the way the leaves have all deserted them.
Some continue shedding bark that's pink
like insulation, even as light slips

from a streaked sky — all will rot in common,
those velvet epaulettes now seeming the print
of something ominous, of blackened lips.

K.E. DUFFIN

K.E. Duffin's poems have appeared in *Poetry*, *Partisan Review*, *Ploughshares*, *The Sewanee Review*, *Verse*, and many other journals. In 2001, she was a finalist for the National Poetry Series, the Walt Whitman Award, and the Colorado Prize. In recent years she has had residencies at The Millay Colony and Yaddo.

Forum on Business & Economics

Charles K. Davis

MBA Certification: Boon or Boondoggle?

An organization called the International Certification Institute (ICI) of Mocksville, North Carolina, recently made a very big splash in the world of business education by announcing its intention to provide and promote a certification exam for candidates in, or graduates of, Masters of Business Administration degree programs. The idea has been compared to medical boards for doctors or the bar for lawyers, a way of measuring and assessing an MBA's fitness to serve and of holding MBA schools accountable for what they teach. In a world wracked by the Enron, Tyco, and Worldcom scandals, this idea has a certain appeal. But it also raises some hard questions.

THE MBA: BUSINESS BOOTCAMP

First, let's consider what an MBA degree really is. The MBA degree was originally envisioned as a vehicle for providing solid business education to individuals who had earned undergraduate degrees in non-business areas. As professionals in any field rise to positions of leadership and business responsibility, they begin to realize that they may not progress much further in their careers without an understanding of the principles and methods of business. This demand first materialized in the engineering professions, and schools of business designed the MBA degree initially for engineers. For example, when engineers became managers in engineering or manufacturing firms, they could pursue the MBA both to gain an understanding of business for their work and to prove to all potential critics that they were prepared and indisputably qualified to manage. Other professions were not far behind — lawyers running law firms, artists running art galleries, computer scientists running computer companies, even doctors running clinics or hospitals. Most of these people came to the MBA classroom with little or no formal business education. And they had to learn everything from scratch.

So, what is an MBA? The MBA is a business "bootcamp" that crams most of an undergraduate business degree, plus advanced coursework in one's major (often called a "concentration"), into an intense two-year, full-time program. The first year of most MBA curricula is similar in that business foundations in each subject area must be covered. The first year or so generally includes basic courses in accounting (financial and managerial), economics (micro and macro), management (including organizational behavior), management science (which includes sophisticated business statistical methods), marketing, information systems, and a basic course or two in business law. All degree candidates take this (or a similar) sequence. In most cases, these foundational courses must be completed successfully before moving on to the upper-level coursework in the second year of the MBA.

Even within this framework, though, the potential for variation is significant because different schools emphasize different areas of specialization. The content of the basic courses can vary importantly and legitimately from school to school. This difference is illustrated by the so-called Techno-MBA degrees that were all the rage a few years back, in which mathematical modeling and information technologies were strongly emphasized across the MBA curricula of some schools.

THE ICI'S GOALS AND OBJECTIVES

ICI believes that its certification program, the CMBA, will inspire confidence in an MBA-qualified job candidate's mastery of basic business skills and thus in the candidate's performance potential on the job. The Institute further maintains that the CMBA confirms for MBA students and employers alike that the candidate has a certifiable command of business fundamentals and is "Certified for Success" (their words found on www.certifiedmba.com at the time of this writing). ICI also believes that a certification of MBA graduates can "level the playing field" and make it possible for MBAs from less-prestigious universities to compete with graduates of the top tier, neutralizing the effect of graduate-program reputation in hiring.

These are lofty claims. There is no doubt that, with the economy in decline, an abundance of MBAs is available in the job marketplace. Employers would love to have a way to differentiate between the ones that will be most successful in their businesses and those who will not. At first blush, the idea is interesting because of this hiring quandary. If employers could know, on the basis of an objective test, who is likely to be successful and who is likely to fail, then such a certification would be valuable indeed. Such testing could alleviate a fundamental and costly problem in personnel management, that of hiring the wrong person for a key job.

PROBLEMS WITH ICI'S APPROACH

ICI proposes to assess the business understanding of an MBA candidate or a recent graduate. How can this be accomplished? The Institute proposes to develop an exam to verify mastery of the core material in typical MBA coursework. This verification (they say) would include assessing

one's understanding of financial reporting, analysis and markets, human behavior in organizations, and a few other first-year topics that are usually taught in MBA curricula. The focus is on testing one's understanding of the common foundational material found in most MBA programs.

It is difficult to see how one can make the logical jump from testing someone's grasp of first-year basics to predicting that person's ultimate success in a business organization. Suppose we actually do test a group of MBAs in this way. Assuming we get a range of scores on the exam, what precisely would a high or low score on such an exam tell us? More importantly, what would it tell us about individuals' potential for success beyond their undergraduate GPA and, for that matter, their MBA GPA as well?

Also, it should be noted that the overall curriculum of an MBA degree varies widely from school to school. Most MBA's include a concentration or even two, in subject areas such as accounting, marketing, management, information systems, finance, and the like. Companies hire people in business to do specific jobs based upon their advanced coursework in these areas of concentration. ICI claims that the CMBA could help businesses better evaluate MBA job candidates and improve their MBA hiring decisions. But it is difficult to envision how one could better screen candidates for (say) an accounting position using a test that by definition does not test advanced accounting theory, principles, and practice. The same is true for the other disciplines. It simply does not seem possible that such a test could provide much, if any, additional insight into an MBA's understanding and content knowledge that would be relevant to the hiring decisions at corporations.

Now, could such a testing program really level the playing field between the top-rated business schools and lesser institutions? This claim is also very difficult to substantiate. How could such a test possibly make an Emory or Penn State MBA equivalent to a Harvard or Stanford MBA in the eyes of corporate recruiters? Nothing against Emory or Penn State; they are fine schools. But a test over some standardized first-year MBA curriculum is simply not going to matter at all to corporate recruiters in this equation.

The question of standardization really gets to the heart of the issue. Who decides the standard for the first-year curriculum anyway? Certainly not ICI, I suspect. In an Associated Press article on the subject (S. Giegerich, 10/29/02), several business-school administrators decry the specter of business-school faculties "teaching to the test." A standardized test, they argue, would pressure schools to conform to whatever standard had been assumed in creating the test, limiting flexibility and adaptability in curriculum as business practices and technologies evolve in the future. This kind of standard would be a dangerously restrictive idea for universities, and I cannot imagine colleges of business moving in this direction.

What about the idea that a CMBA is something like the medical boards for doctors or the bar for lawyers; does this make any sense? I do not think that the medical boards test one's mastery of just the first year of medical school, and the bar exam certainly goes well beyond the first year of law-school instruction. Also, one cannot even practice these professions legally without passing the required boards. That is certainly not the case with the proposed CMBA.

WHAT RECRUITERS REALLY WANT

The Wall Street Journal and Harris Interactive surveyed corporate recruiters on the attributes that they believed were most important in hiring decisions for MBAs (www.harrisinteractive.com/bschools/). The top ten in a long list of results from the survey in descending order of importance were the following: Communication and interpersonal skills, ability to work well on a team, analytical and problem-solving skills, ability to drive results, quality of past hires from a given school, leadership potential, fit with the corporate culture, strategic thinking, likelihood of recruiting stars from a given school, and "chemistry" (that is, the recruiter's general like or dislike of the candidate). In addition, *BusinessWeek* annually ranks university MBA programs (www.businessweek.com/bschools/). The procedures used for these rankings reiterate the importance of teamwork ability and the importance of analytical skills in hiring decisions. The *BusinessWeek* ranking procedures also focus attention upon understanding ethical issues as a key factor in recruiting today's MBAs.

It seems very unlikely that a test devised to measure one's understanding of the first year of course content in a hypothetical standardized MBA curriculum would measure any of these critical factors beyond a purely cursory level. Yet these are the capabilities that really matter in corporate recruiting. Furthermore, it does not take very long in an interview to eliminate a candidate who is less than knowledgeable in the business fundamentals. In fact, in most cases, the pool of applicants will surely be screened initially for both GPA and work experience. Only the top candidates are then invited to interview. So the likelihood of individuals being selected for an interview who are ignorant of the basics is nearly zero. Under these circumstances, certifying the first year of MBA coursework does not seem very useful or worthwhile.

CONCLUSION

The basic questions remain. I fear that certifying MBAs in this manner is wrongheaded and inherently meaningless. How could an exam (and subsequent certification) of this kind possibly differentiate in any way between those destined for business success and those destined for business failure? And what could it possibly add to the hiring decisions facing corporate recruiters? The answers to these two questions are surely "it cannot" and "nothing," respectively.

Charles K. Davis is a professor in the Cameron School of Business at the University of St. Thomas in Houston, Texas, and is a past chapter president of Phi Kappa Phi. He has taught previously at the University of Houston and held analyst and management positions with IBM, Chase Manhattan Bank, Occidental Petroleum, Pullman Incorporated, and Deloitte & Touchè

Forum on

Science & Technology

Daniel Berger

And Now for Something Completely Different . . .

Last summer I spent an extended period doing pure research, for the first time in six years. I had a wonderful time and discovered a few things about myself and about chemistry.

I worked with an old friend who teaches in a department without a graduate program, but who — unlike me — does have a research lab. He tells me that research can be a frustrating process at a primarily undergraduate institution. It takes time to go from teaching mode to research mode, and by the time things are in full swing, the summer is over. Certainly I found this to be true after a six-year layoff: it seemed as though we had just gotten going when we had to quit. Nevertheless, it was a productive summer, and I plan to go back.

According to the fashionable model of the teacher/scholar, I should have come back from my sojourn invigorated, chock-full of ideas to communicate to my chemistry students — primarily sophomores in Organic Chemistry, and a few juniors and seniors in Advanced Organic Chemistry. I did come back refreshed, but sadly lacking in new pedagogical or content ideas.

The problem is that the work I did last summer is too advanced for sophomores, unless they are research workers focused on a particular problem. Much of the information we generated does not even fit into the format of my *advanced* course because it is too specialized. Furthermore, I do not have the equipment to convert any portion of last summer's work into a teaching lab, and the chemicals we used are too toxic for teaching laboratories.

My summer's research did benefit my teaching in one way: it provided a break and a thorough mental reorientation. I came back to teaching refreshed. But one is forced to ask whether a different diversion would have accomplished the same thing. For example, short courses are not only invigorating (when well taught, and attended by congenial colleagues) but are *designed* to directly benefit my students by giving me ideas and topics to incorporate into my courses. And trips to visit my family or my in-laws are not only relaxing and refreshing, but also have the advantage of allowing me to spend time with, instead of away from, my children and wife.

Indeed, the glaring problem with the way I spent last summer was that preparation for my fall courses was jammed into about four weeks, with occasional stolen moments during the rest of the summer. As for my spring courses, two of them are simply carryovers from last spring with minor modifications. The third, which is new to me, required a month or more of shoveling current work—including this essay—onto the "hold" pile, because there was no time for preparation during the summer.

Regular research provides a number of things, some beneficial, some not:

- Regular research provides a feeling for what works and what does not, allowing a more informed critique of the professional literature. This is true, however, only in areas in which one is actually working; for the rest, one gets critical sense by listening to trusted sources and thinking carefully. Furthermore, this sense does not directly or indirectly benefit one's students; they must develop their own nonsense detectors, during their scientific apprenticeships in graduate school or on the job.
- Regular research provides opportunities for undergraduates to work on projects over a longer term than three hours. However, the use of multi-week and semi-independent projects in the teaching laboratory can have the same benefit in the absence of physical and temporal space for "original research."
- Regular research provides an excuse to neglect necessary work around the house. This is especially true when one is commuting to someone else's lab, rather than working in a lab of one's own.
- Regular research provides an excuse to put off the full-time job of preparing to teach properly.

Here's the crux: I cannot *afford* to get too involved in research. Teaching and research are both incredibly labor-intensive occupations, requiring upwards of fifty to sixty hours per week, and in the top tiers we find many teachers and researchers who simply put their lives on hold for extended periods of time. And success at one in no way guarantees competence at — or even interest in — the other. The myth of the teacher-researcher has been thoroughly debunked, for example in Murray Sperber's *Beer and Circus*.

Sperber quotes a psychologist at a large research university. When asked whether it wasn't bothersome that huge, impersonal lecture courses in introductory psychology were contributing to a dearth of psych majors, the psychologist retorted, "That's the point. Who wants a bunch of undergrad majors running around the department, getting in the way?"

Faculty at my institution, which stands or falls on its quality of instruction, cannot afford to take that attitude. My colleagues and I are expected to put most of our energies into *teaching* — preparing interesting

problems, grading papers, and maintaining close relationships with students. Our promotion and tenure guidelines reflect this: 50–75 percent of every tenure evaluation is based on pedagogical quality.

This is not to say that research and teaching cannot be combined. There are a number of excellent institutions at which teaching is in full flower where productive research is also expected of faculty. Their secret is that faculty members have half-time expectations for both teaching and research; they are not held to the same research productivity standard as faculty at, say, Ohio State University, nor to the same teaching-time requirements as faculty at my college. At these institutions faculty can realistically spend thirty or even forty hours per week on pure research without short-changing their students. And there are and continue to be a *limited* number of academics, even at first-rate research schools, who excel at both teaching and research.

Most research institutions pay only lip-service to teaching. Star research faculty regularly receive bogus "teaching awards" to perpetuate the myth of the teacher-researcher; but watch what happens in tenure decisions for those who actually put significant amounts of time into their teaching. At most or all such "schools," faculty are rewarded with course reductions!

A few institutions have separate faculty tracks: professors, expected to be primarily researchers, and instructors, who teach full-time. Unfortunately, at most such places instructors barely rise to the status of second-class citizens. These places at least claim to recognize that teaching and research feed each other, but not necessarily in the same individual.

Here is the key. It is good to be exposed to research, whether as a researcher or as the colleague of one, to help keep current in one's field and to keep the mind active. With that in mind, and because I had a load of fun doing it, I hope and expect to continue the collaboration begun this past summer.

But research is "something completely different" from teaching, and it is insane to expect every academic to be good at both, especially when there is only time enough in most lives to do one of them well.

Dan Berger is a professor of chemistry at Bluffton College. Like any other teacher, Dan likes to answer questions. Send comments to bergerd@bluffton.edu.

Forum on the Arts

Robert Burns

Preserving the Recent Past

Until now, I have refrained from writing about my personal creative work in these pages. Aside from the unseemliness in tooting one's own horn, there are sound reasons for this policy. While I had the benefit of a vigorous professional whelping in one of America's best offices during the 1960s, I have completed a limited number of architectural commissions under my own banner, most of them modest in scale and none of earth-shaking significance, though a few peer recognitions for their design have come my way. As a full-time educator, my primary focus has been on my students and secondarily on my personal design practice.

A recent experience has given me the courage (perhaps others would term it chutzpah) to devote my last column to a project that seems to offer useful lessons in how to preserve a valuable example of an endangered species — twentieth-century modern architecture. This is not to suggest that all of the architectural work of the past century is about to disappear, nor that all of it is worthy of preservation. But the reality is that much modern architecture built in the United States over the past seven or eight decades, even internationally significant work, is fast disappearing or at risk simply because it was produced relatively recently and its values are unappreciated by many of today's decision-makers and clients. The Fallingwaters and the Jefferson Arches will certainly be protected, but what of the larger legacy of those well-designed structures, public and private, that define an era and have been seen as an integral part of our recent history and culture? What follows is one encouraging model.

The project in question is the Kamphoefner House, completed in 1950 and thought to be Raleigh's first true "modern" house. Designed by Henry L. Kamphoefner, the founding dean of the North Carolina State School of Design, it is a rigorous, elegant work of domestic architecture that incorporates such innovations as "Thermapane" (insulated) windows, radiant heating, and a unique natural ventilating system. These special design features, in addition to its low-slung lines and natural materials, reveal its profound debt to the house-type created in the 1930s by Frank Lloyd Wright and named "Usonian" by that great master, which signified a creation uniquely American in character. At the completion of its construction, it was published nationally and hailed as a progressive work of contemporary design.

Dean and Mrs. Kamphoefner lived in the house until their deaths in the late 1980s. During their lives, the house was the site of notable events. Distinguished visitors from all over the world were entertained here: even Wright himself came and spent a couple of nights in the guest room on the occasion of his 1950 address to an audience of 5,000 in the university's fabled basketball arena, Reynolds Coliseum. Presiding in the spacious living room every Tuesday evening for a quarter of a century, Dean Kamphoefner guided his soon-to-graduate students through his memorable course, "Seminar on Ideas in Design." As a student in the 1950s and later as professor of architecture, I spent many stimulating hours in the house. Dean Kamphoefner was my dean, teacher, and, from 1965 until his death in 1989, my close and revered friend. This association has given me a deep appreciation for the house and the unique place it holds in the architectural heritage of the state and city.

Remarkably, the house had remained almost unchanged for fifty years. It was listed in the National Register of Historic Places in 1996 and had been designated as a Historic Landmark by the county's Historic Preservation Commission. And yet its future was by no means assured. Because it was relatively small and occupied a beautiful and highly prized site overlooking the sixteenth fairway of the city's premier golf course, it was a prime candidate for demolition and replacement by a new megahouse. Fortunately, Dean Kamphoefner's heir had wisely donated a protective covenant on the house to Preservation North Carolina, giving this private preservation society final approval in perpetuity on any changes to the property. While this had the effect of limiting the sale price for the property somewhat, it offered protections and compensatory tax benefits. The house became available for sale in 2000, and a young family, attracted to its special architectural qualities, decided to buy and modify it to meet their specific needs.

When I was asked by the new owners to design an addition, I saw it as an opportunity to ensure that the integrity of the original house was protected and that necessary changes would complement its existing character. With the support of a sympathetic client, I believe that we achieved those goals.

First, the new plan expanded but did not inflate inordinately the property. The original construction comprised 1,630 square feet (sf) of conditioned space plus 350 sf of carport and related storage space. The new design added 540 sf of new conditioned space for a master bedroom suite and renovations to the existing carport for an enlarged kitchen and breakfast area. The original kitchen, in the manner of many efficient houses of the post-World War ll era, was

minute. A new carport of approximately 400 sf was also included in the plan. Other than the kitchen expansion, the original house was unchanged except for refinishing existing wood surfaces, repointing brickwork, and reroofing the flat portions of the roof.

Second, the addition has been configured to maintain the scale of the site and general appearance from the street. The new piece is connected to the leading edge of the original carport wing, extending the horizontal roof overhangs and distinctive visual features around its perimeter. The addition hugs the setback line on the northwest side of the property aligning with the original. The plan offers a surprising benefit that in fact enhances the original. The paved courtyard, in the past used for visitors' parking, became a garden and family domain that greets visitors who now enter by way of a new walkway and a previously unused brick stairway.

Finally, materials, dimensions, and details were selected to harmonize with those of the earlier design. Copper roofing, wood siding, and windows selected for their compatibility with those existing associate the offspring with the parent. At the same time, the sophisticated visitor may note the subtle recesses and adjustments where the new and the old come together. We sought a result that would be fresh but ultimately harmonious.

A word about the design review by Preservation NC: the society's officers enthusiastically supported the proposed changes as the best way to protect this valued modern landmark and ensure its preservation for at least another generation. The new design also received approvals from the county's preservation commission and the State Historic Preservation Office. These actions reflect recent enlightened preservation philosophy that allows appropriate change to historic properties.

While this building's story has a happy ending, many similar buildings have been less fortunate. Just across this same golf course, a grand modern house of mid-fifties vintage was recently razed to make way for a tasteless baronial monstrosity. This offense is repeated regularly throughout the United States. If we are to understand and profit from our architectural heritage, it is critical that we preserve a substantial body, not just the rare exceptional works, of the recent past.

Robert Burns is a professor of architecture at North Carolina State University. He is a Fellow of the American Institute of Architects and a recipient of the Holladay Medal for Excellence, the highest award made by the university to faculty members. Professor Burns was selected as Phi Kappa Phi's National Artist for 1998–2001.

New wing and courtyard, Kamphoefner-Petrocella House. Robert Burns, photographer, 2002.

New entryway, Kamphoefner-Petrocella House. Robert Burns, photographer, 2002.

Exterior view, Kamphoefner House. Photographer unknown, archival photo c. 1950.

Phi Kappa Phi Forum Welcomes

Andrea Ickes-Dunbar

Forum on Education & Academics

Jennifer M. Stolpa

Andrea Ickes-Dunbar teaches seventh and eighth grade English and Spanish to a second generation of students in a multi-generational K-8 California public school. Her passion is languages. In Mexico and Chile, she learned Spanish. In the arctic wilderness, she learned conversational phrases in raven caw and wolf howl.

Jennifer M. Stolpa is an assistant professor of English at the University of Wisconsin-Marinette, where she also teaches Spanish. She can be reached at jstolpa@uwc.edu.

Larry Chambers

Forum on Business & Economics

Anthony J. Dukes

Larry Chambers is a freelance financial writer living in Ojai, California. He has authored more than 800 magazine articles and thirty-four business books. Two of his books remain specialty best sellers, and three have found their way into book-of-the-month clubs. One of his books, *The First Time Investor*, was named one of the top five books for "investing on a shoestring" by Chuck Myers, Knight Ridder, *Washington Review*.

Anthony J. Dukes is visiting assistant professor at Carnegie Mellon University's Graduate School of Industrial Administration (Business School). He holds a PhD in economics from the University of Pittsburgh and currently conducts research on the economics of advertising and commercial media.

New Columnists

Devlin M. Gualtieri

Forum on Science & Technology

Evelyn Tiffany-Castiglioni

Devlin M. Gualtieri received an undergraduate Physics degree and a PhD in Solid State Science from Syracuse University. He is currently Senior Principal Scientist with Honeywell, Morristown, New Jersey. Dr. Gualtieri has been a member of Phi Kappa Phi for thirty years, and he can reached at gualtieri@ieee.org.

Evelyn Tiffany-Castiglioni, PhD, is associate dean for Undergraduate Education and head of the Department of Veterinary Anatomy and Public Health, College of Veterinary Medicine, Texas A&M University. She conducts research on the neurotoxicity of environmental contaminants. She is on the editorial boards of *Neurotoxicology* and the *International Journal for Developmental Neuroscience*.

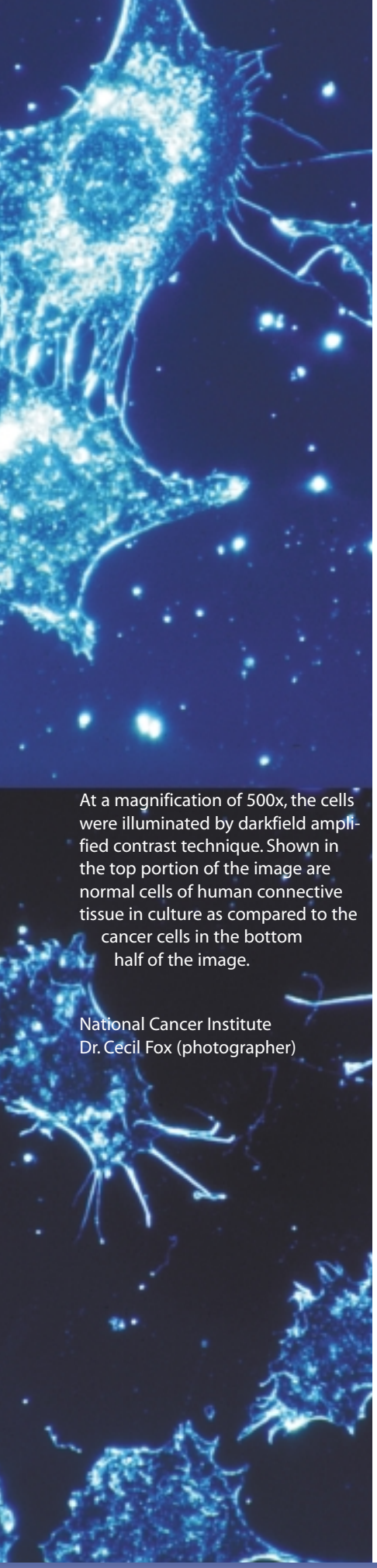
Heidi Motzkus

Forum on the Arts

David Thurmaier

Heidi Tolles Motzkus is a PhD candidate in Cultural Studies at Claremont Graduate University. She teaches in Los Angeles and has held the positions of dramaturge and theatre critic.

David Thurmaier teaches Music Theory at Lawrence University and is a PhD candidate in Music Theory at Indiana University. His primary research focuses on the music of Charles Ives.



At a magnification of 500x, the cells were illuminated by darkfield amplified contrast technique. Shown in the top portion of the image are normal cells of human connective tissue in culture as compared to the cancer cells in the bottom half of the image.

National Cancer Institute
Dr. Cecil Fox (photographer)

Peggy Vaughn

Extraordinary Opportunities in Cancer Research

National Cancer Institute

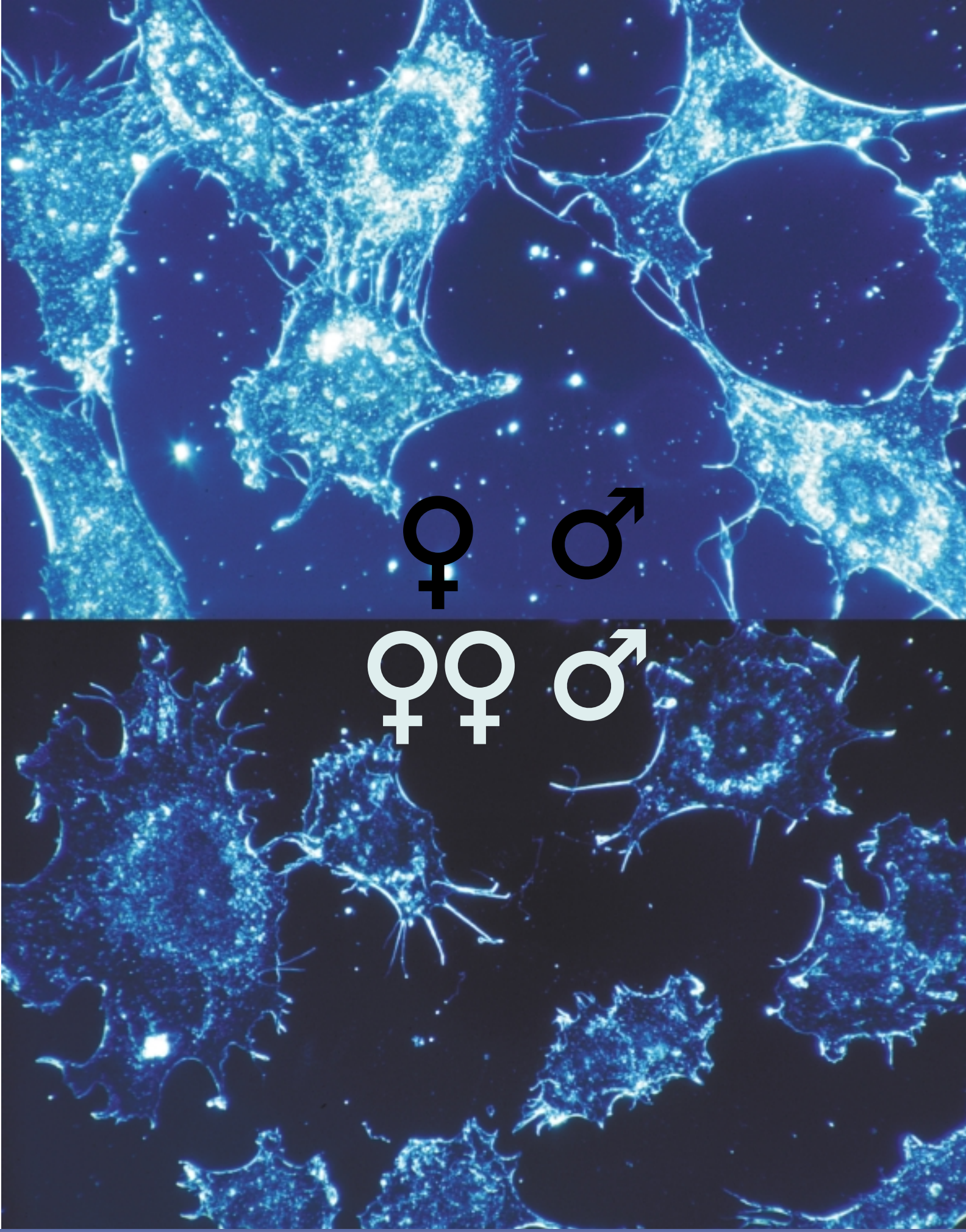
Cancer statistics paint a daunting and seemingly overwhelming picture. One out of every two men and two out of every three women will be diagnosed with cancer during their lives. Nearly 25 percent of all deaths in the United States result from cancer, and medical expenses for cancer cost our nation up to $60 billion a year. With our aging population, the number of people diagnosed with cancer is expected to double from 1.3 million in 2000 to 2.6 million by 2050.

With recent advances in cancer research, however, a comprehensive solution to the problem of cancer is increasingly within reach. The National Cancer Institute (NCI), the federal government's primary organization for cancer research, is in the forefront of that effort. We both conduct and fund research on multiple fronts, from basic laboratory studies to large clinical trials involving thousands of patients. Just as importantly, we strive to close the gap between basic research and the translation of the knowledge that we gain from it into practical help for patients at risk for, diagnosed with, or recovering from cancer.

Perhaps our greatest hope lies in the emerging understanding of cancer at the genetic, molecular, and cellular levels. More than 5,000 NCI investigators, working alone or in groups, have embarked on an incredibly challenging intellectual exercise. Their ultimate goal is to treat each cancer tumor according to its unique genetic and molecular fingerprint.

"The paradigm I grew up with as an oncologist was to find cancer and kill it," said NCI Director Andrew von Eschenbach. "Now, we look forward not only to eradicating cancer, but also to modulating and altering the behavior of the disease. This new paradigm uses biology-based interventions to detect, treat, and prevent cancers."

In the coming years, NCI will focus much of its efforts on a half-dozen areas that we believe offer extraordinary potential: genes and the environment, cancer imaging, molecular signatures and targeting, tobacco-related cancers, and cancer communications.



GENES AND THE ENVIRONMENT

Exactly how genetic and environmental factors interact to cause cancer remains a complex puzzle. Mutations in some genes, such as that for *familial adenomatous polyposis*, are so powerful that carriers are almost certain to develop colon cancer. Mutations in other genes, such as *BRCA1* and *BRCA2*, are just some of the many risk factors for breast cancer. Certain environmental factors, such as smoking, are strong but not absolute predictors of cancer.

NCI investigators are working on identifying the cancer risks associated with the interaction between certain environmental exposures and genetic factors. With this better understanding, we can check genetic susceptibility, identify treatments for people at high risk, and develop strategies to avoid adverse exposures. We are also working toward more patient-friendly tools, with such non-invasive methods as screening for lung cancer by sputum samples or sampling DNA from cheek cells.

Various ongoing studies are helping to build the large databases needed to formulate prevention and treatment options. Currently, we are collecting not only data on environmental exposures, but also actual tissue, blood, and other body-fluid samples from some 700,000 study participants. Because genes play such a significant role in the development of cancer, we are tracking cancer trends among 14,000 families enrolled in cancer registries that record family history, demographics, and lifestyle risk factors.

This past summer, NCI reported its findings on a lengthy study — a decade-long investigation into possible environmental causes of elevated breast-cancer mortality rates in Long Island, NY, and surrounding areas. Researchers looked at the current and past exposure of 1,508 local women to contaminated drinking water, air pollution, electromagnetic fields, and other suspected hazards. The study found a negligible connection. There was some increased cancer risk with exposure to pollutants such as cigarette smoke and diesel fuel, but not with other factors such as exposure to pesticides. The project continues with more than a dozen follow-up investigations into the roles played by various genes, lifestyle choices, and contaminants in the development of breast cancer.

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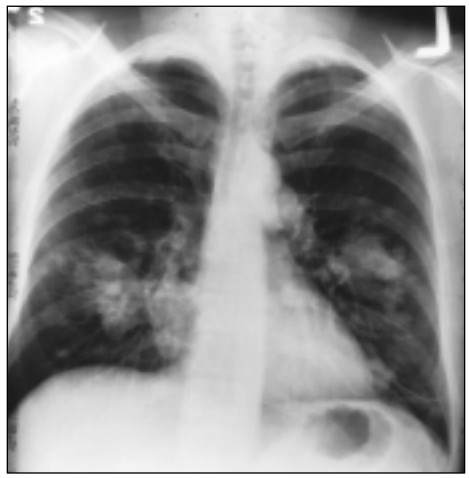
CANCER IMAGING

During the past twenty-five years, imaging technology has advanced from x-ray studies to such recent breakthroughs as virtual colonosocopy, where computerized tomography (CT) is used to scan for colon cancer. NCI investigators also are conducting research into such technologies as "smart contrast agents." Injected into the body, the agents change shape and become fluorescent when they come into contact with certain enzymes present in cancers. One new contrast agent in the pipeline enhances PET imaging by targeting elevated levels of an enzyme present in prostate and other cancers. Sophisticated imaging techniques are also proving vital in determining the effectiveness of cancer drugs specifically designed to prevent the growth of blood vessels that feed tumors.

Several large clinical trials are now underway to evaluate and refine new imaging technologies. In September 2002, the National Lung Screening Trial (NLST) began enrolling 50,000 current and former smokers in a study comparing the use of spiral CT to standard chest X-rays in reducing deaths from lung cancer. Both methods have been used to find lung cancer early, but so far neither method has been shown to



This is an x-ray image of a chest. Both sides of the lungs are visible with a growth on the left side of the lung, which could possibly be lung cancer.

National Cancer Institute
Unknown photographer/artist

reduce a person's chance of dying from the disease. The trial should determine which one imaging tool best reduces a person's chances of dying from lung cancer.

"Lung cancer kills more people than cancers of the breast, prostate, colon, and pancreas combined and will kill more than 155,000 people this year," says the NLST project officer, Dr. John Gohagan, of NCI's Division of Cancer Prevention. "Our hope is that this study will lead to saving lives among the 90 million current and former smokers in the United States."

MOLECULAR SIGNATURES

NCI is expanding research into molecular signatures, or learning how small changes in only a few genes or proteins can disrupt cellular functions and allow cancer to develop. Such knowledge will help diagnose cancer at an earlier stage, help tailor treatments, and help monitor patient recovery.

This effort is resulting in some exciting new technologies. For example, this year work should be completed on a Cancer Chromosome Aberration Map, a genetic map that defines distinct alterations in chromosomes that lead to cancer. NCI makes this and other genetic resources, such as tissue repositories, readily accessible to researchers worldwide.

The discovery and use of biomarkers, or substances in body fluids and tissues that indicate the existence of tumors, are leading to new advances in the early detection of cancer. This past summer, scientists working on a joint NCI and Food and Drug Administration study announced success with a new, thirty-minute test that detects ovarian cancer from proteins found in blood samples.

This new technology combines proteomics — the study of proteins inside a cell — with artificial-intelligence computer programs. Using simple finger-prick blood samples, a computer has correctly identified a pattern of just a half-dozen or so proteins, among thousands found in a person's blood, that correctly identified the presence of ovarian cancer. This process has now been expanded to test for prostate cancer, and in the future, may be used to diagnose other cancers.

MOLECULAR TARGETING

Research is also entering a new era of molecular targeting, where drugs are designed to target specific molecular features of a cancer cell while sparing healthy tissue. NCI is encouraging this development by supporting more than forty research groups working in this area. One group is exploring an aberrant protein that enables cancer cells to evade apoptosis, or the natural death that comes to damaged cells. Others are examining proteins found in unnaturally high levels among cancer cells to determine what role they play in cancer growth.

NCI is taking that vital next step by translating discoveries made in laboratories for use in the clinical care of patients. One novel gene-therapy approach currently being tested delivers a pair of therapeutic "suicide genes" to prostate tumors. The genes sensitize malignant cells to specific cancer drugs and radiation.

Another new approach is to replace a patient's immune system with cancer-fighting cells that aid in shrinking tumors. Certain immune cells taken from a patient's tumor, then grown and strengthened in the laboratory, are injected back into the patient's body to attack cancer cells. This experimental technique, known as adoptive transfer, has shown promising results in patients with metastatic melanoma who have not responded to standard treatment. With further research, scientists hope that this approach may have applications to many cancer types, as well as to infectious diseases such as AIDS.

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Warning Label, National Cancer Institute. Bill Branson (photographer), March 1987

TOBACCO AND CANCER

The devastating impact of tobacco use and tobacco-smoke exposure on the incidence of cancer is as compelling as it is conclusive. Tobacco use is responsible for nearly one in five deaths in the United States. NCI is especially concerned about the health of former smokers, people who have managed to kick the habit yet still comprise about half of the estimated 170,000 lung-cancer patients diagnosed this year.

Lung-cancer studies are a primary focus of much of our research on tobacco-related cancers, but the findings are often applicable to other cancers. As with other cancers, we find that genetic make-up plays a role in not just the progression of lung cancer, but the predisposition to become a smoker. Research has shown smokers with certain genetic traits start smoking almost two years earlier than others, so NCI is studying this genetic predisposition to devise tailored approaches to smoking cessation.

NCI is expanding support for studies that test ways to prevent tobacco use among the young and those willing to quit. With more than fifty research grants in this area, NCI is finding evidence that both social and genetic factors are predictors of tobacco use among youth. One study shows that the optimal age for smoking-prevention interventions is between ten and fifteen years of age, much earlier than most programs target. Another shows that middle schoolers who view more tobacco use in movies are more likely to smoke.

While costly and time-consuming, studies that include genetic and biomarker factors are invaluable in understanding cancer risks and exposures to carcinogens before a diagnosis of cancer. The Prostate, Lung, Colorectal, and Ovarian screening trial, for example, is examining the genetic factors that influence smoking and how genes might be involved in nicotine dependency.

Unfortunately, the best smoking-cessation treatments are effective for fewer than a third of all smokers trying to quit. For that reason, NCI is funding behavioral, pharmacological, and community treatment efforts that tailor interventions to the unique needs of individual smokers. One NCI program providing computer-assisted feedback to smokers resulted in success rates almost 33 percent higher than cessation programs without it.

CANCER COMMUNICATIONS

It is not unusual for today's cancer patients to arrive at their doctor's office complete with printouts of information from NCI's award-winning cancer-information Web site, www.cancer.gov. NCI's Cancer Information Service provides personalized answers to questions about cancer, in English and Spanish, at the toll-free number 1-800-4-CANCER. By providing accurate and easily accessible cancer information, NCI helps to empower patients faced with making decisions about prevention, treatment, survivorship, and end-of-life issues.

NCI is also working towards ending the digital divide with cancer-information programs designed to serve people who frequently lack access to computers. These programs are offered to parents of Headstart students and residents in economically depressed urban and rural areas.

Our NewsCenter Web site, with its downloadable images, audio clips, and press releases, is intended to aid the media in accurately reporting cancer news. Benchmarks, an added feature at this site, reports in detail on emerging technologies in cancer research, such as proteomics and nanotechnology. These sites additionally serve as powerful educational tools for the general public.

To ensure maximum benefits from our investment in research, we are strengthening our partnerships with voluntary health organizations, HMOs, and community-health practitioners. One such joint project is testing a new smoking-cessation program for older smokers. It includes a written, evidence-based guide tailored to smokers fifty and older, as well as one for Spanish-speaking Medicare beneficiaries.

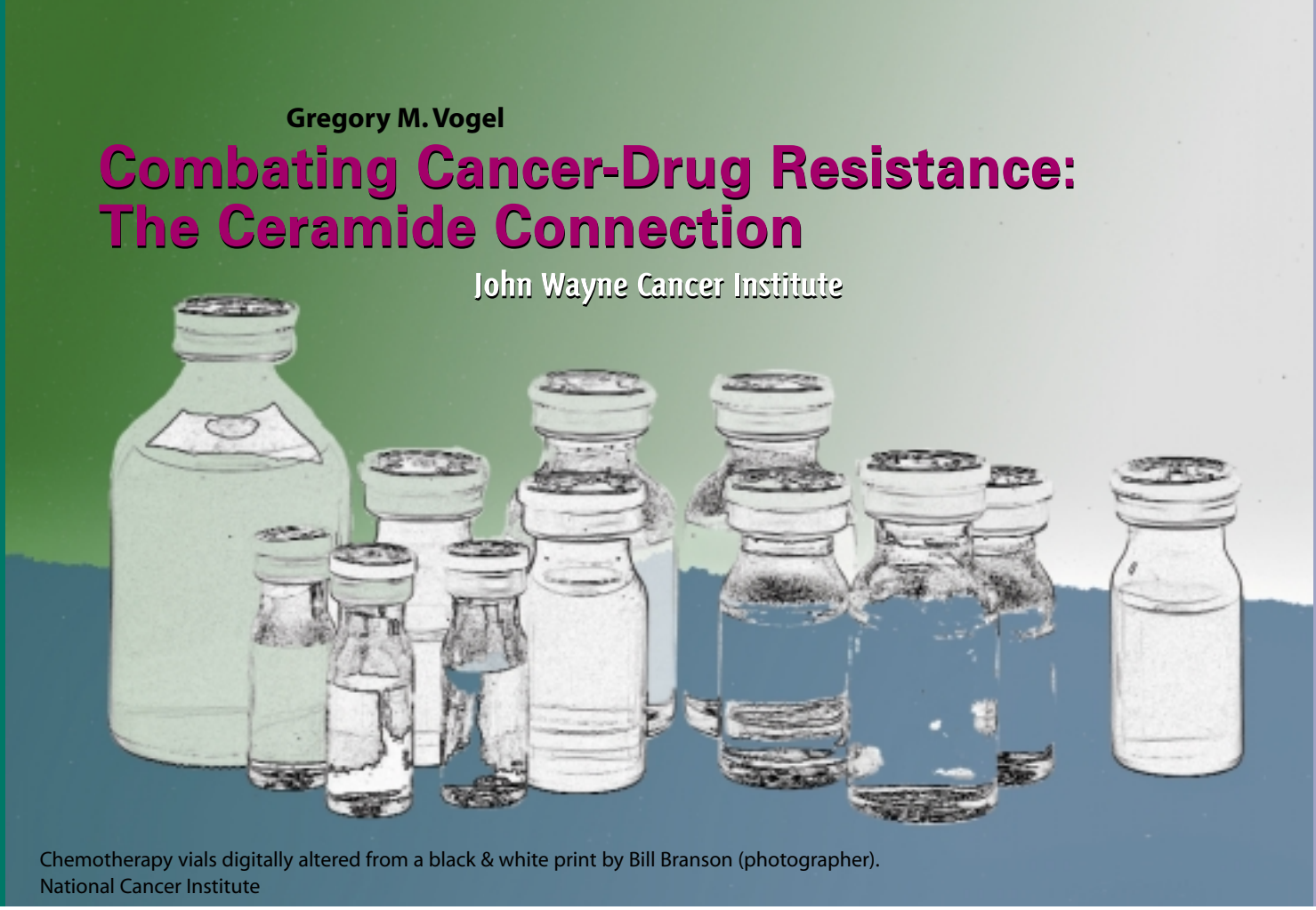
While the focus and methods may change as science evolves, NCI remains committed to reducing cancer's terrible burden on our nation and its citizens. By building on these areas of extraordinary opportunity, we hope to achieve our vision of a future where all cancers are uncommon and treatable. With the courage of our cancer-research and care community, and continued strength of our resources, hope is stronger than ever that the years to come hold promise beyond our imaginations.

Peggy Vaughn is a press officer in the Press Office of the National Cancer Institute in Bethesda, Maryland.

Gregory M. Vogel

Combating Cancer-Drug Resistance: The Ceramide Connection

John Wayne Cancer Institute



Chemotherapy vials digitally altered from a black & white print by Bill Branson (photographer).
National Cancer Institute

The phenomenon of drug and biocide resistance arising in biological systems is widespread. With surprising rapidity, organisms evolve defenses to protect themselves from toxins of all kinds. Increasingly, drug-resistant bacteria and viruses (for example, tuberculosis, *Staphylococcus*, HIV), pesticide-resistant insects (lice, mosquitoes), and herbicide-resistant weeds pose a serious and growing threat to human health and the ecosystem. Emerging cases of resistant organisms are everyday news.

However, it surprises people to learn that many forms of cancer are also drug-resistant, and as in other living things, this resistance can be acquired.

The statistics are not encouraging: 40 percent of operable cancers and 80 percent of inoperable cancers are drug-resistant. Metastatic breast and ovarian cancers are common in the United States; the American Cancer Society estimates 40,600 deaths from breast cancer in 2002. While surgery is an early course of treatment, drug therapy (chemotherapy) may become the only treatment option available in advanced cases. In ovarian cancer, about 70 percent of patients who achieve remission after systemic treatment with chemotherapy will have a recurrence after five years. Most of these patients will be lost as a result of either acquired or intrinsic resistance to chemotherapy.

In breast-cancer patients, 42 percent demonstrate primary resistance to Adriamycin™, the most widely used anticancer drug in the world. Among patients who do respond well to Adriamycin, some will have a recurrence several years later; of these, 58 percent will show resistance to the same drug that seemed to work initially. In advanced breast-cancer patients who fail to respond to chemotherapy, more than 95 percent will develop metastatic disease. In these cases, survival is poor.

TREATING DRUG RESISTANCE AS A DISEASE

Resistance to chemotherapy, the underlying cause of treatment failure, presents an enormous clinical problem that, if solved, could significantly improve survival rates. Researchers at the John Wayne Cancer Institute (JWCI) in Santa Monica, California, have taken the position that drug resistance must be treated as a separate disease. Their goal is to improve responses to chemotherapy in breast- and ovarian-cancer patients who demonstrate either intrinsic or acquired resistance to treatment.

The challenge is considerable. Cancer cells can draw upon their primordial genetic resources for survival and proliferation, and develop ingenious defense mechanisms to avoid the toxic or static

effects of chemotherapeutic agents. In some cases, such as gastrointestinal-tract and kidney-tumor cancers, cells are intrinsically resistant to chemical agents, having evolved to tolerate natural cytotoxins in foods consumed intentionally or by accident. In addition, many kinds of cancers are able to acquire resistance to the very drugs used to kill or suppress them.

The earliest model of multidrug resistance in cancer identified one of the defensive agents at work: a membrane-resident protein molecule called P-glycoprotein, which acts as a drug efflux pump, chemically drawing cytotoxic drugs out of the cell. This process effectively lowers intracellular drug levels to sublethal concentrations and protects the cell against further exposure. Other known resistance mechanisms include the overexpression of "multidrug resistance-associated protein," changes in the activity of certain enzymes, modifications of metabolic pathways, and the expression of other proteins, including mutant forms.

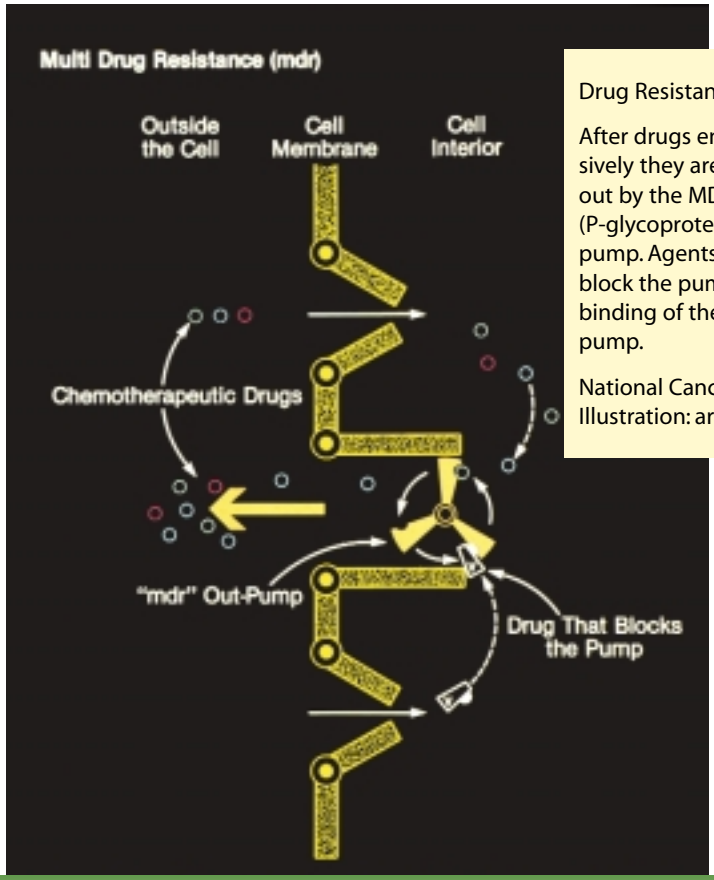
Distressingly, as with other kinds of acquired resistance, cancer treatment itself is a selective force that promotes the evolution of resistant survivors. If 99 percent of a cell type are killed by chemotherapy and 1 percent survives, those surviving cells can form the nucleus of a recurrent growth. The new cancer growth will be impervious to the chemotherapy that was previously effective.

Over the past several years, research at JWCI's Breast Cancer Research Program, under the direction of Myles C. Cabot, Ph.D., has focused on cancer-drug resistance with particular emphasis on the role of a lipid known as ceramide. A dysfunction in the normal metabolism of this lipid is believed to contribute to multidrug resistance and may be a key to restoring the effectiveness of anticancer drugs in difficult cases.

THE TWO FACES OF CERAMIDE

Many beauty creams and lotions today are made with ceramide, a fatty molecule found naturally in the human body, with somewhat higher levels in the skin. Cosmetics manufacturers promote the inclusion of ceramide in their formulas as a beauty remedy; many preparations are claimed to produce "younger-looking skin." But ceramide's role in human biology, including cancer, is far more than skin deep. Ironically, a biochemical marketed to beauty-seekers hoping to maintain an appearance of youth is intimately involved in cell death.

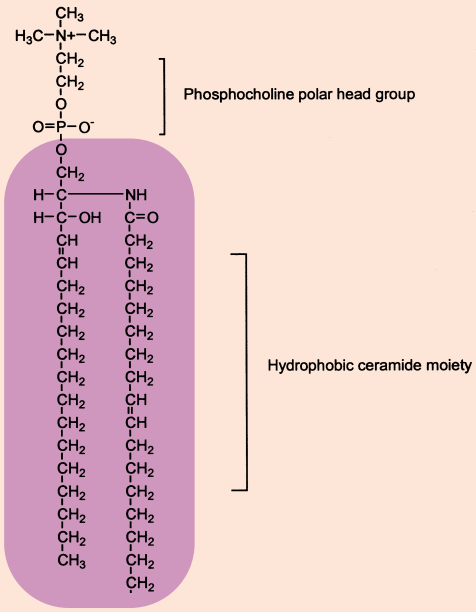
In the body, ceramide, chemically known as N-acyl-sphingosine, is a key intermediate in the biosynthesis of the sphingolipids, which are part of cell membranes, and sphingomyelin, which is abundant in the fatty myelin sheath around nerve cells. But in recent years, ceramide has been identified as a chem-



Drug Resistance Pump (left)

After drugs enter the cell passively they are actively kicked out by the MDR gene product (P-glycoprotein), which acts as a pump. Agents such as verapamil block the pump by inhibiting binding of the drug to the pump.

National Cancer Institute
Illustration: artist unknown



Chemical structure of sphingomyelin

Sphingomyelin is an important fatty (lipid) molecule that contains ceramide as its primary component. Ceramide, a key factor in regulating cell growth and death, is synthesized by the body directly, or by the breakdown of sphingomyelin into its primary components. Many cancer cell lines can inactivate ceramide, thereby resisting chemotherapeutic agents that act as "ceramide generators."

ical messenger as well. Ceramide participates in the process of cell signaling, in which chemicals released by cells and tissues stimulate metabolic activities in nearby or distant regions of the body. Neurotransmitters, hormones, peptides, cellular factors called cytokines, and other biochemicals act as messengers in a chain of "signal transduction" events. A signal carried by a messenger such as ceramide, when chemically transmitted and amplified, can ultimately trigger a cascade of enzymatic and transcriptional activity (the first step in protein synthesis, with an unlimited scope of biochemical impacts).

Myles C. Cabot, Ph.D.

Through recent research, ceramide has been identified as a secondary messenger in the chain, acting by modifying different target proteins. Ceramide-mediated cell signaling is now known to be a critical control mechanism in human biology, influencing many phases of cell-cycle regulation, including cell differentiation, transformation, proliferation, and apoptosis, or programmed cell death.

Apoptosis is the process by which a cell actively commits suicide. Proper regulation of cell death is essential to normal development and necessary for tissue health. In the fetus, for example, apoptosis occurs in the cells between fingers and toes so that individual digits can separate from the early limb bud. In cancer, the regulation of apoptosis is impaired, allowing cells to proliferate unchecked.

Many different stimuli promote the generation of ceramide in the body, either creating it via the enzyme ceramide synthase, or as a product of the breakdown of sphingomyelin. Phenomena that stimulate ceramide formation include the action of cytokines, growth-factor deprivation, heat shock, tumor necrosis-factor alpha, ionizing radiation, and chemotherapy itself. The increase in ceramide also initiates ceramide-mediated signaling pathways that lead to cell-cycle arrest and ultimately apoptosis. In fact, the direct addition of ceramide to cancer cell cultures *in vitro* can cause cells to die. Given to humans systemically as a drug, however, ceramide would likely be degraded before it could reach its target, a problem that currently limits its usefulness in chemotherapy. Improving delivery methods and synthesizing more robust derivatives could solve this dilemma.

Clinically important chemotherapeutic agents used in cancer treatment that stimulate production of ceramide include daunorubicin, doxorubicin (Adriamycin), vincristine, vinblastine, etoposide, tamoxifen, suramin, fludarabine, taxanes, irinotecan, and okadaic acid, as well as ionizing radiation used in radiation therapy. At least some of these agents' cancer-killing activity comes from their ability to activate ceramide-mediated pathways, either by promoting ceramide synthesis directly, by activating the enzyme sphingomyelinase (which regenerates ceramide from sphingomyelin), or by blocking the formation of an inactivated, modified form of ceramide called glucosylceramide (GC). This latter pathway became a focus of interest several years ago in the JWCI Experimental Therapeutics Laboratory, directed by Dr. Cabot.

GC is produced in the body by the action of an enzyme called glucosylceramide synthase (GCS), which adds a sugar group to ceramide in a process called glycosylation. This simple conversion of ceramide to GC is enough to turn off the cell-killing power of ceramide by blocking the normal signaling process in cell regulation. Deactivating cytotoxic ceramide by converting it to GC allows cancer cells to escape from ceramide-induced programmed cell death, permitting them to grow and spread.

In the 1990s, Cabot and his collaborators at JWCI found that levels of GC were unusually high in breast carcinoma cells resistant to Adriamycin, the world's most widely employed cancer drug. Further, GC levels were also high in carcinoma cells resistant to the chemotherapeutic agent vinblastine, and in tumor specimens from patients showing poor response to chemotherapy.

In the 1990s, Cabot and his collaborators at JWCI found that levels of GC were unusually high in breast carcinoma cells resistant to Adriamycin, the world's most widely employed cancer drug. Further, GC levels were also high in carcinoma cells resistant to the chemotherapeutic agent vinblastine, and in tumor specimens from patients showing poor response to chemotherapy. Later, high GC levels were also discovered by other researchers in ovarian and

colon carcinomas. Conversely, cancer cells that are sensitive to chemotherapy do not stockpile GC.

In targeting ceramide, the JWCI researchers had found a clue to the problem of drug resistance hiding in an unremarkable, yet apparently critical, cellular mechanism. Realizing that GC could serve as a biochemical marker for drug resistance, JWCI researchers alerted the scientific community through a landmark 1996 publication in *The Journal of Biological Chemistry*, and were awarded a patent, "Sphingolipids as markers for drug-resistant cancers." Now, the glycosylation of ceramide became a focus of intense research interest. If production of GC could be halted, it would interrupt at least one mechanism by which cancer cells resist chemotherapy. Both the gene regulating GC and GCS, the enzyme responsible for producing it, became targets.

MAKING ANTISENSE OF GCS

The field of antisense DNA research involves taking a gene and scrambling its genetic code so that it literally no longer makes "sense" — that is, once reinserted into the genome, it can no longer code for a normal product, an expressed protein of some sort. With the expertise provided by molecular biologist Yong-Yu Liu, M.D., Ph.D., at the John Wayne Cancer Institute, the gene coding for GCS was identified using the National Center for Biotechnology Information GenBank® database. Officially known as Accession Number D50840, this gene normally codes for a protein containing 394 amino acids, which is the enzyme GCS.

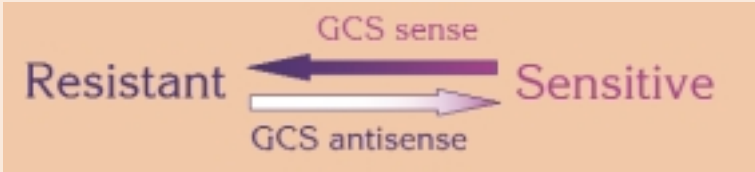
Researchers at many other cancer and scientific institutions generously contributed materials, cell lines, and biochemicals in support of the laboratory's work. A rearranged full-length GCS gene was prepared and introduced into cultures of MCF-7/AdrR breast cancer cells, a line of cells known to be resistant to Adriamycin as well as other important anticancer agents.

The scrambled gene was taken up by the cells in a process known as transfection. When the cells expressed the product of the antisense GCS gene, they were now manufacturing a nonfunctional GCS enzyme, instead of the "correct" enzyme.

These cells were then tested for sensitivity to various chemotherapeutic agents. Sensitivity in the antisense-treated cells improved markedly as GCS levels decreased. Response to Adriamycin increased 28-fold; responses to several other chemotherapeutic agents were even higher, including a 50-fold increase in sensitivity to vincristine, a natural alkaloid from the Madagascar periwinkle *Vinca* plant; a 115-fold increase in sensitivity to the related alkaloid vinblastine; and a more than 240-fold increase in sensitivity to Taxol®, the semisynthetic derivative of yew tree bark extract.

To confirm the results, the reverse process was also tested: non-resistant MCF-7 human breast cancer cells were transfected with a "sense" gene coding for production of the GCS enzyme. Now armed with the genetic ability to convert ceramide at an accelerated rate, the cancer cells showed an 11-fold increase in their resistance to Adriamycin. A similar experiment transfecting already drug-resistant breast-cancer cells produced a small yet significant increase as well.

The proof that sense and antisense genes could respectively increase or lower GC levels, and concomitantly, resistance to chemotherapies, confirmed the role of the GCS gene in contributing to multidrug resistance in the particular lines of breast-cancer cells studied. It also served as a foundation for further research. Currently, JWCI's Experimental Therapeutics Laboratory is designing an antisense "minigene" version of GCS. The native gene, 1182 nucleotides long, is far too large to be administered as a drug. A more practical minigene version would need to be only twenty nucleotides in length, but it would carry bits of code sufficient for the basic functions of initiating and stopping transcription. If laboratory studies of an antisense GCS minigene are successful, JWCI researchers hope to offer patients clinical gene-therapy trials sometime in the next five years.



GCS Sense and Antisense Experiments

Researchers at John Wayne Cancer Institute added an antisense gene for glucosylceramide synthase (GCS, the enzyme used by cancer cells to inactivate ceramide) to drug-resistant cancer-cell cultures. The antisense gene impaired the cells' ability to generate GCS, making them drug-sensitive and treatable by chemotherapy. The reverse also proved true: adding a GCS sense gene coding for over-production of GCS made previously sensitive cancer cells drug-resistant.

THE DIRECT APPROACH: ENZYME INHIBITION

In addition to genetic therapy, other avenues are available to combat the production of GC either by blocking the GCS enzyme directly, or by controlling pathways that block formation of GC from ceramide. Interestingly, molecules that prevent GC

production include a range of familiar and new candidates, including other anticancer agents, antibiotics, antifungals, and antiestrogens.

The chemotherapeutic agent Tamoxifen, used widely in the treatment of breast cancer, also decreases GC production in vinblastine-resistant cells. Clinical concentrations of other antiestrogens including Toremifene, mifeprisone (RU 486, the "morning-after pill"), the beta-blocker verapamil, and the immunosuppressive agent cyclosporine A also decrease GC levels and raise concentrations of ceramide. Additionally, some drugs increase the sensitivity of resistant cancers to other chemotherapies, making them useful adjuncts in treatment regimens.

Interestingly, there seems to be a connection between drugs that target P-glycoprotein (interfering with the drug efflux pump mentioned earlier) and ceramide metabolism. While a number of pathways that influence the metabolism of ceramide are activated in response to various chemosensitizing agents, the mechanisms at work are not clearly understood. Nevertheless, using known pharmaceuticals to inhibit GCS holds great promise, as many of the agents of interest are already chemically and medically well characterized.

Another encouraging prospect for discovering new GCS inhibitors exists in the National Cancer Institute's Anticancer Drug Discovery Database, a resource of more than 70,000 natural and synthetic compounds with possible anticancer activity. The Experimental Therapeutics Laboratory at the John Wayne Cancer Institute is currently working with the NCI to identify compounds with a likelihood of interfering with GCS production, including plant toxins, deep-sea sponge extracts, and other unusual biochemicals. Considering that the earliest chemotherapeutic agents (as well as some of the latest) are derived from natural sources such as the *Vinca* plant, some of the most intriguing discoveries about ceramide may be on the horizon.

Gregory M. Vogel is a science writer-producer in Los Angeles. Currently vice president of the International Association of Business Communicators/LA, he holds master's degrees in biology (College of William and Mary in Virginia), journalism and public affairs (American University), and film and television (UCLA). He recently created and co-produced "Science at the Edge," a three-hour international television series about advances in medicine, astronomy, and physics. He can be reached at gmvogel@aol.com.

ALARMS

Starting at quarter to six,
the clock radios begin to sound.
The guy above me has one that squawks
like a wounded pterodactyl,
the guy to the right plays classical,
the guy below stays locked
on country-pop. Half the time
I wake early, thinking of you,
thinking of the sadness
of so many single men so close
together, the way we cough
and scratch ourselves and keep on
hitting the snooze button,
preferring distant dreams
to morning, postponing
that eventual small summons
of bravery that allows us
to pull back the covers,
find a reason to get up.

DAVID STARKEY

David Starkey teaches in the writing program at the University of California–Santa Barbara and in the MFA program at Antioch University–Los Angeles. He is the author of a textbook, *Poetry Writing: Theme and Variations* (NTC, 1999), as well as several books of poems from small presses, most recently *Fear of Everything*, winner of Paslanquin Press's Spring 2000 chapbook contest. He has published more than 250 poems in various literary magazines.

TEXAS COAST BENEATH CRESCENT MOON

The crisp, uncompromising lights of offshore rigs
perforate the horizon, dividing the black sky
from the blacker sea, while the great jellyfish
of Galveston basks luminescent under the stars.

Where the dark sand of the withdrawn water
slides into the sea, white ropes of foam
roll up the shore's skin, and lines of tangled
seaweed shiver in the gusts of the fishy wind.

The gray cloud-rags drag themselves across
the dark, and our thoughts, too, trawl among the stars,
hauling in the drifted-away notions
of eons of ocean-gleanings and night musings.

The great, warm animal of the planet is raked by horizontals,
stroked from side to side by the neap and flood of tides.
Where water seeks its depth, the earth's rotation coils it
into whirlpools, from Gulf depression to washbasin drain.

The world-beast hold us close, so that we lie
on the resisting sand without fear of floating off,
though Scorpio rears up on the curl of his extravagant tail
and satellites coast between the still-seeming stars.

There is no sound like the uneven gush of surf —
no silence like that of the pelicans who have sailed
above us in three huge wedges, their gray wings
wide and soundless on the star-pricked night.

The Milky Way is sprayed dazzlingly on the sky,
and inside our heads the bright horns of our wonder
impale the dark, and the poise of our adoration
raises us slightly above the earth, like an incoming tide.

JEANNE EMMONS

Jeanne Emmons is a professor of English at Briar Cliff College and is poetry editor of the *Briar Cliff Review*. Her book of poetry, *Rootbound* (New Rivers Press 1998), was winner of the Minnesota Voices Project competition in 1997 and was subsequently given a 1998 Pippistrelle Best of the Small Press Award. Her poetry has appeared recently in *American Scholar*, *Calyx*, *Cimarron Review*, *Cream City Review*, *Wisconsin Review*, *College English*, and other journals.

News from the Sidney Kimmel Cancer Center

Valerie Matthews Mehl

Bullseye!

Researchers Nab the Gene, Develop Therapy for Lethal Leukemia

Among cancer statistics, acute myelogenous leukemia (AML) ranks as the most common form of leukemia. But, with just over 10,000 cases per year, it is dwarfed by the lung, breast, prostate, and colon cancers that seem to monopolize media coverage, major scientific journal reports, and the attention of major drug companies. But, when viewed in human terms, through the eyes of the people who have the disease and the researchers who have made a cure their life's work, it is every bit as devastating and every bit as worthy of treatment-advancing discoveries.

"Knowing that a disease is less common brings no solace when you're the one who has it," says Donald Small, M.D., Ph.D., a cancer researcher in the Kimmel Cancer Center at Johns Hopkins and an expert in the treatment and biology of AML, an aggressive cancer of the blood and bone marrow. To the patient, that just means that the odds were not in their favor from the start. Adding insult to injury is the inevitably slow pace of clinical studies because of the limited number of patients on whom to do them. This lack of patients is the frustration now facing Dr. Small and his colleagues Doug Smith, M.D., and Mark Levis, M.D. They have recently developed a targeted therapy that could transform this deadly leukemia into one of the most treatable forms of the disease — if, that is, they can get the word out to enough patients and physicians so that they can carry out clinical trials.

The clinical trial focuses on a drug which blocks the action of a gene called FLT3 that results in a very aggressive, treatment-resistant form of AML. He and his colleagues mistakenly believed that results of laboratory studies showed such promise that physicians would begin referring patients to Hopkins. They have since learned that many oncologists, even those in prestigious institutions, are unfamiliar with the role of FLT3. The discovery of FLT3 and its direct impact on AML is so new that many cancer centers do not even test their AML patients for the gene mutation, according to Small. And, in a sea of experimental new therapies, despite its promise, the FLT3 trial has been lost to many. As a result, Small has taken to the road, speaking at clinical and research conferences to get the word out, and has enlisted the help of colleagues at MD Anderson in Texas who have now begun enrolling patients in the study as well.

Small first came upon the key gene almost by accident, while working on ways to combat blood- and bone-marrow toxicity common to cancer-drug treatments. While identifying molecular targets involved in blood-cell development that could be used to help patients recover from the life-threatening and treatment-limiting decline in blood cells brought on by anticancer drugs, he came upon FLT3 and found it to be frequently mutated in AML. Continued studies of the altered gene in his laboratory revealed it to be the trigger for the relentless, treatment-resistant growth of certain AML cells.

Yet another breakthrough came last year in Small's laboratory when he and Levis identified and tested a drug that interferes with the function of the mutated gene. "By blocking the action of the FLT3 gene, it's as if the mutation no longer exists," says Small. It was the long-awaited payoff for more than a decade of research to pinpoint the genetic alterations associated with this type of leukemia.

Early laboratory tests on the drug, an FLT3 inhibitor known as CEP-701, showed remarkable activity against FLT3-affected leukemia cells. These promising outcomes led to the first clinical trials of FLT3 inhibitors involving patients who had relapsed after standard therapy. The first preliminary results in patients are equally impressive, according to investigators, and will be presented this month at the meeting of the American Society of Hematology. The results come after just two months of low-dose treatment

What is Acute Myeloid Leukemia?

Acute myeloid leukemia (AML), like all leukemias, is a malignancy, or cancer, of the bone marrow and blood. Leukemia is the uncontrolled growth of blood cells, increasing in such large numbers that they crowd out normal, healthy blood cells. The term myeloid refers to the type of blood cell that has gone awry. Acute means that it is a rapidly progressing cancer that quickly fills the blood and marrow with an accumulation of immature, functionless myeloid cells that prevent the bone marrow from producing large enough quantities of normal, red, white, and platelet blood cells. A lack of these normal cells impairs the body's ability to get oxygen and nutrition to vital tissues and organs, to fight infection, and to control bleeding.

AML is the most common form of adult leukemia. Approximately 10,000 people are diagnosed each year. Treatment with anticancer drugs and bone marrow transplantation is successfully used in many patients. Still, many others do not respond to therapy or relapse a few months to a few years after treatment. Patients over the age of sixty-five are generally not candidates for curative therapies because of the intensity of the treatment.

[This] was the long-awaited payoff for more than a decade of research to pinpoint the genetic alterations associated with this type of leukemia. . . .“We have turned the tables on this cancer so that the very abnormality that makes it so deadly could be what also makes it curable.”

with the drug in patients who were quite ill and with no remaining treatment options available to them, according to Smith, who is overseeing the clinical arm of the research.

Smith and Small say that CEP-701, and its action on FLT3 AML, is scientifically analogous to the drug Gleevac, which made headlines two years ago when it blocked the effects of a gene mutation in chronic myeloid leukemia and brought about rapid remissions. “I believe we can make the same impact on FLT3 AML as Gleevec made on CML,” says Small. At the same time, he realizes that it takes more than leukemia cells in a test tube and a few patients to make the case. And, he also realizes that human trials for less common cancers hinge on the referrals of patients from oncologists throughout the country and, as a result, often take longer to complete. Still, knowing these things doesn’t make it any easier to wait. “I really believe in this therapy, and its ability to save lives,” says Small. He adds, “We have turned the tables on this cancer so that the very abnormality that makes it so deadly could be what also makes it curable.”

On the Trail of a Cancer Starter

HPV Linked to Head and Neck Cancer

Maura Gillison, M.D., Ph.D.

For Dr. Maura Gillison, the human papillomavirus was a smoking gun. Having proven that the virus is present in tumor cells of a subset of patients with head and neck cancer — those patients who did not fit the risk profile for the disease — this new faculty member has now set out to discover how this new finding will affect screening, prognosis, and treatment of head and neck cancers.

A common factor among one quarter of all head and neck cancers is the sexually transmitted human papillomavirus (HPV). Maura Gillison, M.D., Ph.D., assistant professor of oncology in the Kimmel Cancer Center at Johns Hopkins, intrigued by evidence of HPV DNA in head and neck cancers, wanted to find out what role this virus might be playing in this form of cancer. “The fact that the virus had been detected in some head and neck cancers was no secret, but most scientists attributed it to laboratory contamination. I couldn’t help but wonder, what if it wasn’t,” she says.

When she began the experiment, Gillison truly expected the results to be negative, that she would not find HPV in the tumor cells. Instead, her studies not only confirmed the presence of HPV, but also uncovered another interesting fact. She was able to prove that infection with the virus was associated with head and neck cancers, primarily oropharyngeal cancers, including those of the pharynx, tonsils, and base of tongue. And to her surprise, she also found that patients with these cancers typically fared better than those with non-HPV head and neck tumors.

Though she does not currently have an explanation for the better cure rates, her research findings indicate that having an HPV-caused tumor translates to a 60-percent or greater reduction in death rates. “This suggests that HPV-positive head and neck cancers may comprise a distinct molecular, clinical, and pathologic disease very different from other types of the disease,” says Gillison.

This research, the first detailed studies of the relationship between HPV and head and neck cancers, earned her the recognition of, and a $1.2 million grant from, the Damon Runyon Cancer Research Foundation, which named her one of only five physicians worldwide to receive its

inaugural Clinical Investigator Award. More recently, it has earned her funding from Maryland's Cigarette Restitution Fund (CRF) for continued research of the disease, which strikes at alarmingly high rates in Maryland's urban communities.

Gillison is performing oral screenings in the community to determine whether HPV infection can be detected before cancer develops. She suspects that HPV infection of the upper airway and oral cavity precedes cancer development, altering the cell's ability to detoxify certain carcinogens such as alcohol and cigarettes, and putting the person at higher risk for cancer development. What she envisions is an oral pap smear. Gillison is testing several methods, similar to the cervical pap smear that detects HPV in cells of the cervix, from oral rinses to a brush that collects cells from the tonsils. Such tests would reveal the virus in cells and allow physicians to closely monitor those who tested positive for changes that could be the onset of cancer. In addition, she is collecting blood samples from volunteers to test for antibodies that would indicate HPV exposure to see how frequently exposure to the virus leads to upper-airway infection.

In a joint CRF-funded project with the University of Maryland, Gillison is doing a detailed study of patients with oropharyngeal cancers and healthy volunteers. A key element of her research is a unique computerized questionnaire that gathers information from participants about lifestyle behaviors associated with HPV and head and neck cancers. By comparing behaviors in individuals with cancer with those without cancer, she hopes to identify exposures that lead to HPV-related cancers , as well as other exposures, such as smoking and drinking, that combine with infection to trigger cancer development.

HPV infection of the oral airway may occur through oral/genital contact. In fact, other investigators, intrigued by Gillison's findings, began tracking changes in tonsillar cancer rates, the type of cancer Gillison showed was most related to HPV. They found that tonsillar cancer rates consistently increased by 2.7 percent per year, particularly among African American men, between 1974 and 1995, a period correlating with changes in sexual behavior in the United States.

Gillison anticipates a three-pronged attack against these cancers, including both public health and clinical approaches. She expects these studies to reveal a better understanding of the exposures that lead to HPV infection of the oral cavity and of new methods for detection of infection before cancer develops; in 2003 she plans to start clinical trials of immune-based therapeutic vaccines that target infected cancer cells.

A Serving of Broccoli a Day, Could Keep the Oncologist Away

There is a whole new reason to eat your vegetables!

Johns Hopkins researchers, who formerly identified a compound in broccoli and other vegetables believed to prevent cancer, have now figured out how it works.

Scientists from the Johns Hopkins Bloomberg School of Public Health have identified the specific genes and enzymes involved in this naturally occurring cancer-prevention mechanism.

They have developed a blueprint mapping the specific genes and the enzymes that they produce, which enable sulforaphane, a compound found in broccoli and other vegetables, to remove toxins from cells and prevent cancer. "Carcinogens mutate the DNA in genes, which leads to cancer. Now, we know sulforaphane present in broccoli can affect an extensive network of genes and pathways and rid the body of carcinogens," says Shyam Biswal, Ph.D., CRF investigator and assistant professor of environmental health sciences.

The discovery, funded in part by the CRF, was made using new "gene chip" technology that allows researchers to monitor the complex interactions of thousands of proteins within the entire genome. This first-ever gene profile of a cancer-preventing agent provides a new understanding of the body's defense mechanisms and could lead investigators to other cancer-preventing food compounds and strategies. Biswal says, "With this study, we have identified the specific genes regulated in response to a chemopreventive agent, telling us how the process of cancer chemoprevention occurs within the human body. And, it provides us with a novel strategy for evaluating other potential prevention agents in the future."

Photo from the National Cancer Institute, photograher unknown.

Bea Gaddy's Legacy, Saving Others From Her Fate

Bea Gaddy, city councilwoman and lifeline to Baltimore City's poor and homeless, knew that she had cancer long before she sought any medical attention, according to her daughter Sandra E. Briggs. Sandra is helping to ensure that something good comes of her mother's death with the opening of the Bea Gaddy Cancer Prevention and Education Center.

Sandra Briggs speaks at the opening of the Bea Gaddy Cancer Prevention and Education Center in Baltimore.

"My mother knew she had a lump in her breast, but she always put others' needs before her own," says Sandra. The forgotten of Baltimore City — the poor, homeless, and mentally ill — turned to Bea for food, shelter, and other needs while Bea, so focused on caring for others, ignored her own health concerns. Bea could feel the lump growing in her breast and suspected that it was cancer, but she told no one, says her daughter. Unfortunately, Sandra did not realize her mother was ill until the cancer had invaded so far into Bea's lymph nodes and tissues under her arm that she could no longer move her arm. In 2001, Bea Gaddy died. To honor her life of service, the Bea Gaddy Cancer Education and Prevention Center, which held its formal opening on June 6, 2002, is one of seven community sites providing free cancer screening and education to Baltimore City residents through the Maryland CRF.

There to celebrate the opening, among the local politicians, community and business leaders, and community residents, was Janice Owens. Like Bea, Janice found a lump in her breast. Like countless city residents before her, she went to the Bea Gaddy Center. This time, it was Bea's daughter, not Bea, ready to extend a helping hand. "I immediately recognized the signs in Janice — the look of fear and uncertainty in her eyes, the way she held her arm — that I had missed in my mother all of those years," says Sandra. "I knew I had to do something, at that moment, or like my mother, Janice would be lost, too." Sandra helped her arrange the necessary tests, and Janice is now receiving treatment.

"Bea Gaddy, a champion for the poor even after her death, lends much-needed notoriety to the countless and 'nameless' others who suffer from poor health — or even die — because they don't have money or feel they cannot access the medical community," says Jean Ford, M.D., Director of Community-Based Prevention in the Kimmel Cancer Center at Johns Hopkins.

Sandra agrees: "For a variety of reasons, many of the people we see do not feel comfortable going to big hospitals like Johns Hopkins. They will come to us and other community centers, though, and through our partnership with Hopkins and the CRF, we can help them get the information, screening tests, and if necessary, the treatment that they need."

Since the opening, Sandra reports an ongoing stream of visitors participating in breast, oral, and prostate-cancer screenings and obtaining information. "One day, we had 140 people come through in just two hours," she says. "Now, clearly that demonstrates both interest in and need for such programs in our community."

The first to take advantage of the prostate screening and examination was forty-eight-year-old Eric Dunn. Though Dunn has known many people who have had cancer and even has had some health training, it was the first time he had undergone a cancer screening. The first thing he did when he returned home was tell his sons about his experience. "Our streets are filled with misinformation. I want to send a message to all black men, but particularly to my own children, to get the truth. Prostate cancer is a real problem in the black community. We can't ignore it any longer. We need to take care of ourselves." He says that centers such as Bea Gaddy's are invaluable to the success of community cancer screening because they provide a comfortable, non-intimidating setting for community residents and Hopkins experts to come together. Dunn says, "Only time will tell if it's successful, but unquestionably we are at last moving in the right direction. This is about more than just curing a disease. It's about curing our community."

Valerie Matthews Mehl is senior writer and publications editor at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins.

Becky Levine

Stem Cells: Working to Improve Nature's Miracle

Duke University Medical Center

Dr. Joanne Kurtzberg speaks of miracles as though they were decidedly routine. In her upside-down world, they are. Her little shop of wonders houses sixteen tiny rooms where children are rescued daily from the brink of death, saved in part by modern science and in large measure because Kurtzberg earnestly believes that they can be.

Desperate parents seek her out because they have heard that she is willing to test the boundaries of modern science, to take leaps of faith where others can't or won't. Within minutes, a day at most, Kurtzberg responds to pleas from desperate parents — up to a dozen per day — who are begging for a sign of hope when others claim that none exists.

"We really believe we can treat and cure these children," she says with characteristic humility. She is speaking of her life's mission at Duke University Medical Center, saving children with rare immune deficiencies, metabolic diseases, and blood-borne cancers, all by using the same technique — infusing them with precious stem cells derived from umbilical-cord blood.

Once discarded as the refuse of childbirth, umbilical-cord blood is now viewed as the Garden of Eden for progenitor cells, a source teeming with stem cells that can transform into virtually any type of cell in the body. These wondrous little cells know just where to go, homing in on defective tissue in need of repair. Accordingly, Dr. Kurtzberg has applied their immense capabilities to cancers of the blood and genetic disorders that have previously been viewed as utterly hopeless.

Mouthfuls of obscure diseases tumble from Kurtzberg's lips as though they were days of the week — adrenoleukodystrophy, metachromatic and globoid leukodystrophy, to name a few. When pressed for details, she casually confesses to being the first in the world to use cord blood from an unrelated donor to treat and cure several of these rare metabolic diseases. So prolific is her transplant experience that cord blood is now considered standard care for recurrent leukemia, lymphoma, and neuroblastoma.

The numbers speak of her overwhelming success. In a decade, Kurtzberg's team has performed more than 460 transplants using umbilical-cord blood, nearly quadruple the number performed by any other medical center in the world. Indeed, her break-neck pace belies the warmth and compassion that she exudes to families and children, who often claim there must be multiple clones of her to accomplish so much in a single day.

Yet in her laboratory she heralds the cures that support her success, and she continually tests the limits of science with even bolder technology aimed at broadening the scope of stem-cell use.

IMPROVING ON MOTHER NATURE

Mother Nature created a near-perfect thing in stem cells, but Kurtzberg seized upon a way to make them even better. By manipulating stem cells in the lab, she is nudging them in the direction she wants them to go, coaxing more of them into becoming fighter T-cells.

"We lose kids most often because they have no T-cells to fight infection," says Kurtzberg. "It takes thirty to ninety days before the immature stem cells engraft and become immune-system cells capable of fighting for themselves. We want to reduce that precarious window by making cells engraft sooner."

So Kurtzberg pondered, is there a way to bolster cord blood's restorative powers so that it engrafts sooner than it would on its own? The answer appears to be yes.

With a little help from modern science and technology, Kurtzberg's team is literally growing cord-blood cells in a laboratory incubator to increase the number of immune T-cells it produces, reports Kirsten Krapnell, a research fellow at Duke. The expanded pool of T-cells will then be infused into the patient within a few hours of the transplant to speed up the patient's ability to fight infections.

Krapnell serves as the master chef of this cord-blood concoction, mixing the bricks and mortar of the recipe and then adding a pinch of vital ingredients that will promote T-cell growth.

The cord-blood expansion process begins with what appears to be an elf-sized muffin tray. The tray has twenty-four small wells, in which the patient's skin cells are placed. Krapnell then irradiates the skin cells to stop them from dividing, yet they continue to produce important growth factors that are critical to the recipe's success.

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Next, she puts a million white blood cells — derived from the cord-blood sample — into each well, along with five growth hormones and chemical messengers called cytokines. Just as a baker would test her product, Krapnell samples the mixture's readiness at ten, fifteen, twenty and finally, twenty-five days. In a little less than a month, she has a hundred-fold increase in T-cells. A high-tech process

called flow cytometry confirms the number of T-cells by detecting markers on the surface of cells that distinguish one type of cell from another.

The ingenious part about the recipe is that Krapnell uses the patient's own skin as the framework for growing the T-cells. Skin cells provide the meshwork on which white blood cells grow, but just as importantly, they produce their own growth factors and cytokines that would be nearly impossible to reproduce in the lab.

"We are recreating in the lab what the body does naturally," states Krapnell. "We couldn't possibly isolate and reproduce all the hundreds of important factors that cells produce, so we're doing the next best thing by allowing skin cells to create them on their own."

The first test of the recipe's viability will come from experiments in sheep. Kurtzberg's team will transplant expanded human T-cells into sheep and track them to see where they go and what function they perform. Testing in humans should begin within the next six months.

"All the components we are using to expand stem cells either belong to the patient or are substances that are currently being used in other clinical contexts, so there is no risk to the patient," says Kurtzberg. "We use the patient's own skin cells to ensure that the child won't reject them as foreign invaders, and cord-blood cells are closely matched to the patient's HLA type to reduce the chances of rejection and graft-versus-host disease."

STEM-CELL PLASTICITY

Exactly why doesn't the patient reject cord blood and its fledgling stem cells as foreign invaders? Why don't the stem cells attack their new host? And how do stem cells instinctively know to become the blood or immune cells that they need to be?

It is a biological paradox that stem cells can be at once so compatible, making themselves at home in a foreign host, yet so versatile that they transform themselves into almost any cell that the body requires.

The answer lies in stem cells' immaturity. Because they are young, they lack the requisite knowledge and power to wage war on their new host's body. Meanwhile, their youthful inexperience allows the body to nurture their development in the direction most needed.

"There is convincing evidence that cord-blood cells extend much farther than the blood-forming and immune systems, and that they can differentiate themselves into brain, heart, liver and bone cells," says Kurtzberg. "We believe they are actually correcting genetic defects that arise in these organs."

This notion of stem-cell "plasticity" sprang, in part, from clinical observations of children with metabolic diseases, who appeared to respond better to cord blood than to bone marrow. Such children are missing critical enzymes needed to break down complex sugars in various cells. As sugar accumulates in vital organs such as the liver, heart, and brain, cells become damaged and die.

"We had observed that kids with metabolic diseases who receive cord blood tend to advance more rapidly than kids who get bone marrow," Kurtzberg explains. "Their brain function seemed to be restored more rapidly. We believe that stem cells are traveling to the brain sooner, and that more of them are responding to signals that differentiate them into brain cells. The new cells then produce the needed enzyme."

Kurtzberg needed hard evidence to confirm her clinical observations, so she used x-ray imaging to illustrate that nerve cells in the brain were actually forming new myelin sheaths — the coating on nerve cells that is damaged if the enzyme is missing.

Can she prove that stem cells from the donor's cord-blood are responsible for improved brain function? Not definitively — yet. But she is well on her way to doing so. By studying heart and brain tissue donated from children who have succumbed to their diseases, Kurtzberg will be able to determine whether donor cord-blood cells have successfully infiltrated other organs and transformed themselves into nerve, liver, or heart cells.

"We are looking for specific cell-surface markers that indicate what type of cell it is, and whether that cell originated from the patient or the donor," says Kurtzberg.

Specifically, her research team will look for subtle differences, known as HLA (human leukocyte antigens), that differentiate one person's blood type from another's. If the HLA markers on a particular cell match the donor's, they will know that the cell originated from the donor-cord blood. The most convincing evidence will come from sex-mismatched donors, in which the donor is of the opposite sex to the recipient. Testing for gender is much easier and more clear-cut than HLA typing, says Krapnell.

Already, preliminary data are showing that stem cells from donor-cord blood have crossed the blood-brain barrier and differentiated into nerve cells in the brain, says Kurtzberg. Just as exciting, her laboratory is attempting to grow cord-blood stem cells into non-blood cells, such as heart and muscle cells.

Using distinctive markers on a cell's surface, scientists can tell whether a stem cell is destined to become a blood cell or another type of tissue cell. Kurtzberg's team will use these markers to select cells that are slated to become non-blood cells. Then, she will manipulate them in such a way that they become the desired cells.

"We would use these cells to repair damage in the brain or other tissues that are damaged by chemotherapy and radiation," says Kurtzberg.

Proof of stem cells' migration to other parts of the body will mark an enormous clinical milestone, as well as an important economic victory for patients whose insurance companies refuse to pay for so-called "experimental" therapy.

Indeed, Kurtzberg believes her therapies are by no means experimental. She has living proof in the form of 235 children who are alive and thriving. Five years ago, 50 to 60 percent of her children died. Today, that number is 25 percent.

Such rapid progress would have been impossible without external funding to cover the huge expense of transplantation, states Kurtzberg.

"Many of these diseases are so rare and obscure that enrolling enough patients to conduct a clinical trial would take decades to conduct, as well as millions of dollars in NIH funding that are simply not available for the study of obscure diseases," she notes. "In the meantime, we would have needlessly lost thousands of patients."

"Insurance companies have a moral obligation to pay for treatments, even if they have not withstood rigorous clinical testing," she adds. "Parents take out health insurance with the expectation that it will cover unforeseen illness, and these diseases clearly represent the unexpected."

GROW, CELLS, GROW:
One Child's Fight for Survival

Tommy Bennett's big brown eyes and sweet demeanor make it that much harder to accept his plight. Just three years old, he blithely endures the constant barrage of drugs, needles, and tests as though he instinctively knows that they are destined to cure him.

Born with a rare, degenerative disease called Sanfilippo syndrome, Tommy lacks a critical enzyme needed for proper organ and brain development. Without the enzyme, Tommy will die by adolescence. With the enzyme, Tommy's brain may unlock the potential to allow him to talk, dress, and care for himself.

Such skills have eluded his two affected siblings, four-year-old Hunter and six-year-old Ciara. Ciara had just been diagnosed with Sanfilippo syndrome when their mom became pregnant with Tommy.

Since that time, theirs has been a desperate search for someone willing to take a chance on helping Ciara, Hunter, and Tommy. The Bennetts found hope at Duke University Medical Center, the only program in the country willing to apply the benefits of stem cells — derived from newborn babies' umbilical cords — to treat this disease.

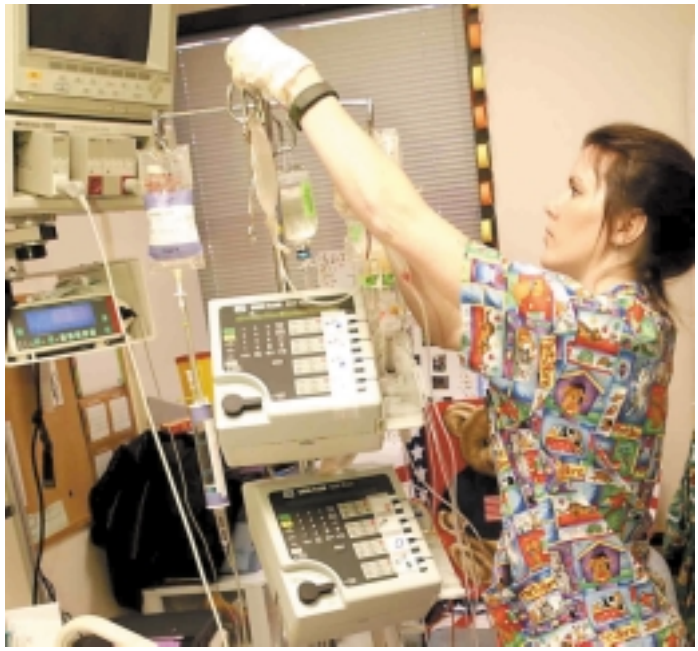
Proof of a Sanfilippo cure remains elusive, and Tommy is only the sixth Sanfilippo patient ever to have received a stem cell transplant. Yet if the transplant is to help, Tommy is a good candidate. He is young enough that the disease has only just begun to wreak havoc on his brain and organs. His siblings have progressed too far to be helped. Still, the sting of disappointment was palpable when doctors deemed Tommy the only viable candidate.

Thankful as they are for the opportunity, the Bennetts have embarked on a costly gamble — financially, emotionally, and physically. The Bennetts uprooted their kids and moved 900 miles away from family and friends to undergo a series of grueling tests before Tommy's transplant could begin.

It is also clear that Kurtzberg's passion is stirred by her patients, not just their diseases. Her program has enjoyed widespread acclaim because she has assembled a critical mass of people who are dedicated to taking care of patients and their families.

"Our team members aren't doing this for the money," says Kurtzberg. "It's quite a difficult job, so you have to truly care about the families you're treating. Our staff has both a diverse and highly specialized set of skills to deal with the incredible scope and diversity of the diseases we treat. And I think that's what makes us unique."

Becky Levine is a science and medical writer at Duke University Medical Center. She holds a B.A. from the University of Michigan, Ann Arbor, and a master's degree in journalism from the University of Maryland, College Park.



Photos in this article are courtesy of Duke University Medical Center.

Then came the real test of endurance. Confined to the hospital unit for four straight weeks, Tommy's small body was ravaged by toxic doses of chemotherapy designed to wipe out his immune system and make way for a new one that might provide the crucial enzyme.

Alicia took on hospital duty, caring for Tommy night and day, and catching a few winks of sleep as time permitted on a pull-down cot. John assumed full-time care of Ciara and Hunter at a rented apartment nearby, no easy task given Ciara's penchant for 3 a.m. awakenings.

The process is clearly daunting, yet the transplant itself is deceptively simple. It takes just fifteen minutes for a bag of red liquid to drip intravenously into a child's bloodstream. Nurses literally squeeze every last drop from the bag, lest they lose a single stem cell that floats amidst a billion blood and supporting cells.

Every parent knows that stem cells hold the key to their child's survival. If they grow, the child has a fighting chance to live. If they do not, the child has probably exhausted his or her last resort at a cure.

Then comes the wait, and the familiar refrain: "Grow, Cells, Grow." The words resonate within the halls, grace the walls of every room, and are sprinkled throughout cards of love and hope. Parents recite them like a battle cry designed to incite soldiers to action.

Indeed, stem cells are like tiny soldiers who descend upon bone marrow and rescue it from near-certain demise. So powerful are stem cells that it takes only ten to a hundred of them to restore a child's entire blood-forming and immune system — in Tommy's case providing the missing enzyme. Moreover, they know exactly where to go and what function to perform.

Yet such remarkable power is not without its drawbacks. Stem cells can attack the last remnants of the child's immune system, a complication called graft-versus-host disease. Stem cells take time to grow and mature, leaving the child's developing immune system vulnerable to minor infections that could prove deadly.

Children also suffer mightily from the dangerously high levels of chemotherapy needed to wipe out their immune system. Often, their mucous linings literally slough off from within, causing severe diarrhea and vomiting. Nausea, painful sores, fatigue, and stomach pains also plague the children as the chemo exerts its effects.

Luckily, Tommy endured far less of the usual symptoms of his transplant, but only time will tell if the new cells have become his own. A year must pass before his new immune system will be running at full force. A lot can happen in that time, but hope, prayer, and a will to overcome will be on their side.

MY NEIGHBORS

I'm positive the only force holding them up was
their own momentum as they leaned forward
and in a lovely fluttering manner Venus and
Aphrodite glided across the busy boulevard
confident of the joy they'd bring to the Lotharios
in the local watering holes. They however
looked right through me.

Their graceful athletically slim bodies did not
begin to feel any strain — much of their stored
energy readied for the night ahead. Several
moments of merriment were in the offing for
them I thought.

I alone am the one who can explain the craving
and desire I felt when I saw them with their light
fluffy dresses swirl and cling to their legs in some
places revealing their sinewy thighs while rushing
across the avenue laughing about whatever thrills
awaited them on that sultry eve O how I longed
for their attention.

The hurrying pair resembled wind chimes being
jostled in a summer breeze when they dodged
those speeding autos. The youthfulness the playful
mood the energy the throw-caution-to-the-wind look
the focus they bore only reinforced my belief
the duo would pass my door again and again night
after night unaware I ached to be with them.

RONALD K. BURKE

Ronald K. Burke is professor emeritus of speech communication at Syracuse University. He is now a free-lance writer residing in West Hollywood. Burke has articles published in academic journals, and he has written books on antislavery activists. Several of his poems can be found in small presses.

THE PRINCESS WHO "RAN AWAY"

to join the circus wouldn't have it any other way.
Stephanie of Monaco didn't sidle or sulk — it was by no
means a carefully considered decision, a thoughtful
weighing of pros and cons. No concern that joining the
circus was yet another illusion: that "ever since grade
school all [she'd] ever wanted was . . ." and if wrong,

what of future imaginings? "I will be happy when. . .";
the reality is *never* and *not*. Nobody musing "Steph's
kinda clumsy though not entirely mistaken." Fleeing the
"stuffy" palace (is there any other kind as even
Cinderella might discover): was Stephanie driven by a
praiseworthy desire to pare down? Had she read *The
Practice of the Presence of God* by a blessed pot
scrubber perhaps in Cinderella's own scullery? What's
    best to hope for, to want?

The princess citing Picasso, something arty to tart up
her escape — his blue period painting of a juggler.
She can never quit the circus now, too many other false
starts (clothing designer, rock singer, perfume
entrepreneur). Having no credibility better? All she
wants is simplicity though it looks like humiliation.
Like a spiraling down ending in total defeat.
        Spiritually superior but it hurts.

MARY WINTERS

After working as a lawyer, Mary Winters is currently a reading specialist in an East Harlem elementary school. Her poetry has appeared in *Anthology of Magazine Verse & Yearbook of American Poetry*, *Cimarron Review*, *Commonweal*, *Gulf Coast*, *Massachusetts Review*, *Quarterly West*, *Seneca Review*, and *Washington Square*. Her book *A Pocket History of the World* was published by Nightshade Press. She was a featured poet in the Palanquin Press pamphlet series, and two of her chapbooks were contest prizewinners.

Stephanie J. Bond

Bully Pulpits and Cancer

Many well-known people have used their celebrity to create awareness about certain types of cancer. Katie Couric, anchor of *TODAY* on NBC, immediately comes to mind. Since her husband's death from colon cancer, she has done a number of programs to make the public aware that a simple screening procedure, a colonoscopy, can detect colon cancer early before it becomes deadly. To prove her point about how easy it is to have a colonoscopy, she had one on national television. With *TODAY*'s millions of viewers, Couric has quite possibly saved hundreds of lives.

Breast cancer, the second-leading cause of cancer death in women, and prostate cancer, the second-leading cause of cancer death in men, have had their celebrity spokespersons. Usually survivors — Bob Dole, for example — point out that screening procedures such as PSA or mammography can detect these cancers early when, such as with colon cancer, there is a fighting chance for a cure.

As I have watched these spokespersons and applauded them for their efforts at raising public awareness, I always wonder, where is lung cancer's spokesperson? Lung cancer is the leading cancer killer of both men and women. Yet, you rarely hear someone telling you what to do to fight lung cancer — to catch it before it kills you. Unfortunately the reason for this may be that right now there is precious little that can be done to detect lung cancer early and not a whole lot that can be done after a diagnosis. I am sorry to say that I know this from personal experience.

YOU DON'T HAVE TO BE A SMOKER TO GET LUNG CANCER

In 1993, by a very lucky fluke of getting a chest x-ray before an outpatient procedure, my husband was diagnosed with lung cancer. The spot on his lung was minuscule. It would not have ordinarily been discovered until he had some sort of symptoms. He was not a smoker after all, so he did not get regular chest x-rays as part of his physicals. Because it was discovered very early and a lobe of his lung was removed, his prognosis was brighter than that of most people who have lung cancer. "Go home, forget about this, and enjoy your life," the doctor told him. No one ever mentioned that there was a 50-percent chance of a recurrence. And in our efforts to forget about this terrifying time, neither of us read up on the disease to find that fact out for ourselves. The regular check-ups were scary-enough reminders.

The chest x-ray in June 1996 had been fine, although my husband seemed concerned about it — for no reason that he could explain. A nagging backache made him get an MRI in August, which showed that the lung cancer had recurred. Now in both lungs and down his spine, his prognosis could not have been worse: six to eight months to live, perhaps as much as a year with chemotherapy.

While being handed his death's ETA was gruesome enough, my husband's weekly chemotherapy was absolutely grueling. He was determined to live a "normal" life (like this was even vaguely possible), but the chemo stopped him in his tracks. After four months of a new treatment, x-rays and MRIs showed that the cancer was gone. He was in remission. Everyone was amazed. The oncologist counseled caution, but she was delighted with the results.

Then, in what is often lung cancer's natural progression, the cancer came back with a vengeance, this time in his brain. As the cancer spread, it was like watching someone go through Alzheimer's at Mach one. Within a three-week period, he lost the ability first to talk, then walk, then chew, and then control his bodily functions. A man who was a history professor, teacher, and administrator, whose stock in trade was his intellect and verbal abilities, was robbed of everything that made him — him. Such a cruel, cruel disease. He died seven months after the recurrence was discovered.

Words cannot begin to describe the profoundly awful experience of watching someone you love

Photograph by Ted Bodner.

Gordon C. Bond. November 17, 1939–March 27, 1997.

suffer and die from cancer. It makes me wish with all my heart that no one else will ever have to suffer that way. I understand completely the need of people who have media access to go public with any information that might prevent another person from such pain and suffering.

TAKING MY BULLY PULPIT BY THE HORNS

Because this space is as bully a pulpit as I am ever going to get (unless Katie Couric calls to offer me air time on *TODAY* to get a chest x-ray or an MRI), I want to encourage everyone to be more aware of your lung health. Obviously, smoking is not good for you. You say quitting is hard. I'm sure it is; I'm sure I can't even begin to imagine how hard. But lung cancer is vicious.

If I thought for one minute that giving the horrifying and gruesome details of death by lung cancer would cause even one person to put down his or her cigarettes, I would write about them. I'm fairly sure that the scare tactics won't work, however. But as I watch students on the campus where I work, especially the women, holding their cigarettes as if they think that they are the most sophisticated chicks to come down the pike, I want to tell them that sophisticated is the last thing that lung cancer metastasized to the brain is. It is an especially mean way to die.

Increasingly, nonsmokers such as my husband are being diagnosed with lung cancer, and more women, for some unknown reason, are in this group. Perhaps it is from exposure to some airborne chemical pollutant, perhaps from a genetic predisposition — who knows? Does it really matter how someone gets lung cancer? That lung cancer is the leading cancer killer is the important point. Like most forms of cancer, lung cancer has no regard for race, creed, tax bracket, or national origin.

While little has changed since 1993, either in early detection of an initial lung-cancer diagnosis or of recurrences, pre-operative chemotherapy before lung cancer surgery is looking like a promising method of preventing recurrences. And MRIs are now the approved follow-up screening instead of just chest x-rays, so recurrences can be found earlier. The sad truth remains, however, that lung cancer recurrences are incurable.

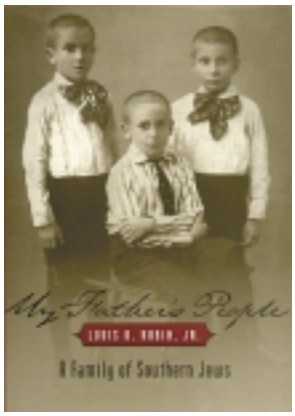
Maybe soon new advances will be made, and a celebrity spokesperson will be able to make the public aware of new early-detection procedures that will give doctors a fair fight with lung cancer. Until then, please be kind to your lungs. And get a physical.

Stephanie J. Bond is an associate editor at *Phi Kappa Phi Forum*. **She wishes to thank Edith F.K. Graves, M.D., for reading this article for accuracy.**

Book Reviews

LOUIS D. RUBIN, JR. *My Father's People: A Family of Southern Jews*. Baton Rouge, LA: Louisiana State University Press, 2002. 139 pages. $22.50.

Louis Rubin has long been known as a leading scholar and proponent of Southern Literature. What is somewhat less well-known is his nurturing of contemporary southern writers, such as Annie Dillard, Lee Smith (see the review on page 41), and Jill McCorkle, through his encouragement as a teacher and his founding of Algonquin Books, which he ran from 1982 to 1989 before selling it to Workman Publishing because of financial difficulties.



In *My Father's People*, Rubin turns away from literature and criticism to write an affectionate remembrance and analysis of his father's family — an eccentric, talented group of siblings who overcame poverty growing up in Charleston, South Carolina, to succeed in their very different fields. The poverty that the family experienced (brought on by their father's illness and debility and seven mouths to feed) early on was so profound that three of the children — Dan, Manning, and Louis Rubin, Sr. — were sent away to live in the Atlanta Hebrew Orphanage for three years until other children were old enough to work and help support the family. The three boys' experience in being "orphaned" profoundly affected their characters.

Rubin spends most of the time in the book concentrating on his uncles and the one aunt he knew best, Dora. The youngest two of his aunts, Esther and Ruthie (the only Rubins of that generation to finish high school), he knew less well, and he spends barely a paragraph or two on them. Esther was married to a compulsive gambler who eventually went to prison, while Ruthie (called that to distinguish her from her brother Harry's wife, Ruth) never married. For the other siblings — Dora, Harry, Dan, Manning, and Louis Sr. — he paints a vivid picture of fiercely independent individuals shaped by the stigma of their childhood poverty.

Dora, the oldest of the children, is characterized as a kind, affectionate person who coped with her parents' poverty by essentially denying it in her own mind, a practice that became a life-long habit. She worked as a secretary her entire life, never married, and lived with her two younger sisters later in her life. Harry, the oldest boy, took on the role of family patriarch after his father died. One of only two of the brothers to marry, he worked for a wholesale dry goods house and yearned to be known as a "Person of Consequence" (31). He became an arch-conservative segregationist, and "The Old South, with its aristocratic ideal and martial bearing, was [his] El Dorado" (29).

Dan, who is Rubin's favorite uncle, was a newspaperman who became a very successful playwright in the 1920s and a screenwriter in the 1930s. He saved the money that he made in Hollywood and invested wisely enough so that he could return to writing plays full-time in the 1940s, writing two plays a year without fail. Yet he never had another play published or staged. Manning was another newspaperman who eventually rose to the position of assistant editor of the *Charleston Evening Post*, and like Dan he was a lifelong bachelor. He could have been named editor, but that position required a level of social interaction that Manning would not or could not handle. He was a solitary man who felt more comfortable with children than with adults, though he had none of his own, and above all was a man who kept his own counsel.

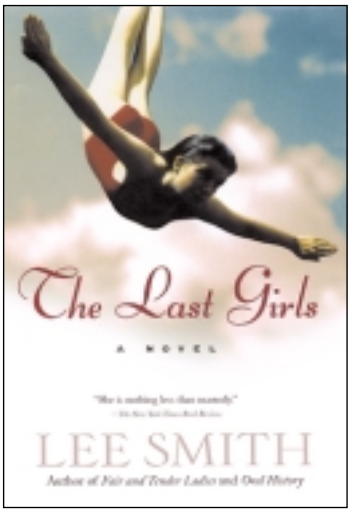
Rubin's father, Louis Sr., was initially a successful businessman who, after being felled by a life-threatening illness, witnessed the failure of his electronics business through mismanagement of the man whom he left in charge. Fearful of duplicating his own father's failure as a provider, however, Louis had purchased enough disability insurance so that "his family was adequately provided for, and if not well off, certainly reasonably comfortable" (100). Louis, in stark contrast to Dan and Manning, loved the spotlight and was always doing something to get his name in the news. He eventually became a long-range weather forecasting pioneer by studying the effects of volcanic eruptions on the weather. He even wrote and marketed a small booklet called *How to Forecast the Weather*, which was distributed to millions of people, including school children, until his death in 1970. A book on weather forecasting that he had been writing with a collaborator was published shortly after Louis died.

As much as anything, *My Father's People* is about Rubin himself trying to understand what made these people who they were. He spends a good deal of time analyzing why his Uncle Dan's later attempts at writing plays were such dismal failures, when he had earlier enjoyed such tremendous success. He concludes that Dan's self-imposed total isolation during the time that he was actually writing was deadly to his ability to write plays because in doing so, he deprived "himself of the one element that could make possible an ongoing deepening of his dramatization of human life as he experienced it — his own continuing imaginative participation in that life" (56). Of his Uncle Manning, perhaps the oddest of all the Rubin brothers, he says, "In a deeper, more complete, and perhaps more ultimate way than anyone else I have ever known, he was *alone* — more so even than Dan, for whom isolation was a deliberately willed condition" (80). Louis Senior, though he was as outgoing as Dan and Manning were introverted, is described as equally self-absorbed, to the point that he "tended to view his children as adjuncts to his design" (120).

My Father's People is a beautifully written book that pays tribute to but does not whitewash the lives of a remarkable southern family who also just happened to be Jewish. It is well worth a few hours of your time.

Pat Kaetz is the editor of the *Phi Kappa Phi Forum*. He was fortunate to have had his doctoral dissertation directed by one Louis D. Rubin, Jr.

LEE SMITH. *The Last Girls: A Novel*. Chapel Hill, NC: Algonquin Books, 2002. 284 pages. $24.95.



While Lee Smith was one of Louis Rubin, Jr.'s students at Hollins College, she and fifteen other "girls" decided to take a raft down the Mississippi River from Paducah, Kentucky, to New Orleans, Louisiana. Inspired by *Huckleberry Finn* and the idea of a coming-of-age quest, the girls embarked on a trip that Lee Smith describes in *The Algonkian* (Fall 2002) as "the only journey I ever made that ended as it was supposed to. Subsequent trips have been harder, scarier."

These harder, scarier trips into adulthood are the stories of the four now middle-aged women who have come to say good-bye to a fifth in Smith's *The Last Girls: A Novel*. Four former college suitemates are recreating the raft trip that they took as young, seemingly carefree undergraduates. Now adult women with plenty of mileage and on the *Belle of Natchez* steamboat instead of a raft, they come together to scatter the ashes of Baby Ballou, the group's wild child — or that is the role the group ascribed to her.

None of the character's stories is exactly what the others think it is — either as undergraduates and now as grown women. Lee Smith is a wonderful storyteller. She effortlessly pulls the reader into the girls' more innocent undergraduate world at the fictional Mary Scot College, when "They expected to be taken care of. Nobody had yet suggested to them that they might ever have to make a living or that somebody wouldn't marry them and look after them the rest of their lives. They all smoked cigarettes. They were all cute. They headed down the river with absolute confidence that they would get where they were going (18)." This was 1966, when young women were still called "girls."

Then Smith delves back into their adult lives, in which things have not always turned out well, despite outward appearances. One has never married; one has the picture-perfect life that is just that facade and no more; one is professionally successful to avoid having a personal life; and one has been married three times. Some sneak a cigarette in times of stress. Some color their hair. These women come alive as real people, and Smith's writing style is so intimate and smooth that the reader feels as if she is dishing the dirt with a friend about them.

If I have any criticism — and maybe it is just a matter of Smith writing the story her way and not mine — it is that Smith could have put greater emphasis on how different those times were for girls/women. For example, I wonder at Baby's promiscuity at a time when birth control pills were not readily available to single women, and abortions were still illegal.

Publishers Weekly describes *The Last Girls* as "*The Big Chill* meets *Huckleberry Finn* in a moving novel inspired by a real-life episode." I would add that *The Last Girls* also has a generous helping of *A River Runs Through It* and a dollop of *The Divine Secrets of the Ya-Ya Sisterhood* tossed in for good measure. But *The Last Girls* has its own unique flavor, and it all comes down to the stories that we all have — and the stories that everyone knows about us — which may or may not bear any relation to what our stories actually are.

The Last Girls is a good read — in turns funny, sad, poignant, and honest. Alas, *The Last Girls* is probably "chick lit," and will not have a big audience among men. That is unfortunate, because *The Last Girls* is an honest portrayal of the non-linear way girls grow into women. And while the characters in this story are privileged and educated, their struggles are universal.

Louis Rubin, Jr. must be very proud of Lee Smith.

Stephanie J. Bond is an associate editor at *Phi Kappa Phi Forum*.

FORTHCOMING ISSUES

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PROFESSIONAL ETHICS

Summer 2003
ARCHITECTURE

Fall 2003
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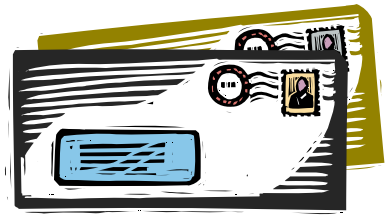
Winter 2004
IS DEMOCRACY IN DANGER?

Letters to the Editor



ANTHROPIC QUESTIONS

I read with interest this article about the anthropic questions raised by the "just so" state of the universe that allows for human life ["Anthropic Questions" by Gordon Kane, "Big Space/Little Space," Fall 2002] Dr. Kane speculates much on the various reasons that this could have happened by chance. He dismisses those who think that there may be design with two sentences: "If you win the lottery, you may feel very grateful, but someone had to win, and no one selected who that was, except randomly. Just because a universe has a unique set of laws and parameters should not lead one to wonder whether that set was designed" [p. 24]. You mean when I see all the beauty and complexity in the universe and in life itself, the inappropriate response is wonder? And to wonder how it could all come to be is a question that is out of bounds? Hmm. That seems a bit narrow to me.

But I will grant that the physicists and astronomers may someday be able to explain all the universe by reference to law and equations and that there would be nothing that remained a mystery. Would that eliminate the question of God? I think not.

May I suggest an analogy? Let us take a simple piece of piano music by Bach only two pages in length, Prelude No. 1 in C major. There is much to explain about this piece. I can describe the Baroque period in which he lived, the cultural milieu in Germany where he wrote, and all who influenced him. I can describe the physics of the piano and how it is constructed and why sounding various keys produces different notes and how the ratios of the vibrations of the strings produce tones and overtones. I could go into music theory and reveal how the various chord sequences in the piece are pleasant to the human ear, and then I could explain why the human ear responds the way it does to produce pleasure in the listener. I could delve into the anatomy and physiology of the human hand and mind that allows us to play such pieces. Etc., etc., etc.

But all this does not explain one thing: the genius of the composer. In fact explaining all the above only casts his genius into clearer focus, for he created a masterpiece using all these as his tools to make a beautiful composition that we admire 300 years after his death.

Dr. Kane thinks that if he could explain all of the universe he would eliminate the need for thoughts of a Designer. In actuality, his ruminations make the evidence for a Designer even more clear. The universe is a *wonder-producing* combination of law and chaos, and I am not amiss in attributing it to a Master Designer, in spite of Dr. Kane's objections.

Allen E. Shepherd, MD
Berrien Springs, Michigan

BIG SPACE/LITTLE SPACE

Congratulations on the fall issue of *Forum* ["Big Space/Little Space"]. I found it extremely interesting, having just tackled Hawking's book on *The Universe in a Nutshell*. You are timely, and I commend you on the policy of centering issues on themes. I appreciate that that simple policy is very taxing and requires much careful thought in advance.

George W. Williams
Durham, North Carolina

The Fall 2002 issue, cover-to-cover, had a common theme: relative to, relativity, and relativism. Einstein's "Theory of Relativity" perhaps is the worst-named theory in science. Any human applying only a minimum of natural reasoning must accept that "relativism" is, of logical necessity, the "true" state, as opposed to "absolutism." He also must, for peace and harmony in his soul and within society, accept that standards (under the guise of absolutism) are useful artifacts, else there can be no judgment, no evaluation. The only real bone of contention is who gets to define the standards (aka absolutes).

Theoretical science applies "thought experiments." Let's apply one. Suppose the smallest life-form we know had the equivalent of human intellect, and suppose that this life-form existed solely within the tissue of our life-form. What grand model of cosmology would this pea-brain perceive, conceive, theorize? Would it be the same as ours? Would it exist within the same cosmos as the human? Would each model be relativist or absolutist? Which would be solid-gold and diamond 100 percent *true*?

The first Letter [to the Editor] was near pure absolutist; popular standards well transmitted and integrated. Others were mixed relativist, but Zinn's article was worth the journey among free ideas. Confession: My aged pea-brain couldn't quite handle the dazzle of the cosmic articles, but they also were worth the journey.

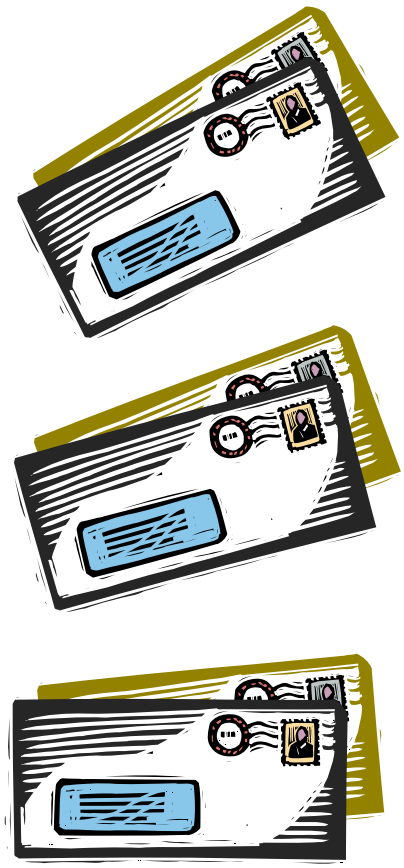
Louis G. Dooley
Ocala, Florida

ABSOLUTELY THE FINAL LETTER ON HOWARD ZINN'S ARTICLE THAT WE WILL PUBLISH

As an American citizen who cares deeply about the national security of the United States, I am insulted and embarrassed by the letter written by Malcolm Muir, Jr. in response to Professor Zinn's "A Just Cause, Not a Just War" ["Terrorism," Spring 2002]. To suggest that Zinn should move to Iraq or Syria instead of criticizing the actions of a government with which he disagrees is not only

insulting to all Americans, but is precisely the brand of arrogance and self-righteousness practiced by the Bush administration. The freedom to disagree publicly with a government that is leading us into an ill-advised and dangerous war is exactly the type of freedom that American soldiers have died to protect! Disagreeing on policy is not anti-American. Rather, what is anti-American is to use tired rhetoric in an attempt to stifle any opinions that may disagree with your own. Mr. Muir, if you truly care about the future of your country, you should not run from open discussion on U.S. foreign policy. Why not present argument against Mr. Zinn's conclusions, instead of ignorant shock over the fact that he disagrees with you?

Aaron Zeichner
Minneapolis, Minnesota



COAL TOWN, 1926

Night in Coal Town, Hunkie Row.
In a spill of uncut pitch we live,
floating ash from the alps of slag
the wet moon loops above as an
omen we cannot read. Here,
the cornsnow ricks dingy drifts
and a man grovels for ten-hour
turns in the space of a tomb. Here,
a swampslash of carbon defines us,
blesses us with its dark rainbow;
its oily grit flavors us like stew.

And here, tonight, a lone woman
at a lop-legged table cribbed with
cap boards like a piece of bad top
moon-watches, breathes in the ash,
the odors of stove polish and Hardwater
Castille Soap. She smiles at the way
lean flames of oil lamps flinch behind
curved glass. Her face is shining.
In the barn a blind pullhorse named
Doll stands asleep. Fresh-paid men
shuffle in line before the Yates' whorehouse.

DAVID BOND

David Bond is a member of Phi Kappa Phi from Southern Illinois University at Carbondale, where he received an MFA in Creative Writing. He is currently Interlibrary Lending Manager at Morris Library. He has recently published poetry in *Black Dirt*, *Clark Street Review*, *Valparaiso Poetry Review*, and *Branching Out*. His book *Colors* is available at bookstores and online at www.greatunpublished.com.

THIS JOURNEY

It is,
of course, one of
the well-worked
metaphors
employed by poets;
The long and pained journey.
The whorl of road ahead.
The grand and stony
insurmountable summit.
The horizon which seems
always to occupy
the most distant point
of our seeing.
Sometimes a stretch
of desert for effect.
The path is always
rocky, muddy after
an endless rain.
Or baked by a sun
without remorse.
There is fog,
thick as a cataract.
A wind like a
palm, pushing us back.
And we poets
are almost always
going it alone.
The sweet, unbearable
solitude, our crucifix,
our nourishment.
But today,
I will not make
another entry into
the log of my
own many miles,
but say, rather,
that I have arrived at
that very place I
once saw in a dream.
It is as I had imagined.
And there was
someone waiting.

DANIEL THOMAS MORAN

Daniel Thomas Moran is the author of five collections of poetry, the most recent of which, *From HiLo to Willow Pond*, was released in the spring of 2002 by Street Press of Sound Beach, New York. He is Literary Correspondent to Long Island Public Radio and is the vice president of The Walt Whitman Birthplace Association. His poem "no title yet–for Billy Collins" (*National Forum*, Summer 2001) has been nominated for a Pushcart Prize.

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HIGH FLIGHT

Oh! I have slipped the surly bonds of Earth
And danced the skies on laughter-silvered wings;
Sunward I've climbed, and joined the tumbling mirth
Of sun-split clouds — and done a hundred things
You have not dreamed of — wheeled and soared and swung
High in the sunlit silence. Hov'ring there,
I've chased the shouting wind along, and flung
My eager craft through footless halls of air ....
Up, up the long, delirious, burning blue
I've topped the windswept heights with easy grace
Where never lark, or even eagle flew —
And, while with silent, lifting mind I've trod
This high untrespassed sanctity of space,
Put out my hand, and touched the face God.

— Pilot Officer John Gillespie Magee, Jr., RCAF

In Memoriam

The crew of the space shuttle *Columbia*
February 1, 2003

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