DukeMed MAGAZINE

VOLUME 4
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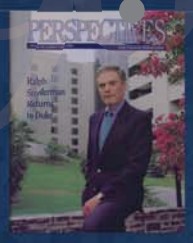
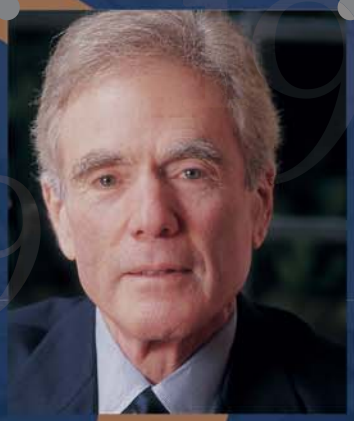
SPRING/SUMMER 2004

ADVANCES IN RESEARCH, EDUCATION, AND PATIENT CARE AT DUKE

Looking back on Ralph Snyderman's

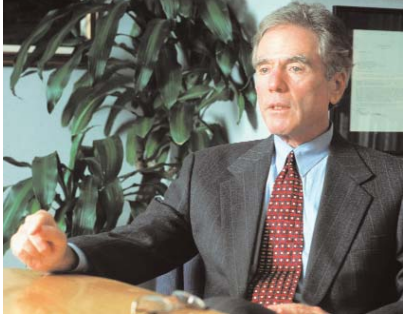




15 YEARS AT THE HELM

Duke's longtime chancellor for health affairs steps down June 30

PLUS: THREE FEATURES ON THE LATEST FINDINGS IN CANCER RESEARCH
Targeting breast cancer • Transplant therapies • Drug discoveries



Still in awe

For the past 15 years, I have used this column to talk with you about one of the most remarkable places I know, Duke University Medical Center and Health System, and the extraordinary people who work here. Typically, with each issue of this magazine, I've told you about some of the many accomplishments of this amazing institution, briefed you on the challenges facing us and our nation's health care system, or introduced you to one of our talented physicians, scientists, nurses, and other caregivers.

But now, after 15 years, I am retiring as chancellor. This time, for my final column, I want only to tell you how much this experience has meant to me and to express to you my very deep and heartfelt gratitude.

Being chancellor for health affairs at Duke University has been, quite simply, one of the greatest privileges of my life.

It was almost 40 years ago when I first set foot on the Duke campus. A senior medical student from the SUNY Downstate Medical Center in Brooklyn, I was here to interview for a medical internship. After a particularly grueling session of gallop rounds with Dr. Eugene Stead, I had serious doubts about any future I might have had in medicine at Duke. But that changed when the chief resident took me on a tour.

As we walked the halls of the hospital, the clinics, and the few small research labs, I could sense an unmistakable aura about the place. From the physicians, the nurses, the orderlies, the housekeepers, and others, I picked up the definite feeling that Duke was a place where wonderful things were happening, a place destined for medical greatness. For me, the deal was sealed when the chief resident ended the tour by walking me out the front door of the Davison Building and onto the main quad of the Duke campus.

As I looked down the quad and then back up at the Davison Building, my jaw dropped. I was completely awed. For this boy from Brooklyn, it was the most beautiful place I had ever seen. I knew this was where I wanted to be. And except for brief sojourns to the National Institutes of Health and to Genentech, I have been here ever since.

Virtually every workday morning for the past 15 years, I have gone out of my way to come in to work through those same doors. Every day, I have looked down the quad and up at the Davison Building, and every day I have been as impressed with this medical center as I was on that day so long ago.

I was in awe when I started at Duke. I'm still in awe as I step down as chancellor.

Throughout my time here, from that first visit to today, the source of that awe, the source of that palpable Duke aura, has been the people who work here. Yes, the Duke stone helps, but the real aura about this place can't be mined in any quarry.

From the very beginning, when Dean Wilburt C. Davison was just launching this adventure, right to the present, Duke University Medical Center has been a story about remarkable people, joining together for a great and common purpose. Whether department chairs, physicians, nurses, researchers, cafeteria workers, or housekeepers, all are engaged in the important work of helping and caring for other human beings.

I am honored to have been a part of this team. Whether you are an alumnus, a referring physician who entrusts us with the care of your patients, or one of the thousands of people who work throughout the Health System, please know how deeply grateful I am to have served as chancellor and to have been able to work with you. For all that you do for Duke, for the hard work you do for our patients and for one another, and for your friendship and support over the past many years, both for me and for this medical center, I thank you.

RALPH SNYDERMAN, MD
CHANCELLOR FOR HEALTH AFFAIRS,
DUKE UNIVERSITY
PRESIDENT AND CEO,
DUKE UNIVERSITY HEALTH SYSTEM

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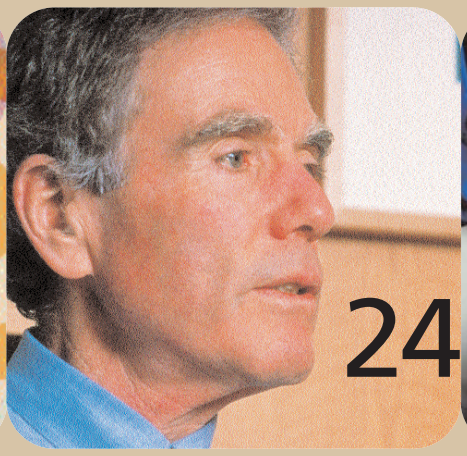
Targeting breast cancer

Early detection remains the key to survival—and new techniques are finding breast cancer earlier than ever.

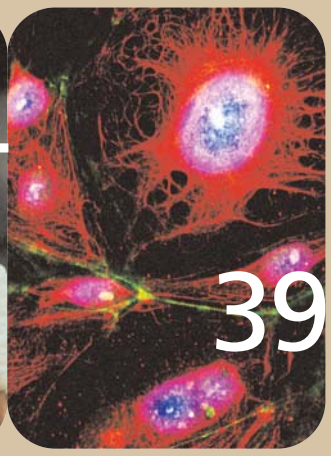


The Snyderman legacy

Looking back on Ralph Snyderman's 15 years at the helm of the Duke health enterprise.

What's bred in the bone

The new generation of transplant therapies in the fight against cancer.



Wrecking alien cells

Creative strategies to battle malignancies are emerging from the new understanding of cancer's aberrant cellular machinery.

More on health on DukeHealth.org

DukeMed Magazine comes out just twice a year—but if you want more health information and medical news from Duke, there's a great new place you can go 24 hours a day, seven days a week: DukeHealth.org.

Recently launched by Duke University Health System, DukeHealth.org is a redesigned and retooled Web site created to help consumers and patients stay informed and healthy. The site combines a broad range of continually updated health content, with information on all hospitals, clinics, physicians, and medical services offered through Duke University Health System. Its content is continually updated to reflect the newest research, medical innovation, and health information produced by Duke.

At the core of DukeHealth.org is a health information gateway called Health Portal. Currently, DukeHealth.org has five portals, including heart, cancer, women, children, and orthopedics. Online visitors selecting a health portal receive an array of information and resources in one of these areas, such as feature stories on patients and treatments, related news and research generated by Duke, health tips, available clinical trials and a spotlight on a physician who specializes in that area. The new DukeHealth.org also offers extensive drug and herb libraries, as well as a disease encyclopedia with descriptions, treatments, and preventive medicine for hundreds of diseases and ailments.

The new DukeHealth.org is a major component of Duke's information technology agenda, providing patients and the community with better and more personalized access to health information and services via the Internet. The evolution of Dukehealth.org will give patients secured access to their medical records, personalized health progress data, prescribed medications, physician referrals and lab results as well as the ability to request physician appointments online.

As Asif Ahmad, vice president and chief information officer of medical information systems at Duke University Health System, says, "Dukehealth.org moves us a step closer to creating a complete network of personalized care for our patients where we are not just improving our standard of services but creating an entirely new definition of health care at Duke."

Visit the site at http://dukehealth.org.

DukeMed Magazine is online at **dukemedmag.duke.edu**

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Acting Editor:
Dorothea W. Bonds

Designer:
Regina Barnhill

Contributing Editor
DukeMed Now, People
& New Physicians:
Sherry Williamson

Contributing Editor,
Clinical Update section:
Catherine Macek, PhD

Creative Director:
Jeff Crawford

Production Manager:
Margaret Epps

Publisher:
Dorothea W. Bonds

Contributing Writers:
Neil Chesanow
Dennis Meredith
Catherine Macek, PhD

Contributing
Photographers:
Butch Usery
Chris Hildreth

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DukeMed Magazine
DUMC 3687
Duke University Medical Center
Durham, NC 27710
919-419-3271
dukemedmag@mc.duke.edu
Web: dukemedmag.duke.edu

WILL MCINTYRE

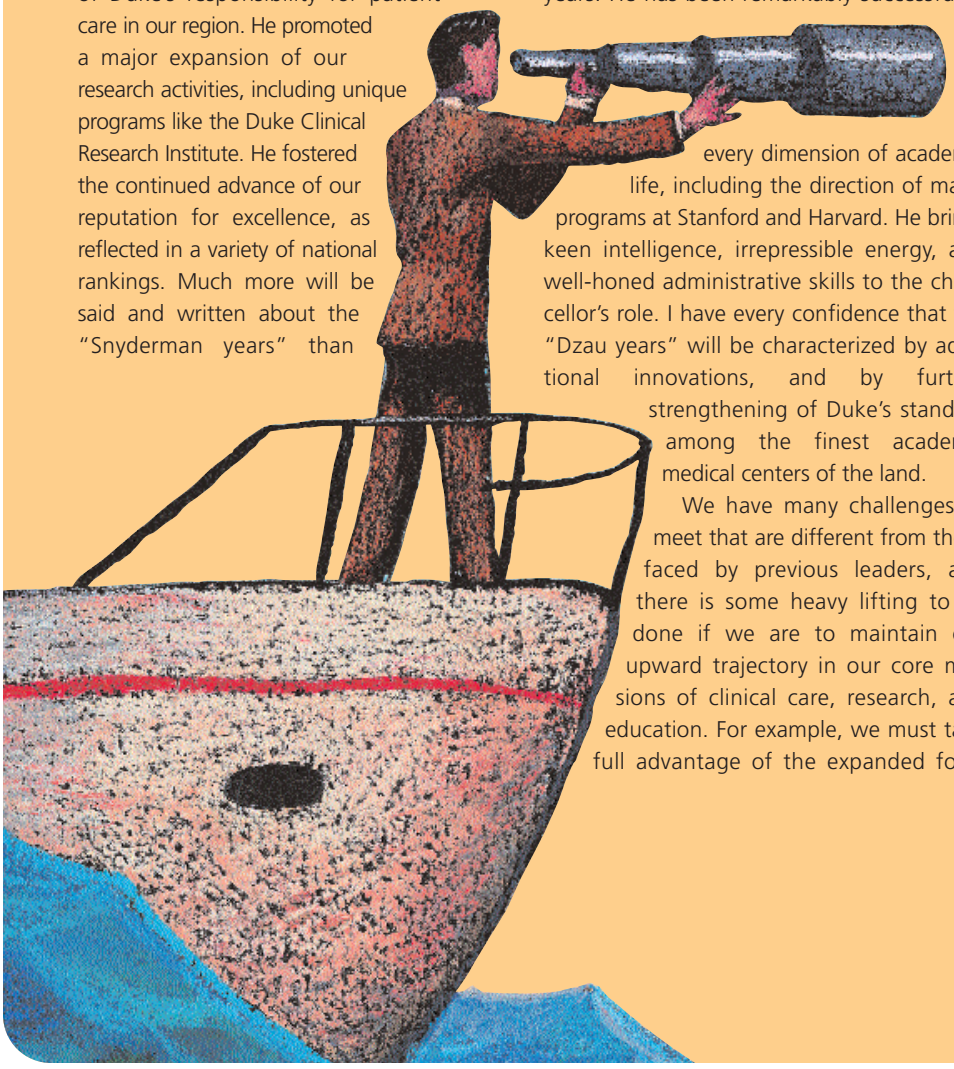
Of chancellors, challenges, and change

by R. Sanders Williams, MD
Dean, Duke University School of Medicine
Vice Chancellor for Academic Affairs,
Duke University Medical Center

THIS SUMMER, Ralph Snyderman will step down as chancellor for health affairs and CEO of the Duke University Health System, and Victor Dzau will arrive in Durham to take up the reins of this vast and complex enterprise. It has been my privilege to work closely with Dr. Snyderman over the past three years, and I greet the future under Dr. Dzau's leadership with high enthusiasm.

Dr. Snyderman leaves a legacy that includes many tangible and important achievements. He led the founding of the Duke University Health System and the resulting extension of Duke's responsibility for patient care in our region. He promoted a major expansion of our research activities, including unique programs like the Duke Clinical Research Institute. He fostered the continued advance of our reputation for excellence, as reflected in a variety of national rankings. Much more will be said and written about the "Snyderman years" than I can detail here, but suffice it to say that those of us who sail on at Duke under a new admiral will do so on a rising tide.

I have known Dr. Dzau for more than 25 years. He has been remarkably successful in every dimension of academic life, including the direction of major programs at Stanford and Harvard. He brings keen intelligence, irrepressible energy, and well-honed administrative skills to the chancellor's role. I have every confidence that the "Dzau years" will be characterized by additional innovations, and by further strengthening of Duke's standing among the finest academic medical centers of the land.

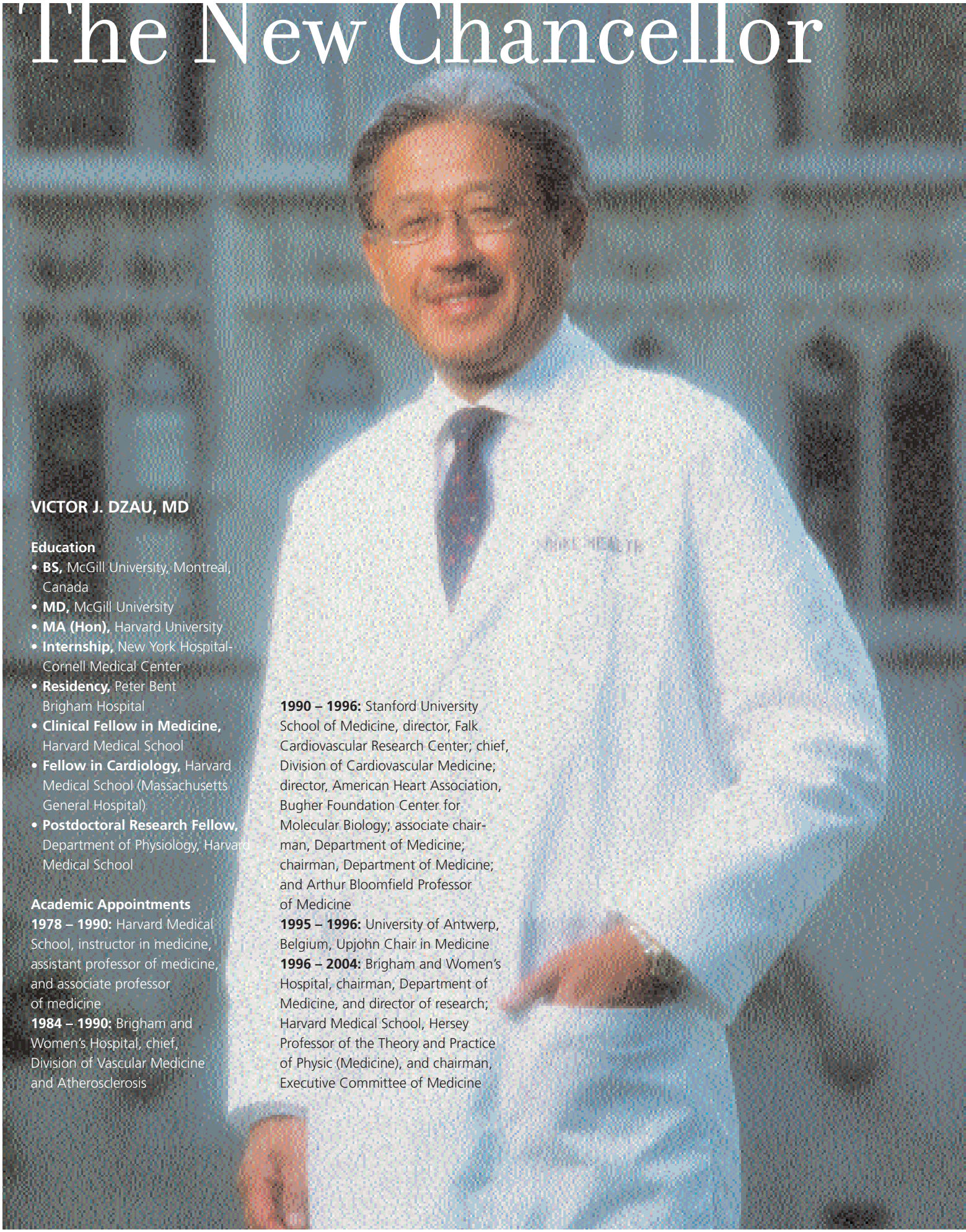


We have many challenges to meet that are different from those faced by previous leaders, and there is some heavy lifting to be done if we are to maintain our upward trajectory in our core missions of clinical care, research, and education. For example, we must take full advantage of the expanded footprint in regional health care provided by the three hospitals of the Duke University Health System in a way that advances our academic aspirations.

Likewise, we must find ways to foster a sense of common purpose within a rapidly expanding network of outlying clinics staffed by physicians of the Private Diagnostic Clinic and others affiliated with Duke. We must find new mechanisms to provide stable financial support for the fragile enterprises of medical education, basic research, and clinical investigation that cannot be self-sufficient from revenues provided solely by tuition and NIH grants. We must provide fair and competitive compensation to faculty, maintain our outstanding residency programs, and support scholarship in a changing financial environment in which time-honored practices of distributing revenues from clinical practice are proving inadequate. We must tune our activities to prosper in a time of increasingly stringent regulatory standards and compliance demands.

Is Dr. Dzau stepping into a difficult job? You bet he is! However, it is a wonderful opportunity and he is well suited to the task. In addition, I am certain that he will be heartened by similar emotions to those I found when I came to Duke three years ago to take up my role as Dean. He will quickly note, as did I, that he is surrounded by women and men of great talent, enterprise, and good will—individuals who are fiercely dedicated to making Duke a national model for success as an academic medical center.

The New Chancellor



VICTOR J. DZAU, MD

Education

- **BS,** McGill University, Montreal, Canada
- **MD,** McGill University
- **MA (Hon),** Harvard University
- **Internship,** New York Hospital-Cornell Medical Center
- **Residency,** Peter Bent Brigham Hospital
- **Clinical Fellow in Medicine,** Harvard Medical School
- **Fellow in Cardiology,** Harvard Medical School (Massachusetts General Hospital)
- **Postdoctoral Research Fellow,** Department of Physiology, Harvard Medical School

Academic Appointments

1978 – 1990: Harvard Medical School, instructor in medicine, assistant professor of medicine, and associate professor of medicine

1984 – 1990: Brigham and Women's Hospital, chief, Division of Vascular Medicine and Atherosclerosis

1990 – 1996: Stanford University School of Medicine, director, Falk Cardiovascular Research Center; chief, Division of Cardiovascular Medicine; director, American Heart Association, Bugher Foundation Center for Molecular Biology; associate chairman, Department of Medicine; chairman, Department of Medicine; and Arthur Bloomfield Professor of Medicine

1995 – 1996: University of Antwerp, Belgium, Upjohn Chair in Medicine

1996 – 2004: Brigham and Women's Hospital, chairman, Department of Medicine, and director of research; Harvard Medical School, Hersey Professor of the Theory and Practice of Physic (Medicine), and chairman, Executive Committee of Medicine

PHOTOGRAPH BY CHRIS HILDRETH

Meet the next chancellor for health affairs at Duke University—Victor J. Dzau, MD, a distinguished physician-scientist and academic and administrative leader that Duke University President Nannerl O. Keohane describes as combining "a remarkable breadth of professional experience with the personal qualities and vision needed to lead one of the world's great academic medical centers."

Since 1996, Dzau (pronounced "Zow") has been the Hersey Professor of the Theory and Practice of Physic (Medicine) at Harvard Medical School, and chairman of the Department of Medicine, physician-in-chief, and director of research at the Brigham and Women's Hospital. An authority on cardiovascular diseases, he also serves as senior academic officer, director of academic collaborations, and member of the board of trustees for Partners HealthCare System, which includes the Brigham and Women's Hospital, Massachusetts General Hospital, and several other hospitals and physician organizations in the Boston area. On July 1, Dzau will officially take office as chancellor for health affairs and president and CEO of the Duke University Health System and begin building on the University's strengths in teaching, research, and patient care. Below are a few of his thoughts about his future at Duke.

WHY DUKE? "Duke is the best place to be in American medicine. Under [current Chancellor for Health Affairs] Ralph Snyderman's leadership, Duke has established itself as a premier academic medical center and health system. Duke is young; full of energy, vitality, and optimism. It has much to look forward to. It aspires to be the best. It is the best. I am honored to be chosen by President Keohane and President-elect [Richard] Brodhead to lead the Duke University Medical Center and Health System at this challenging yet exciting time for academic medicine and biomedical research."

HOW CAN THE DUKE VISION OF "THE FUTURE OF MEDICINE, DELIVERED TODAY" BE REALIZED? "First, we must build bridges that will bring together the many strong components of DUHS, and harness the powerful synergies that exist at Duke such that the whole enterprise becomes much greater than the sum of the individual parts. This is the true meaning of a health care system—the medical school, Duke University Hospital, the community hospitals, the faculty, the scientists, and the physician practices and networks. We also must reach out to our patients, make connections with the community, and develop a stronger network.

"Duke has led in many areas of research innovation and knowledge discovery. As a medical center, we must facilitate and increase the translation of basic research and discovery to clinical application. We need to build more bridges between basic science, clinical investigation, and clinical adoption. We must aspire to be the first and the best in the translation and adoption of new evidence-based methods of diagnosis and therapies such that Duke medicine remains at the cutting edge. In so doing, we can provide our patients with the best, the latest, and the safest care.

"These bridges must extend to the rest of the University. Silos must be broken down in order to promote interdisciplinary and multidisciplinary research. We must take advantage of the University's strengths in quantitative, physical, and social sciences and the humanities and many other areas so as to develop novel, collaborative models of research, as exemplified by the recently established Institute for Genome Sciences & Policy.

"Our medical school and nursing school are among the very best. Our trainees and young faculty are our future. The 'Future of Medicine' will be defined and realized by them. We must continually challenge ourselves and ask if our curricula meet the needs of our students, whether we are preparing them properly for the future, and if we have successfully mentored our young faculty and facilitated their career development. Our training program must provide strong links and bridges from basic science to clinical care, from bedside to ambulatory care, and we have to teach our students to understand the importance of social and economic factors in health and disease."

HOW CAN DUKE FACE THE MANY CHALLENGES IN AMERICAN HEALTH CARE? "The Chinese word for challenge or crisis is made of two characters: danger and opportunity. In Duke, I see many opportunities. We will create the environment for our clinicians, educators, and scientists to not only weather these difficult times, but to thrive and to lead the changes locally and nationally that will address and improve health care in North Carolina, in the U.S., and globally. Together with all of the dedicated Duke faculty and staff, I look forward to meeting these challenges."

Farewell to a transformational dean

Chancellor for Health Affairs Ralph Snyderman, MD, (top right) considers the recruitment of Mary Champagne, RN, PhD, FAAN, (left) as dean in 1991 as a crucial turning point for Duke's School of Nursing. Both Snyderman and Champagne are stepping down from their leadership positions on June 30. Champagne (below, right) talks with a nursing student.

WHEN MARY CHAMPAGNE, RN, PHD, FAAN, arrived at Duke as the new Dean of Nursing in 1991, the School of Nursing was floundering. The school's bachelor's degree program had been closed for several years, leaving only a handful of students and faculty in master's-level programs.

Since her arrival, Champagne has done for the School of Nursing what nurses are trained to do for patients: Evaluate their individual strengths and weaknesses, try proven solutions, work with others to reach shared objectives, and, even while attending to the smallest details, never lose sight of the big picture—achieving a positive outcome.

After 13 years under Champagne's watch, her patient is doing remarkably well. As Champagne prepares to step down from the dean's position on June 30, vital statistics show:

- Eleven new programs of study
- #6 and #8 rankings, respectively, for nurse anesthetist and gerontology programs in the 2003 *U.S. News & World Report* rankings
- 71,500 square feet of new space in the planned $22 million future school headquarters facility
- 374 students and 38 faculty members—up from 50 and five, respectively, in 1991
- $18.4 million raised for initiatives like faculty projects, scholarships, and endowed professorships.

These numbers represent far more than rankings, dollars, and square footage; they represent lives Champagne has touched—directly and indirectly.

"Many students have benefited directly from Mary's efforts, and thousands upon thousands of patients have benefited and will benefit," says Duke University President Nannerl O. Keohane, PhD. "Her years will be remembered as transformational—a time of intelligent innovation that honored the best of Duke's traditions and history."

Taking a big risk

Ralph Snyderman, MD, chancellor for health affairs, recruited Champagne to Duke from UNC-Chapel Hill, where she had gained national recognition as a gerontological nurse researcher.

"Mary did something that few people would have been willing to do; she put a vibrant research career on hold to take a big risk," says associate professor Ruth Anderson, RN, PhD. "Although the School of Nursing had only five faculty members and about 50 students at the time, Mary clearly saw a lot of potential here."

One of Champagne's first priorities was to strengthen the school's master's-level degree program offerings to meet the growing need for specialized nursing professionals. The 1990s saw the development of primary care, acute care, and tertiary care majors; nurse practitioner programs in acute care, pediatrics, and geriatrics; and specialty programs in oncology, cardiovascular health, and nursing informatics.

In 1993, in collaboration with Duke University Hospital, Champagne led the School of Nursing to establish the Nursing Research Center, which provides staff, support services, and resources to foster scholarly nursing research. Later that year, the school received its first federal research grant.

"Dean Champagne was the architect of this center, and under her leadership, it has gone from receiving essentially no extramural funding to ranking 29th in the nation for National Institute of Nursing Research funding," says Director Barbara Turner, RN, DNSc, FAAN.

Reaching out, moving up

Champagne was instrumental in establishing the Division of Community Health, a partnership with the School of Medicine's Department of Community and Family Medicine, in 1996. This unique division quickly gained recognition at Duke and in the community for its innovative care-delivery models to underserved populations, as well as for the hands-on experience it offers students pursuing health care professions.

Champagne also wanted to extend the school's reach to future nurses in North Carolina's rural, medically underserved areas. So she, along with her then colleague, the late Bonnie Jones Friedman, RN, PhD, obtained Area Health Education Center (AHEC) funding to implement an off-campus family nurse practitioner program. This prepared the school to apply for its first major foundation grant in distance-nursing education.

In 1997, the school was one of only eight schools of nursing in the country to receive a Partnerships for Training grant from the Robert Wood Johnson Foundation. The grant established an innovative distance-education program for family nurse practitioner, physician assistant, and nurse midwifery students in rural counties throughout North Carolina.

By 1998, the school was nationally ranked among other graduate schools of nursing for the first time in its history. The smallest among those listed—and the only one without a doctoral degree program—the school was ranked 32nd by *U.S.News & World Report*. Two years later, its ranking rose to 27th—placing it in the top 10 percent of nursing schools ranked.

In 2000, the school was one of only five sites nationally to receive funding from the National Institute of Nursing Research to create a P20 interdisciplinary research center to address the health care needs of the elderly. The Trajectories of Aging and Care (TRAC) Center occupies 1,700 square feet of research space in Duke Hospital and has launched some 20 pilot studies, the first step on the road to federal funding for junior faculty.

Training new nurses

In 2002, the School of Nursing received the largest gift in its history—$6 million from the Helene Fuld Health Trust, HSBC Bank, trustee. This gift launched an innovative accelerated Bachelor of Science in Nursing (ABSN) degree program that packs the entire degree into just 18 months. The program graduated its inaugural class of students in December 2003, and many of the graduates are now working in Duke University Health System (DUHS) facilities. The school also graduated its first class of certified registered nurse anesthetists in 2003.

National Institutes of Health (NIH) funding also doubled in 2003, from $728,120 the previous year to $1,442,060—moving the school up from number 38 to number 29 in NIH funding among U.S. nursing schools. The school also received full unconditional accreditation from the national Commission on Collegiate Education in Nursing.

In January 2004, Champagne kicked off the campaign for a new School of Nursing headquarters. Her plans for a new facility have been endorsed by The Duke Endowment, with a $3 million appropriation in December 2003 (see sidebar), and community friends who have contributed a total of $12.3 million toward the cost of the $22 million facility.

On the horizon

Because Champagne plans to stay at Duke, teaching and conducting nursing research, she'll get to watch as the fruits of her many years of effort ripen and are harvested. On the horizon are a doctoral degree program, plans to apply for a federally funded P30 research center, and the construction phase of the new headquarters building.

Ralph Snyderman believes Champagne's legacy will be as the dean who revitalized and transformed the Duke School of Nursing.

"Mary Champagne has strategically ushered the School of Nursing into a new era," Snyderman says. "Her vision, her unflagging dedication, and her ability to rally people behind her have made all the difference in the progress the school has seen and the impact it will continue to make for years to come."

Duke Endowment awards more than $20 million to Duke University

THE DUKE ENDOWMENT has awarded more than $20 million to Duke University to support a number of university priorities. They include an expansion of the School of Nursing programs, the growth of interdisciplinary science initiatives, improvements to Perkins Library, and community involvement through the Duke-Durham Neighborhood Partnership.

The Duke Endowment's 2003 gift includes $1 million for the School of Nursing, with a plan to provide an additional $2 million by 2005. Nursing Dean Mary Champagne, PhD, said the money would be used to help support construction of a new building adjacent to Duke Clinic on Trent Drive, behind the nursing school's current facilities.

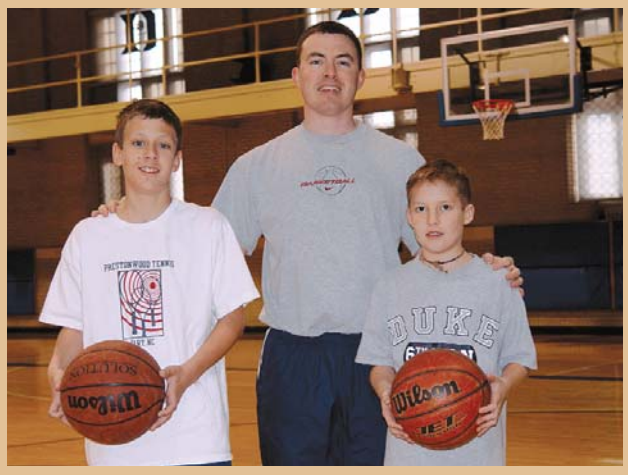
"We are thrilled to receive this endorsement for our critically needed expansion," Champagne said. "Our growth—both in size and caliber of our faculty and programs—is in direct response to societal needs."

On the Medical Center side, Duke received more than $7 million, in 18 separate allocations, from the Endowment. In addition to the nursing school gift, funded programs included the Albert Eye Research Institute, $1 million; a patient safety initiative, $696,000; and the Center for Genome Ethics, Law and Policy (GELP), $1 million.

The Charlotte-based charitable trust also awarded $6 million for an undergraduate science initiative, with the French Sciences Building at the center. The initiative will promote close interaction among scientific disciplines and create new opportunities for interdisciplinary teaching and research.

Proposed new building for the School of Nursing.

Court and spark



Coach Michael Zeillmann (center) teaches young patients new tricks through the Hoop Dreams program.

KATE SHIPMAN, Dana Brown, and Erica Gunter are teenagers who share a skill they're pretty proud of: They can all dribble two or three basketballs at a time. They can even combine that feat with turnarounds and through-the-legs maneuvers. Something else the girls have in common makes their skill on the court all the more remarkable: all are being treated for brain tumors.

Kate, Dana, and Erica are among the young brain cancer patients who have discovered new wellsprings of self-confidence, coordination, and fun through Hoop Dreams Basketball Academy. A basketball skills program designed for children battling life-threatening illnesses at Duke and UNC hospitals, Hoop Dreams is the brainchild of former Durham Academy basketball coach Michael Zeillmann—known affectionately to his charges as Coach Mike or Coach Z—and Duke neuro-oncologist Henry Friedman, MD.

"There's power in learning something like this," says Zeillmann. "One of our girls had trouble bouncing basketballs when she started. Now she's already working with three balls more than 25 dribbles at a time. We try to boost the kids' confidence and make sure they have fun in the process."

Zeillmann, 31, played varsity basketball in high school and college and has long combined his love of basketball and teaching by coaching and mentoring kids seeking to improve their skills. While serving as coach at Durham Academy a few years ago, Zeillmann met and began mentoring Friedman's daughter, Sara.

"I was impressed by Mike's ethics, his behavior with the kids, his personality," Friedman recalls. "And the more I saw what he was doing with Sara and the other kids, the more impressed I became." So, during a one-on-one talk one day, Friedman asked Zeillmann what his dream was.

As chief of neuro-oncology at Duke, Friedman knows a lot about helping people stay focused on their dreams, rather than the daunting obstacles that are often in their way. Besides his family (with his wife, Joanne Kurtzberg, MD, chief of the Duke Pediatric Stem Cell Transplant Program, he has two kids) and fighting brain tumors, he counts basketball as his third driving passion.

So when Zeillmann said that he hoped to some day have a gym where he could work with children and give something back to the community, Friedman saw a unique opportunity. He quickly went into action, contacting friends in the area—including several Duke alumni and parents who are now successful business owners—who could help make things happen. Together, several of them established a nonprofit corporation that would lay the groundwork for Hoop Dreams. "We formed a group bonded by this notion of sports and children," Friedman says.

The Hoop Dreams leadership optioned a 25-acre site at South Roxboro Street and Martin Luther King Drive, where they plan to build a dedicated gymnasium for the program. Fundraising for the facility has begun, and Hoop Dreams board member Anthony Dilweg, a former Duke football player who is now a local real estate developer, has pledged to build it at cost. Meanwhile, Duke Athletics Director Joe Alleva agreed to let Hoop Dreams meet in any available Duke gym, including Cameron Indoor Stadium, until the group's own facility is ready.

Currently, 19 children with life-threatening illnesses, including 13 patients from Duke with brain tumors, leukemia, sickle-cell anemia, and other diseases and 6 leukemia patients from UNC, gather at least once a week to hone basic basketball skills and develop some special tricks. Sometimes Zeillmann gets help from guest coaches, such as former Elon University head basketball coach Mark Simons, who is married to "Coach G," Duke women's basketball coach Gail Goestenkors. Sometimes the kids are joined by members of the Duke teams, who give them good-natured mock competition and sign autographs to boot.

In coming years, Hoop Dreams may expand to include free skills training camps for special-needs children from a broader geographic area, as well as paid camps and classes to help pay for the nonprofit activities.

"We're not going to be developing a feeder system for the NBA," Zeillmann says with a wry laugh. "But we can help kids develop some confidence and learn some special things that average kids can't do well."

If you are interested in helping Hoop Dreams fulfill its mission, please contact the program at 919-479-6069 or send an e-mail to: info@hoop-dreams.net. For more information, visit www.hoop-dreams.net.

What's in a name—Duke care close to home

RALEIGH COMMUNITY HOSPITAL (RCH) has been a part of the Duke University Health System (DUHS) for more than five years and a part of the Raleigh community for much of the past century. This summer, however, the 186-bed hospital is reintroducing itself to Raleigh residents with a new name and expanded services including new cancer and cardiovascular centers.

Effective June 2004, the hospital is renaming itself Duke Health Raleigh Hospital. The new title strongly identifies the facility with the expertise, value, and cutting-edge technology of Duke University Health System, administrators say. The name also reinforces Duke's ownership of the hospital as well as the convenience for Wake County residents of having "Duke at your doorstep."

"Since DUHS purchased the hospital from HCA in 1998, we have expanded the Duke services offered at Raleigh and see the hospital as a vital part of our strategy to increase services in Wake County—the fastest growing county in North Carolina," says Ralph Snyderman, MD, president and CEO of the health system.

Raleigh Community CEO Jim Knight adds that the name is more telling of those expanded services. "Duke Health Raleigh Hospital is a name that speaks to our ability to provide a spectrum of health care options including education, treatment, wellness, and prevention," he says.

New Cancer Center

ONE OF THE EXPANDED services will be the new Duke Health Raleigh Cancer Center, opening in June 2004.

The 22,400-square-foot facility will contain the latest radiation therapy technology, as well as expanded conveniences and support services. The $7.2-million project includes radiation therapy equipment with a new dual-energy linear accelerator and on-site simulation service.

With patient rooms designed to respect privacy and confidentiality, the center's added space also includes areas for on-site social services, nutritional support, and other allied health care workers involved in providing comprehensive, multidisciplinary services for oncology patients and their families. Patients and staff also will benefit from new education suites, as well as conference and medical education space.

In addition, the Cancer Center will introduce the newly created position of patient care coordinator to facilitate patients' treatment and ensure the best delivery of care.

Todd Sigmon, director of Cancer Services, said the center will allow the hospital to better serve patients by providing the most advanced technologies for treating cancer and offering a full array of services. "The new facility also offers a blend of academic and community medicine," he said. "The vast majority of cancer services at our facility are provided by community physicians; the linkages to Duke will enhance clinical quality allowing access to current research and proven protocols here in our community setting."

New Cardiovascular Center

IN ADDITION TO the Cancer Center, the hospital also is opening the new Duke Health Raleigh Cardiovascular Center at the end of May. The centerpiece of this $2.3-million project is a Fixed Diagnostic Cardiovascular Catheterization Lab.

RCH Chief Operating Officer Tom Hanenburg said the addition of the cardiovascular center "dramatically improves RCH's ability to provide comprehensive cardiovascular services to the community."

Intensive Care Unit Renovations

THE HOSPITAL IS not only expanding cancer and cardiovascular services, but renovating the Intensive Care Unit. Scheduled for completion in Fall 2004, enhancements will include expanded patient rooms; an all-encompassing nursing station at the bedside that will allow nurses to do charting, take phone calls, and have computer access; and a centralized physician documentation station with state-of-the-art features. The unit also will contain a new private physician/family conference room as well as a dedicated special procedure room with optimal space for invasive procedures.

In June, Raleigh Community Hospital becomes Duke Health Raleigh Hospital.

Duke Health
Raleigh Hospital

Another Medical Science Research Building on the way

DUKE ANNOUNCED in December that it will construct a second Medical Science Research Building (MSRB). The 165,000-square-foot medical science building will support the growing need for research space for a number of centers and departments, including the Comprehensive Cancer Center, the Stedman Nutrition and Metabolism Center, the Department of Surgery, and the Department of Medicine.

School of Medicine Dean R. Sanders Williams, MD, said that "Duke has recruited outstanding new leadership in these and other departments, and the new research space, including open wet labs, will support those hires. The new lab space also will help us recruit other leading researchers, enhance research productivity, and accommodate the advanced equipment that is central to our research enterprise."

In addition, the MSRB II will support and complement the nearby Center for Human Genetics and Center for Models of Human Disease. The four-level building, which will cost $64 million, will be built on the southeast corner of Research Drive and Erwin Road, near the existing MSRB.

Duke, Durham Public Schools launch new school-based clinic

GETTING SHOTS IS NEVER FUN, but a new school-based health clinic run by Duke University may help ease the pain for both children and their parents.

Jane Ann Moore, MD, a family physician, started seeing students at Durham's E.K. Powe Elementary School in January 2004—much to the delight of principal Brandon Patterson. Patterson described the clinic, which offers both health and mental health services on site, as a dream come true for him and his staff.

"It's an awesome resource to be able to offer the children and families of E.K. Powe," said Patterson, who saw the need for a clinic at his Ninth Street school after referring his students to a similar clinic at nearby George Watts Elementary School. "When children feel better, attendance will improve and achievement will improve."

The clinic is an example of a successful partnership between Duke and Durham Public Schools, Patterson said.

Duke's Division of Community Health is operating the clinic, which will be open when school is in session. The project is supported by a $110,000, two-year grant from The Duke Endowment.

Duke physician Jane Ann Moore, MD, is now seeing students at E.K. Powe Elementary School thanks to a school clinic supported with funds from The Duke Endowment.

Duke's Division of Family Medicine will provide care for E.K. Powe students when the school is closed. Durham Public Schools provides the services of an office manager and renovated the clinic.

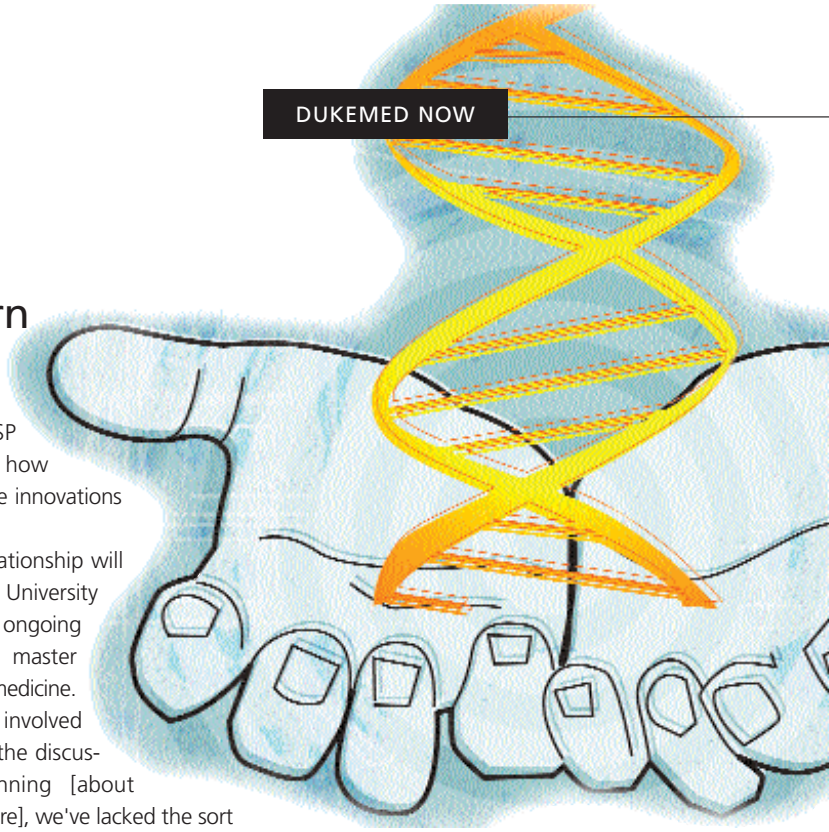
In addition to treating children for physical ailments at the clinic, the wellness center provides mental health services through the Center for Child and Family Health. The Center for Child and Family Health is a collaborative effort involving Duke, North Carolina Central University, and the University of North Carolina at Chapel Hill and specializes in serving children who have been exposed to trauma.

The Center for Child and Family Health staff at the wellness center connects children with other mental health issues to other mental health providers.

Though the clinic is an asset for the school's low-income families, it actually serves the needs of all students, regardless of family income. The clinic charges for its services, billing a student's insurer or family and assisting those who need to apply for reduced charges. No child is denied service based on ability to pay.

Duke's Division of Community Health operates three other wellness centers for the Durham Public Schools: at George Watts and Glenn School, both elementary schools, and at Southern High School.

For more information, contact Susan Kauffman at 919-681-8975 or by e-mail at susan.kauffman@duke.edu.



Center for genomic medicine is born

IN DECEMBER 2003, the Duke Institute for Genome Sciences & Policy (IGSP) announced the formation of the Center for Genomic Medicine (CGM). The CGM, which joins the other key research centers housed within the IGSP, will focus on the translation of genome sciences into clinical practice.

When asked about the impetus for the creation of the new center, IGSP Director Hunt Willard, PhD, says simply, "It represents the finish line. If we're actually going to do genomic medicine, we're going to have to do it in the clinic. Neither we nor anyone else has had in place a unit specifically designed to examine both the science and policy issues relevant to translating scientific findings from the genome arena into a standard of clinical care. To me, this center is the most logical missing piece of the IGSP, and it's long overdue."

Willard cites two relationships as being key to the success of the CGM. The first involves the Center for Genome Technology, where the goal will be to take new developments in genome technology and, once they've achieved scientific muster, hand them off to the CGM. Physicians and physician-investigators within the IGSP will then determine how best to integrate those innovations into clinical medicine.

The second key relationship will be with the Duke University Health System and its ongoing efforts to develop a master plan for personalized medicine. "While we've been involved in various aspects of the discussions and the planning [about personalized health care], we've lacked the sort of focus that comes with having a dedicated unit with a particular faculty champion directing those efforts," says Willard.

Chancellor for Health Affairs Ralph Snyderman, MD, Duke's most vocal and visible proponent of personalized health care, sees the CGM as an important part of the university's mission to reshape clinical medicine. "The Center for Genomic Medicine will play an important role in the transformation of health care, the development of personalized medicine, and individual health planning," he says. "The relationship of both the IGSP and the CGM to Duke Health will enhance the value and impact of all three entities."

For more information, visit www.genome.duke.edu.

Duke Hospital's Emergency Department to expand

The Emergency Department at Duke University Hospital will undergo a $29.8-million expansion and renovation based on a plan approved by the Duke University Board of Trustees in May.

The project will provide for a new, larger space with separate entrances and care areas for adult and pediatric patients; adjacent resuscitation and radiology areas; and a more effective layout to allow for improved staff and patient circulation throughout the department.

With the trustee approval, the Duke University Health System (DUHS) will next apply to the state of North Carolina for a certificate of need. Renovations could begin in January 2005 and be completed in August 2007.

The Emergency Department, located on the hospital's first floor, was built in 1981 and designed to handle 38,000 patient visits per year. Due to increased patient demand and continued growth of the Triangle area, the department currently sees more than 59,000 patients annually. Much of the nearly $134 million in charity and uncompensated care provided by DUH comes through its emergency department, Duke officials said.

Although several major renovations have been made to the original department in the last six years, space requirements for patients and staff have not kept pace with population growth. Recent DUHS estimates suggest the emergency department will see up to 90,000 patients annually by 2015.

The trustees also extended the lease for the Ronald McDonald House at 506 Alexander Avenue for five years. The facility, which the Pediatric-Family Center of North Carolina has operated for the past 25 years, provides a home-like setting for seriously ill children and their families while the children receive medical care at Duke.

Architectural design of planned Duke Hospital Emergency Department expansion and renovation.

Putting physician fatigue to rest

DUKE UNIVERSITY MEDICAL CENTER, UNC Hospitals, and other health care-related entities are collaborating to develop and launch a unique education program intended to improve patient outcomes by promoting physician wellness.

The initiative—called The Model Instructional Program on Physician Fatigue and Impairment and Patient Safety—is being made possible with a nearly $1 million grant from the Josiah Macy, Jr. Foundation. The grant will be distributed over a three-year period. The foundation is a privately endowed philanthropy based in New York City.

The program will attempt to teach medical professionals to recognize, manage, and prevent fatigue, impairment, and burnout in themselves and their colleagues. The program was initially conceived after the Accreditation Council for Graduate Medical Education (ACGME) began an effort in 2002 to educate medical trainees and faculty about fatigue and impairment. It gained further momentum when the ACGME's mandate limiting medical residents to 80-hour workweeks went into effect in July 2003.

"Physicians need to take care of themselves first, so they can be in the best possible condition to care for others," said co-principal investigator Kathy Andolsek, MD, associate director of Duke's graduate medical education program.

"There are significant stressors, such as much sicker patients coming into the hospital today, that put physicians at risk in ways that other professionals and workers are not, so we want them to be able to recognize, prevent, and manage these risks," Andolsek said. "It's also important for graduate medical education programs to understand that although their residents are now adhering to an 80-hour work week, these stressors still exist."

Evidence suggests that burnout and impairment issues start early in medical training, she added.

The program's curriculum—to be delivered through standardized workshops, a Web site, and CD-ROMs—will be developed during the coming three years. The first part of the program is expected to be introduced at Duke and UNC in 2004.

The core curriculum will initially be designed for residents and fellows in specialty and subspecialty training, as well as for medical faculty. It is being created to be easily tailored to meet the future needs of other relevant audiences, including practicing physicians, hospital staff, nurses, medical students, and students in physician assistant and other health profession programs.

Medical faculty from Duke and UNC and staff from the North Carolina Physicians Health Program will assist with the development and implementation of the program, which has been supported by the North Carolina Area Health Education Centers and the Southern Medical Association.

If the program shows a correlation between provider wellness and improved patient outcomes, Andolsek hopes it will serve as a model for academic medical centers around the country.

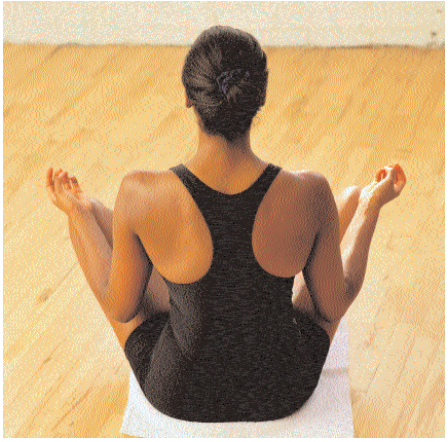
Foundation funds new integrative medicine facility

DUKE UNIVERSITY received $10 million in January from the C.J. Mack Foundation to support a new facility dedicated to the emerging field of integrative medicine. The gift is pivotal to Duke's efforts to develop new models of health care focused on wellness.

The C.J. Mack Foundation is the philanthropic entity of Christy King Mack and John Mack of Rye, NY. Christy Mack is a native of Greensboro, NC; John Mack is a native of Mooresville, NC.

Tracy Gaudet, MD, director of the Duke Center for Integrative Medicine (DCIM), said the center seeks to serve as a catalyst for change in health care, fostering a healing partnership between patients and providers, and encouraging patients to become more active in their own health and wellness.

The new 29,800-square-foot health and healing center will be constructed on the campus of the Duke Center for Living on Erwin Road, where DCIM is now based.



"Duke University Medical Center enjoys a stellar international reputation for its commitment to advancing the practice of medicine," says Christy Mack. "Duke stands out as an example of pushing the envelope in research and clinical practice as well as in education. With the creation of this Center for Integrative Medicine, I believe Duke is poised to become the role model for what the practice of medicine should be: patient-focused with an emphasis on the interconnectedness of mind, body, spirit, and community. I am pleased to play a part in this extraordinary movement, and to partner with the committed professionals at Duke."

The fab four: New drugs show promise in halting brain tumors

RESEARCHERS AT the Duke Comprehensive Cancer Center have shown that four experimental drugs can strongly inhibit the growth of deadly brain tumors in animals, and they expect these promising results to hold true in humans, as well.

In fact, one of the drugs significantly slowed the growth of three different types of brain tumors, a remarkable finding given that brain tumors are very distinct in their biologic makeup, says neuro-oncologist Jeremy Rich, MD, of the Brain Tumor Center.

The new drugs selectively target particular molecules within brain tumors, so they should be more effective inhibitors of tumor growth and carry far fewer side effects for the patient. Three of the new drugs are in a class called small molecule inhibitors, designed to prevent growth factors from activating themselves inside cancer cells.

A trial using two of the drugs in combination will begin testing in patients within the next year, says Rich.

Donepezil bulks up hippocampus in AD patients

DUKE RESEARCHERS have determined that donepezil (Aricept), a cholinesterase inhibitor commonly prescribed for mild to moderate Alzheimer's disease (AD), appears to cause physical improvements in the hippocampus and other brain regions of patients with the disease.

The researchers used magnetic resonance (MR) technology to track brain changes among patients taking the drug. This is the first longitudinal study to use magnetic resonance imaging (MRI) and proton magnetic resonance spectroscopy (MRS) to assess brain function and the impact of a medication upon brain structures of patients with AD. The feasibility of using MR for such studies is likely to improve future research into treatments for AD and other brain disorders, the researchers said.

"We discovered that, among the patients taking donepezil, levels of a brain chemical called N-acetylaspartate increased and the hippocampus deteriorated more slowly than among the patients who received a placebo," says Ranga Krishnan, MD, lead author of the study and chief of psychiatry at Duke. The hippocampus is critical to memory function and is affected earliest in AD.

The study appeared in the Nov. 1, 2003 *American Journal of Psychiatry*.

Do your kids make you fat?

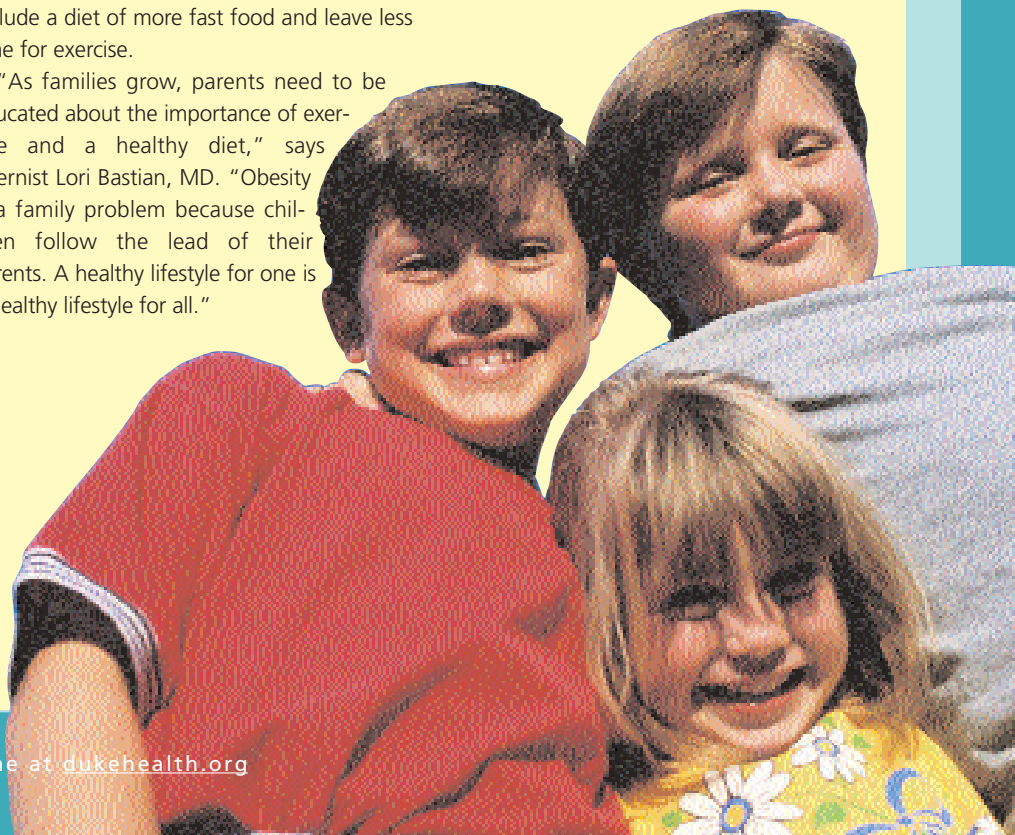
THE MORE CHILDREN a person has, the greater the risk he or she will become obese, according to a new Duke study based on data from the national Health and Retirement Study, a large database of middle-aged Americans.

The Duke researchers found women faced an average 7 percent increased risk of obesity per child and men an average 4 percent increased risk per child. They attribute the weight gain to a busier lifestyle that may include a diet of more fast food and leave less time for exercise.

"As families grow, parents need to be educated about the importance of exercise and a healthy diet," says internist Lori Bastian, MD. "Obesity is a family problem because children follow the lead of their parents. A healthy lifestyle for one is a healthy lifestyle for all."

The research appears in the January/February *Journal of Women's Health*.

According to the National Health and Nutrition Examination Survey, 30 percent of all Americans are obese. Obesity is linked to several major health concerns including diabetes, heart disease and some cancers. An estimated 300,000 adults die of obesity-related illnesses every year in the United States.



Improving treatment for macular degeneration

RESEARCHERS AT THE DUKE EYE CENTER believe a surgical procedure they have refined for over a decade can help restore central vision to those suffering from end-stage age-related macular degeneration (AMD). AMD is an eye disease that may lead to central vision loss and afflicts an estimated 500,000 people worldwide each year.

The two-stage procedure, called "macular translocation surgery with 360 degree peripheral retinectomy"(MT360), involves first internally rotating the retina to shift the degenerating macula to a healthy area, away from abnormally growing blood vessels and scar tissue. In the second procedure, the eye is rotated to account for the ensuing tilt in a person's visual field. The macula is the central portion of the retina and is used for activities that require fine-detail vision, such as reading or sewing.

"This technique often allows us to recover a patient's reading vision. It isn't a cure, but our patients' feedback has been very exciting."—Cynthia Toth, MD

MT360 had been used in patients with recent central vision loss from AMD in their newly affected second eye, but not in those who had undergone previous macular treatment, says eye surgeon Cynthia Toth, MD. "This technique often allows us to recover a patient's reading vision. It isn't a cure, but our patients' feedback has been very exciting."

The latest Duke research into MT360 appeared in the Nov. 1, 2003 *American Journal of Ophthalmology*. The authors reported that patients who have received a round of a standard treatment called ocular photodynamic therapy (PDT) and continue to experience vision loss recovered reading vision after MT360.

Macular degeneration, a disease that may cause blurring of central vision, occurs in two forms, wet and dry. The dry type is more common and occurs when deposits, called drusen, accumulate under the retina. The dry type may set the stage for the less common but more severe wet form in which blood vessels and scar tissue begin to grow abnormally beneath the retina, leading to permanent damage of the macula.

More information is available online at http://mactrans.dukeeye.org.

Stop those senior moments (smoking, too)

THE NICOTINE PATCHES that help smokers quit might also boost the recall of seniors with the mildest form of memory loss, according to results of a preliminary clinical trial on 11 people conducted at Duke. While nicotine itself has not been approved for long-term use, the research could point the way toward other nicotine-like drugs that might improve memory without the side effects of nicotine, according to the Duke researchers.

Previous research conducted by the Duke team and others has found evidence that nicotine might benefit people with a variety of disorders—including schizophrenia, attention deficit hyperactivity disorder, and Alzheimer's disease. However, the latest study is the first to examine the drug's effects on people with age-associated memory impairment (AAMI), a common condition among older people that is characterized by so-called "senior moments."

Geriatrician Heidi White, MD, and nicotine researcher Edward Levin, PhD, emphasize that, despite the possible benefits of nicotine, the results should not encourage smoking. They also caution that nicotine patches have associated health risks—including nausea, dizziness, and increases in blood pressure and heart rate—and have not been approved for long-term use.

"While the results are encouraging, seniors should not try nicotine skin patches until larger studies testing the efficacy and safety of their use have been conducted," Levin says.

The study appeared in the February *Psychopharmacology*.

Appendectomy wins by a lap

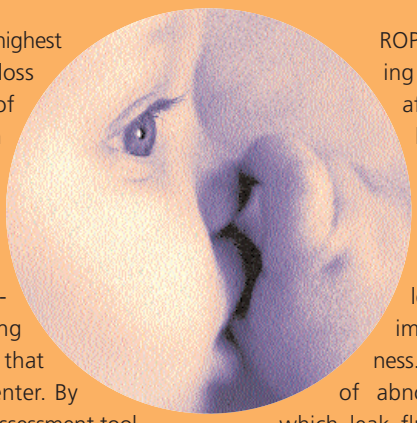
AFTER ANALYZING a nationwide database of more than 43,000 patients, Duke researchers determined that the minimally invasive laparoscopic approach to removing infected appendixes has significant advantages over the traditional open surgical approach.

The researchers found that patients who received laparoscopic surgery were discharged from the hospital sooner, were more likely to be discharged home as opposed to further medical care, and had fewer complications while in the hospital. Just as importantly, the researchers added, the laparoscopic approach was as effective as the open approach in the more serious cases where the appendix is either perforated or where an abscess is present.

The results appeared in the January *Annals of Surgery*.

Early treatment = RIP to ROP

PREMATURE INFANTS at highest risk for severe vision loss caused by retinopathy of prematurity (ROP) retain better vision when treatment is administered at an earlier stage of severe disease rather than at the previously accepted threshold for treatment, according to a 26-center study that included the Duke Eye Center. By using a computerized risk assessment tool to more accurately identify which premature infants were most likely to develop severe vision loss from the disease, researchers were able to target treatment for babies who needed it and avoid treating those whose cases may resolve on their own.



ROP is a potentially blinding eye disease that affects premature, low birth weight infants. The disease is among the most common causes of vision loss in childhood and can lead to lifelong vision impairment and blindness. ROP spurs the growth of abnormal blood vessels, which leak fluid and blood in the back of the eye leading to retinal scarring and increasing the risk of retinal detachment. Retinal detachment is the main cause of visual impairment and blindness in ROP.

The study appeared in the December 2003 *Archives of Ophthalmology*.

Pegging the best Hep C therapy

RESEARCHERS FROM DUKE and Johns Hopkins will lead the first ever direct comparison of the two leading treatments for hepatitis C infection, a study they hope will help refine treatment practices to maximize benefit for patients.

The most common treatment for hepatitis C virus is the combination of two antivirals—interferon and ribavirin. Interferon suppresses and eradicates the hepatitis C virus, whereas ribavirin enhances response rates (although alone it is not effective against the virus). A recent advance in hepatitis treatment is pegylated interferon, which permits more convenient once-weekly dosing. In comparison, standard interferon treatments must be given three times a week.

In the new study, researchers from Duke and Johns Hopkins will compare three treatment regimens in 2,880 hepatitis C patients with one of two available pegylated interferon treatments—pegylated interferon alfa-2b and pegylated interferon alfa-2a. Both treatments will be administered in combination with ribavirin.

The trial, named IDEAL (Individualized Dosing Efficacy vs. flat dosing to Assess optimaL pegylated interferon therapy), is sponsored by Schering-Plough Research Institute. John McHutchison, MD, director of gastroenterology and hepatology research at the Duke Clinical Research Institute, and Mark Sulkowski, MD, assistant professor of medicine at Johns Hopkins, will serve as co-principal investigators for the trial.

For patient referrals, contact McHutchison at 919-668-7177.

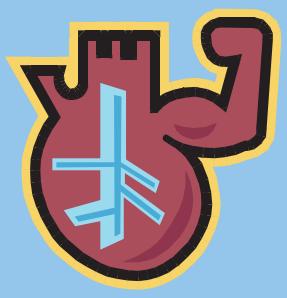
News from the "other ACC"

A number of Duke cardiologists and scientists presented their latest research at the annual scientific sessions of the American College of Cardiology. Among the most recent findings:

- **DURING THE YEAR** after suffering a heart attack, less than half of the patients had been taking beta blockers regularly, according to a Duke analysis of a Council for Affordable Quality Healthcare (CAQH) study of more than 15,000 insured patients. This is a disturbing finding, since numerous clinical trials have proven the effectiveness of beta blockers in reducing the risk of future heart attacks and improving survival, and about 90 percent of heart attack patients receive prescriptions for the drugs at discharge from the hospital.

- **PHYSICIANS ARE** underutilizing aggressive therapies such as anti-clotting drugs and invasive procedures in heart patients, despite blood levels of creatine kinase-MB (CK-MB) and troponin. Both are intracellular proteins that leak into the bloodstream as the cell membranes break apart during cell death; troponin, however, is only released by heart cells, so it is a more specific indication of myocardial injury. In their analysis of a heart attack registry of almost 30,000 patients, Duke cardiologists found that 28.4 percent of the patients had discordant marker results. Furthermore, when the two blood chemical results conflicted, the treatment strategy tended to be determined by the status of the CK-MB, an older and less specific test, and not by troponin, which can identify high-risk patients.

- **IN AN ANALYSIS** of the transfer patterns from more than 100 U.S. community hospitals, Duke researchers found that fewer than one of five high-risk patients presenting with unstable angina or non-ST-segment elevation myocardial infarction were quickly transferred to tertiary facilities with the ability to reopen clogged arteries with an angioplasty or coronary bypass surgery procedure, as recommended by American College of Cardiology and the American Heart Association. An additional 27.2 percent were transferred more than 48 hours after presentation. The results of this analysis, the first such comprehensive look at this issue at community hospitals, highlights a crucial weakness in the delivery of cardiac care that should be addressed to improve the outcomes of patients with heart attacks.

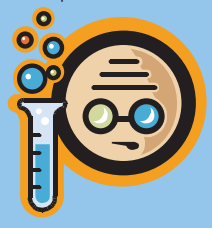


- **THE USE OF** an implantable cardiac defibrillator (ICD) can provide a significant reduction in mortality in patients with congestive heart failure (CHF), according to a study coordinated by the Duke Clinical Research Institute. Treatment using conventional therapy plus an ICD showed a statistically significant reduction in total mortality when compared to standard treatment with a placebo and standard treatment with the anti-arrhythmia drug amiodarone. Currently, more than 5 million Americans suffer from CHF, with more than 400,000 new cases diagnosed annually. Patients with CHF also have a higher risk of an arrhythmia, which often leads to sudden cardiac death. About half of all CHF patients who die do so from sudden cardiac death.

- **DUKE RESEARCHERS** have now demonstrated what many have long suspected—heart attack patients admitted to U.S. hospitals during the winter holidays have higher mortality rates than those admitted during the rest of the year. The researchers also found that during these holiday hospitalizations, patients were less likely to receive drugs and/or procedures that have been proven effective in large clinical trials to save the lives of heart patients. While there are likely many factors involved in these trends during the holidays, the researchers believe that the U.S. health care system is not truly organized to operate around-the-clock for 365 days a year.

- **IN ONE OF THE FIRST STUDIES** of its kind, Duke researchers have demonstrated clearly that hospitals' adherence to national guidelines for treating potential heart attacks saves lives. This finding is important because, while many studies have proven the effectiveness of individual therapies in improving outcomes for heart attack patients, very few have correlated individual hospitals' use of these different therapies with how their patients actually fare.

- **DUKE RESEARCHERS** have uncovered a strong relationship between the severity of heart disease and decreased levels of circulating endothelial progenitor cells (EPC). This relationship could represent an important new diagnostic and therapeutic target for the treatment of coronary artery disease. Since one of the roles of EPCs is to repair damage to the lining of blood vessels, one cause of coronary artery disease may be an increasing inability over time of these EPCs to keep up with the damage caused to the endothelium.



- **AN EXPERIMENTAL** anticoagulant that prevents the formation of blood clots earlier in the coagulation process than other agents has shown efficacy in phase II clinical tests—success that emphasizes its promise as a new treatment for patients with coronary artery disease, according to Duke cardiologists. The agent, code-named DX-9065a, inhibits the action of Factor Xa, a pivotal clotting factor in the complex cascade of biochemical events that ultimately leads to the formation of a blood clot.

- **IN THE FIRST** such analysis, Duke researchers have found that state-mandated programs for continuing medical education (CME) for physicians have little impact in improving outcomes for heart attack patients or in increasing the use of therapies proven effective by clinical trials. Just as interestingly, the researchers found that heart attack patients in states requiring CME were significantly more likely to receive those brands of thrombolytic, or artery-opening, drugs manufactured by drug companies that frequently sponsor CME events. Currently, 34 states mandate that physicians must complete a certain number of CME hours each year, at an annual cost of more than $1.5 billion to the healthcare system, the researchers said. Requirements vary from state to state, with mandated CME ranging from 25 hours to 75 hours each year.

Cancer pain relief—for a few pennies more

FOR A FEW MORE PENNIES a month, health-care providers can consistently manage and control cancer pain much more effectively using guideline-based care instead of more traditional approaches, according to a new Duke study.

Using a mathematical model that describes the interplay of clinical decisions and economics, the researchers found that guideline-based cancer pain management offered effective pain relief in 80 percent of patients, compared to 30 percent effectiveness for the "as-needed" pain management by non-specialty providers. Pain management by oncologists was slightly more effective, but still managed the pain of only 55 percent of patients.

Guideline-based pain management is a targeted approach to addressing pain using a pre-determined treatment plan for patients. In contrast, an as-needed approach by non-specialty providers is less methodical, and its effectiveness varies depending on provider knowledge of pain and treatment intervention as well as patient willingness to report pain and ask for assistance.

The guidelines were based on those issued in 1994 from the U.S. Agency for Health Care Policy and Research (now the Agency for Healthcare Research and Quality) that are based on the World Health Organization's guidelines for cancer pain management called the "WHO Analgesic Ladder." Both sets of guidelines utilize round-the-clock long-acting opioids with doses of short-acting opioids as standard. All patients receive non-steroidal analgesics, like aspirin, ibuprofen, or acetaminophen. Opioid side effects are recognized and treated appropriately.

From a literature review of the topic, researchers cited that oncologists tended to follow the guidelines above, but they more frequently prescribed short-term opioids and analgesics. They were also one-third less likely to recognize neuropathic pain. Pain management by non-specialty providers was more difficult to assess because pain management techniques within this group have not been systematically studied; however, assumptions are that pain is sporadically assessed, and round-the-clock dosing with long-acting opioids, use of short-term opioids, and treatment of neuropathic pain is infrequent.

Costs were calculated based on medication cost and all associated fees for anesthesiology and surgical procedures, radiotherapy, and physical therapy. After analysis, the guideline-based therapy cost an estimated $1.18 per member of a health-care organization per month, compared to oncology-based care at 95 cents and non-specialty "usual care" at 65 cents.

"In the world of managed care, a few pennies per member per month is not insignificant, but when you consider the dramatic increase in pain relief it stops being so much of an economic issue as it is a humanitarian one," says David Matchar, MD, director of the Duke Center for Clinical Health Policy Research and senior author of the study that appeared in the November 2003 *American Journal of Managed Care*.

Targeting Breast Cancer

Duke researchers are finding ways to detect the disease earlier and treat it with more precision

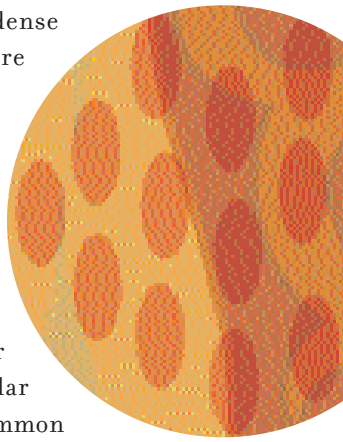
FOR THE NEARLY 200,000 AMERICAN WOMEN diagnosed with breast cancer each year, even the most significant scientific breakthroughs can sometimes seem frustratingly far away from making a difference. As Duke Comprehensive Cancer Center Director H. Kim Lyerly, MD, notes: "The sentiment out there is, 'You've been fighting cancer for years but the death rates are still unacceptable. You say you are unlocking the fundamental keys to cancer, but how about unlocking the fundamental keys to *my* cancer?'"

That's just what investigators in multidisciplinary programs such as Duke's Breast and Ovarian Oncology Research Program are trying to do. "Our focus is on research that is going to have a direct impact on people," says Lyerly, who co-leads the program. "Some people say you have to speak to and touch a person in your research activities to call it translational research. That's what we do here. It involves talking to, touching, and interacting with the lives of patients."

THE BREAST "PAP SMEAR"

Some of the most encouraging projects under way at Duke are aimed at discovering the disease in its earliest stages and then tailoring treatment to the individual. While mammograms and breast exams are currently the standard of care for screening for early breast cancer, these methods are often unable to detect the earliest pre-cancerous changes. Physicians at Duke are using a new research tool called rFNA (random fine needle aspiration) to detect pre-cancerous cells in woman who are at high risk for breast cancer. The tool, which can also be used to determine the effectiveness of preventive drugs in high-risk women, is being used in Duke's Breast Wellness Clinic, which opened in January 2003.

With rFNA, cells are obtained from the entire breast. This new test is considered revolutionary because of its ability to test more effectively for the presence of abnormal cells even in the absence of a breast lump or an abnormal mammogram. It is especially useful for detecting changes in dense breasts, which are typically quite difficult to see using mammography. RFNA is far more sensitive than a mammogram because a pathologist analyzes each cell for specific molecular changes that are common to many breast cancers.



"This is potentially the 'breast Pap smear' that we never had before," says Victoria Seewaldt, MD, associate professor

of medicine and director of the Breast Wellness Center. "Just as we do with a cervical Pap smear, we can now survey cells from the whole breast, examine them under the microscope and test for early changes that often precede breast cancer. Then we can give women a preventive agent to see if we can eradicate the abnormal cells and thus prevent cancer from developing.

> "Mammograms and self breast exams are good tests for looking at cancer, but they don't always do a good job of finding early changes in the breast."
>
> —Victoria Seewaldt, MD

"As women in America, we are all at risk for breast cancer," Seewaldt adds. "Mammograms and self breast exams are good tests for looking at cancer, but they don't always do a good job of finding early changes in the breast."

During the test, the breast is numbed with a local anesthetic. A slender needle is inserted into the inner quadrant of the breast, then is slightly withdrawn and reinserted eight to 10 times in precisely defined segments of the breast. The process is repeated on the breast's outer quadrant to ensure that cells are extracted from the entire breast. This new test will help characterize a cell as it transforms from normal to abnormal, and then eventually into a malignant cell. Understanding how cells behave very early in the process of becoming cancerous can help doctors assess a woman's potential cancer risk—or perhaps even prevent cancer—long before cellular changes have become irreversible.

Developed at the University of Kansas Medical Center and refined at Duke, "the breast Pap smear" will be undergoing clinical trials at Duke, Kansas, and Ohio State University. "Ninety percent of breast cancers occur randomly, without a family history of the disease or a known genetic mutation in the woman," says Seewaldt. "Clearly, we don't understand how most breast cancers arise, and we don't know how the various agents we give to patients actually repair what is malfunctioning. The new test will define what early changes in the breast look like, and furthermore it will tell a woman early on if a preventive treatment is really working in her own body."

While the test is available only at the three sites conducting the clinical trial, Seewaldt hopes it will ultimately be available at numerous sites around the country. The test is inexpensive and simple to administer and analyze so even a basic clinical laboratory could carry it out. Seewaldt says that the ultimate goal of the clinical trial and its associated research is to identify which cellular changes progress to become cancer.

CAMERA WORK

Another early-detection tool under investigation at Duke is a new breast scanner designed to detect subtle changes in breast cells before a lump can be felt by hand or seen with X-ray mammography. Martin Tornai, PhD, associate professor of radiology and biomedical engineering at Duke, developed the device. The new camera has undergone extensive testing in artificial breasts and will begin testing in women this year.

Tornai's device uses nuclear medicine to pick up chemical changes to breast cells that signal the cells are becoming malignant. The camera should be particularly useful for detecting tumors in large or dense breasts, which are difficult to image using traditional mammography because X-rays often cannot penetrate them. Moreover, the geometry of the new device allows for imaging small breasts and the nearby chest wall. It can even image the axillary lymph nodes to look for evidence of metastasis—which traditional mammography cannot do.

The key to the efficacy of the new scanner is its ability to detect changes in the

Women age 35 to 55 at high risk for breast cancer due to family history, abnormal breast biopsy or mammogram, or genetic presence of BRCA1 or BRCA2 may be eligible for a clinical trial of the new "breast Pap smear" (see article above). For information, e-mail scott001@mc.duke.edu.

SPORE Grant

IN 2003, the Breast Cancer Research Program of the Duke Comprehensive Cancer Center was awarded a SPORE (Specialized Programs of Research Excellence) grant by the National Cancer Institute (NCI). Duke's program is one of only 10 in the country to receive a breast SPORE grant, which will provide $9.8 million in funding during the next five years. The grant directly supports research and is awarded "to bring to clinical care settings novel ideas that have the potential to reduce cancer incidence and mortality, improve survival, and improve the quality of life," according to the NCI. SPORE projects must involve both basic and clinical scientists, must include a population-based research component and must focus on translational research.

The SPORE grant will fund four research projects and an ongoing developmental research project within the Duke Breast Cancer Research Program. The new projects are:

- Consequences of Hypoxia in Breast Cancer. This study is designed to determine whether or not lack of sufficient oxygen in tumors is a cause for treatment resistance to chemotherapeutic drugs and whether or not improved oxygenation improves response to therapy in the adjuvant (after treatment of the primary tumor) and metastatic settings. Hypoxia is commonly observed in breast cancer, but it remains undetermined whether it is a source of treatment resistance, although laboratory studies suggest that it may be.
- T helper Responses to HER2/neu in Breast Cancer Patients. The long-term objective of this project is to generate a response to antigen-specific T cells and to demonstrate the clinical benefits of these findings in patients with cancer.
- Hormonal Modifiers of Penetrance of Breast Cancer among BRCA1 and BRCA2 Mutation Carriers. The focus of the study is to examine whether genetic factors involved in DNA damage and repair act as modifiers of BRCA1 and BRCA2.
- Application of Pharmacogenomics to Treatment of Breast Cancer. The goal of this project is to identify pharmacogenomic determinants of drug exposure and utilize the knowledge of these determinants to improve the effectiveness and tolerance of breast cancer therapy.

The ongoing research project that SPORE will support is work on identifying the genetic markers of hormonal therapy resistance.

"The true impact of the SPORE grant is meant to be driving excellent research into applications for patients," says Kim Lyerly, MD, George Barth Geller Professor for Research in Cancer and Cancer Center director. He believes that Duke's collaborative research model "allows investigators to fully engage in cooperative activities that take their observations on the basic science level and drive them into direct applications that benefit people." This model, so different from the every-lab-for-itself approach that often prevails in medicine, promotes excellent research, Lyerly believes.

"What I would hope is that in five years Duke is the leading institution for complex projects that impact human health. The opportunity exists for us because of our large scientific infrastructure, our large clinical operation, our culture of interchange and teamwork, and a dynamic management style that will allow us to take on the hard tasks and do the heavy lifting for society."

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—Kim Lyerly, MD

Duke Referrals

Duke operates toll-free phone lines to help patients and physicians learn about Duke cancer treatment options, or find out about joining a clinical trial. Patients should call 1-888-ASK-DUKE to connect with a service representative in the Duke Consultation and Referral Center. Hours of operation are Monday-Friday 7:30 a.m. to 6 p.m. Eastern Standard Time. Physicians may call 1-800-MED-DUKE. This service has been developed to give physicians and other health care professionals a single telephone number to conveniently access Duke University Health System physicians and services. Hours of operation are Monday-Friday 7:30 a.m. to 6 p.m. Eastern Standard Time.

behavior of cancer cells rather than structural changes, such as tumor masses, which take much longer to develop, says Tornai. "Once you start seeing structural changes using mammography, that indicates the molecular process has been going on for a while," he says. "If we can detect subtle changes in cells before a tumor has developed, we have a better chance of treating the abnormal cells in their earliest stages of malignancy."

To use the device, providers inject a cancer-specific radioactive tracer into the patient's bloodstream. One tracer, called sestamibi, is preferentially absorbed by cancer cells because they have large numbers of mitochondria, the cells' powerhouses. Cancer cells have more mitochondria than normal cells because they are more metabolically active and require more energy to grow and spread. The camera obtains an image by picking up gamma rays—high energy photons or units of light—that are emitted by the radioactive atom attached to sestamibi. The gamma rays easily penetrate the tissue and can be detected non-invasively by a gamma ray camera.

Tornai, along with his Duke collaborators, developed a miniature gamma ray camera and rotating platform system that allows it to completely and closely orbit a breast, creating a high-resolution, three-dimensional image called an emission or functional mammotomogram. In clinical practice, the procedure would take 10 to 20 minutes per breast, and should be more comfortable for the patient than mammography, because the breast is not compressed during the procedure. Patients may not even need to remove their bras, since the device never touches the breast.

"This technology could potentially be applied to screen women who are at high risk for breast cancer, particularly younger women who have denser breast tissue," he says. In addition, Tornai says the device could be useful to monitor the course of chemotherapy or radiation therapy in breast cancer patients because it could detect changes to the cancer cells.

TRACKING GENETIC FINGERPRINTS

A third significant project aimed at early detection and prediction involves a new statistical approach to classifying breast cancers based on profiles of their gene expression. Duke is leading studies using microarray analysis to determine the genetic fingerprint of a patient's tumor. Genetic differences within cancers can give doctors clues about how a patient's tumor might respond to a given drug, or how aggressive the tumor might be. In breast cancer, some differences are already known to relate to prognosis. The microarray chips, similar to computer chips, have a grid pattern of tiny bits of genetic

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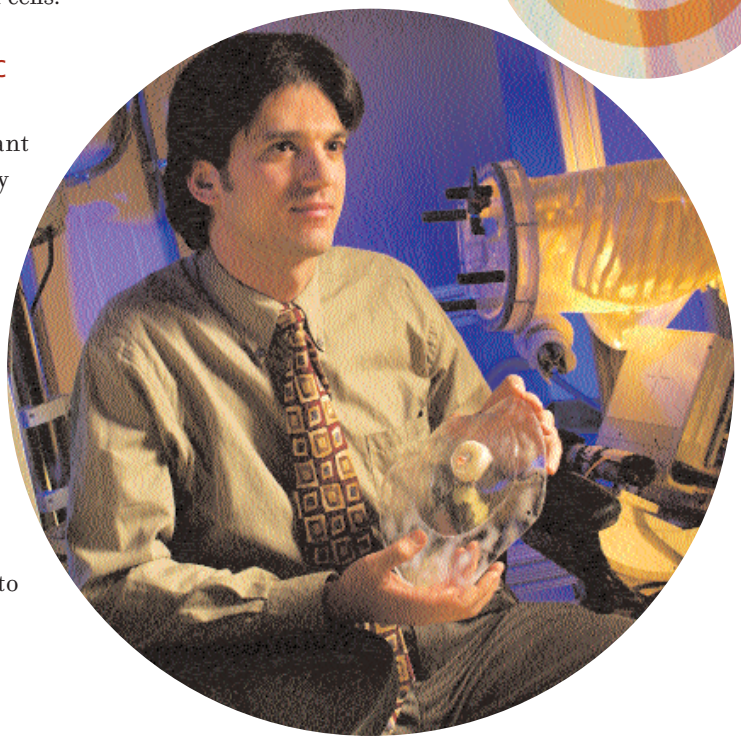
>
> —Martin Tornai, PhD



material that detect the activity of genes in the cancer. Because researchers know which bit corresponds to what gene, they can determine the cancer's genetic fingerprint.

Clinical studies will track these genetic fingerprints with many measures of patient outcome and also test the utility of knowing such information.

Joseph Nevins, PhD, James B. Duke Professor of Molecular Genetics and Microbiology, says he and his colleagues believe the technique will lead to new prognostic tests that can predict the status of tumors with considerable precision, enabling improved diagnosis and treatment.

"This technique goes beyond the standard practice of using visual and clinical data to decide on treatment and outcomes based on that examination," Nevins says. "Since the visual and clinical information that guides a pathologist's diagnosis is largely determined by the gene expression within the tumor, our ability to directly analyze gene expression on a very large scale, and ultimately to analyze every gene that is expressed in the tumor, affords the opportunity to diagnose tumors with much greater detail than now possible.

"Genomics is all about the promise and hope that one can precisely identify and classify a disease state and treat that disease with a much more precise and individualized therapy." □

—from staff reports

Escaping the woes of chemotherapy

Breast cancer is a harsh reality for thousands of Americans, but researchers are finding that a little escapism can relieve some of the hardships associated with treating the disease. The Virtual Reality study, conducted at Duke University School of Nursing and Case Western Reserve Comprehensive Cancer Center, found that women with breast cancer have fewer adverse effects from chemotherapy and less fatigue when using virtual reality as a distraction intervention during treatments.

Nearly 60 percent of chemotherapy patients report some form of symptom distress, including nausea and vomiting, inability to concentrate, and fatigue. For chemotherapy patient Donna Honeycutt of Elon, North Carolina, the stress was enough to make her worry that she wouldn't be able to complete the entire series of treatments she needed to have the best chance of beating her breast cancer.

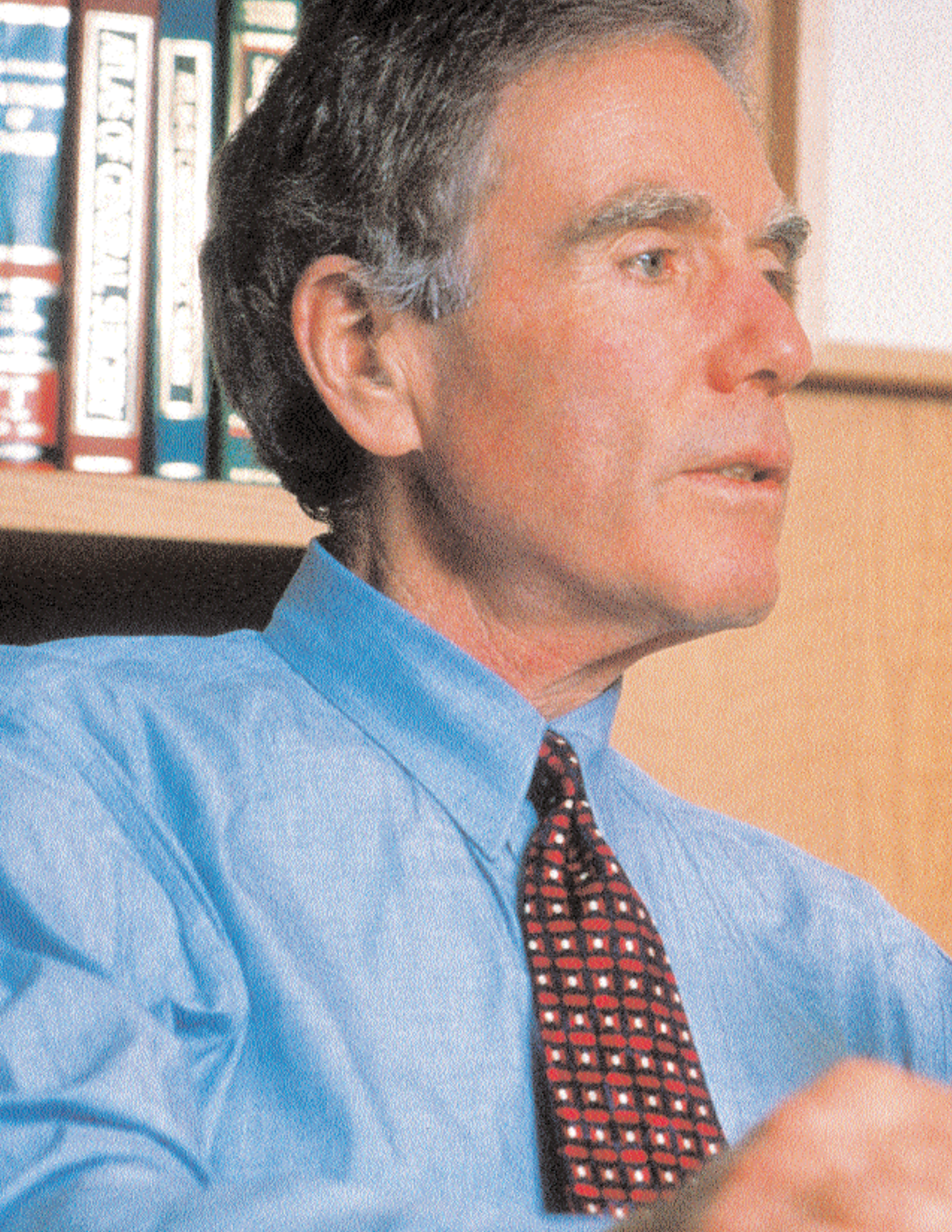
"You're in a room with many other people receiving chemotherapy. Some are very sick and you tend to always look at the individual who's sickest. For me, I felt sicker when I was in this environment," says Honeycutt, who underwent her chemotherapy two years ago and completed a portion of her treatments using virtual reality.

In the study, published in the January 2004 *Oncology Nursing Forum*, the researchers described how chemotherapy patients eased their fatigue and discomfort by immersing themselves in a computer-generated visual and aural environment via a head-mounted display device. In the study, participants could keep their minds off the stresses of chemotherapy by solving a mystery, touring an art gallery, or deep-sea diving in a virtual environment as they underwent treatment. The researchers believe that virtual reality makes for an excellent distraction intervention because it is interactive, engages several senses simultaneously, and immerses participants in a new world, thereby blocking out their current and often stressful environment.

Women who used virtual reality during chemotherapy treatments reported significant decreases in symptom distress and fatigue immediately following treatments. While anxiety levels were not directly impacted by the intervention, according to Susan Schneider, PhD, director of the oncology program at the School of Nursing and lead author on the paper, "One added benefit was that the virtual reality seemed to make patients feel as though time was moving faster. For example, on average, a chemotherapy treatment might last 67 minutes, but patients would perceive that it only lasted 42 minutes."

All the study participants preferred chemotherapy treatments with virtual reality than using no intervention, and 95 percent said they would be willing to use it again.

Honeycutt, who participated in a similar trial of Schneider's at Duke, says she benefited greatly from using virtual reality. "I just did not get sick," she said. "I did not get nauseated. I didn't get violently ill like most people. And I think it's because you separate yourself from that initially. The virtual reality helps take you away from it all."



Looking back on Ralph Snyderman's 15 YEARS AT THE HELM

BY NEIL CHESANOW

ON JUNE 30, 2004, RALPH SNYDERMAN, MD, STEPS DOWN AS DUKE'S CHANCELLOR FOR HEALTH AFFAIRS AND PRESIDENT AND CEO OF DUKE UNIVERSITY HEALTH SYSTEM. DUKEMED LOOKS BACK ON SNYDERMAN'S FIFTEEN YEARS AT THE HELM.

Robert J. Lefkowitz was trying to enjoy his daily jog down Duke University Road, but he had too much on his mind. Lefkowitz, a respected biomedical researcher, was serving on the 1988 search committee charged with finding a new chancellor for health affairs. He feared his team would never find anyone to fit the bill.

The task was formidable. The ideal candidate would be a brilliant scientist, a caring physician, a diplomat, a steely-eyed executive, and perhaps most important, a fearless entrepreneur whose visionary leadership would make Duke a world-class leader in medicine.

With a sudden burst of clarity, the answer came to Lefkowitz. 'Ralph's the guy for the job!' he thought.

Ralph was Ralph Snyderman, Lefkowitz's old jogging partner. He was also the former chief of Duke's rheumatology and immunology division. But Snyderman wasn't being considered for the job, in spite of his groundbreaking research in the field of inflammation, specifically chemotaxis. His departmental management experience was modest, and his chosen field of research was, at that time, not as glamorous as it has since become.

What's more, Snyderman, 48, had recently left Duke. He had been wooed away eighteen months earlier by Genentech, the nation's white-hot biotech company, where he was now a supernova himself, having been recently promoted to senior vice president. He headed R&D and was in charge of 300 scientists, thanks to his lightning fast shepherding of a new Genentech drug through the FDA's clearance process.

But that didn't bother Lefkowitz at all. 'This is beshert!' he thought, using the Yiddish word for destiny. 'The guy loves Duke. He's good administratively. He's a superb academic. Now he has administrative responsibility on the commercial side. And he's very good with money. It makes so much sense!'

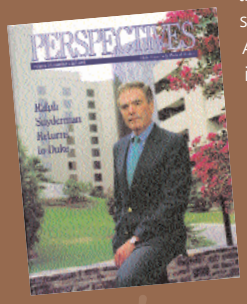
Later that day, when Snyderman returned to his office in San Francisco, he found his destiny in the form of a pink message slip waiting on his desk. Lefkowitz had phoned and requested an urgent callback. Snyderman returned the call.

"Sit down," said one runner to another. "I'm going to change your life."

15 YEARS AT THE HELM

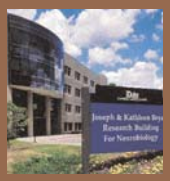
1989

Ralph Snyderman, MD, is appointed Chancellor for Health Affairs of Duke University and Dean of the School of Medicine, succeeding William G. Anlyan, MD. Snyderman is the fourth person to lead Duke University Medical Center since its opening in 1930.



1990

After a national search, Duke University Medical Center recruits **Dale Purves** as the first chair of the Department of Neurobiology (created in 1988). Purves is the first of 25 chairs to be recruited by Dr. Snyderman.



On February 22, Mary Semans, Joseph Bryan, William Anlyan, and Ralph Snyderman formally dedicate the $26.5 million **Joseph and Kathleen Bryan Research Building for Neurobiology**. Over the next 15 years, more than 350,000 square feet of space for basic research is added to the DUMC campus.

1991

Duke University Board of Trustees approve the **Strategic Long Range Plan for DUMC**. Areas highlighted for growth over the next five years include genetics, immunology, signal transduction, neurosciences, and structural biology.

Mary Champagne, RN, PhD, is appointed Dean of the School of Nursing. Under her tenure, the School of Nursing increases its faculty from 5 to 38, and the number of students from 54 to close to 400. By 2005, the school hopes to begin a doctoral program in nursing.

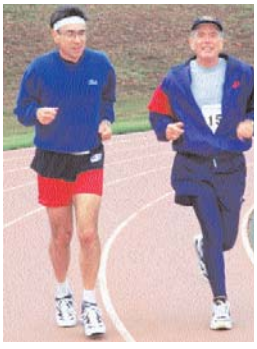
DUMC creates a **new section of Genetics** (which became a full-fledged Department in 1994) and a new **Department of Radiation Oncology**.

Whether you call it destiny or "beshert," Ralph Snyderman returned to Duke, lured by the challenges of being chancellor of the institution he loved. He brought to the job a physician's compassion for patients, a scientist's creativity, and an entrepreneur's enthusiasm and bottom-line focus. Most importantly, he brought the sheer will to help lead Duke's medical center to the top.

"Ralph Snyderman has built a health system at Duke that in many ways is one of the leading examples in the nation," says Edward Holmes, MD, former dean of Duke's medical school and now the vice chancellor at the University of California-San Diego. Duke's medical school ranked fourth and its medical center sixth in the latest *U.S.News & World Report* surveys.

"He's a remarkable man with a tremendous intellect whose mind works at exceptional speed," says R. Sanders Williams, MD, the dean of the medical school, who has worked perhaps more intimately with Snyderman than anyone else. "I see him almost every day in one type of meeting or another. In meetings, he has a commanding presence and is very insightful. During discussions about a topic, Ralph can pull the conversation back to the real crux of the matter that has eluded others. That's a trait great leaders have."

"We couldn't have found a better person to lead the health system," says former vice chancellor for health affairs Jean Spaulding, MD. "In addition to being an amazing visionary and excellent administrator, he's a fantastic physician. He'd take a month each year and go on rounds. I don't know of very many people who run a huge medical center who continue to have that personal touch with patients."



"He's the kind of guy who can't sit still too long," says Robert Lefkowitz, MD (left) of longtime friend and jogging partner Ralph Snyderman. "He has to continuously challenge himself to reach new levels of mastery."

These qualities have translated into a long series of innovations under Snyderman's leadership over the past fifteen years. Key components of the Snyderman legacy include:

- *The Duke Clinical Research Institute, the world's premier academic clinical research unit;*
- *The Duke Office of Science and Technology, which boasts more corporate funded research than any U.S. medical center;*
- *The Duke University Health System, a model for the delivery of cost-effective health care;*
- *The Duke Institute for Genome Sciences & Policy, a university-wide effort to study all aspects of the genetic revolution;*
- *The Duke Center for Integrative Medicine, a pioneering effort to create a more patient-centric, holistic approach to medical care; and*
- *Prospective health care, a plan to transform how health care is delivered.*

Growth in each of these areas has also meant the recruitment of scores of outstanding biomedical researchers who have enhanced the university's medical system

1992

To improve employee communications, **INSIDE DUMC**, a newsletter for staff and faculty, is created.

Responding to the growing emphasis in the U.S. on preventive medicine, DUMC opens the **Center for Living Campus** on Morreene Road.

School of Nursing expands its **Advanced Practice Nursing** programs, offering gerontology in 1992, followed by pediatrics in 1994, neonatal nurse practitioner in 1997, and acute care pediatric in 1998.

DUMC creates a new **Department of Immunology**, reorganizing the department of Microbiology and Immunology.

Duke performs its **first lung transplant** and its **first heart/lung transplant**.

1993

Duke Comprehensive Cancer Center opens the first **outpatient bone marrow transplant clinic** in the nation.

Duke **researchers identify apolipoprotein E** (APOE) as the major susceptibility gene for Alzheimer's disease. This is just one of many genetic risk factors for disease identified at Duke.

Final patient is enrolled in **GUSTO-I**, the largest clinical trial conducted in the U.S. The infrastructure created for the GUSTO-I trial formed the foundation for the Duke Clinical Research Institute, the nation's foremost clinical trials center based in an academic setting.

Duke and US Surgical collaborate to create the **Duke/US Surgical Endosurgical Center**. The center's research and education in laparoscopic and minimally invasive surgery has changed the face of many surgeries, from gallbladder removal and orthopedic surgery to minimally invasive heart surgery.

The **Department of Pharmacy installs a robot** that dispenses medications with an error rate of less than 1 in 400 million.

as well as its basic science departments. The growth in research is underscored by the boom in Duke's National Institutes of Health (NIH) funding, one measure of any university's importance as a research institution. Since 1989, when Snyderman took office, Duke's NIH funding has rocketed 269 percent from $91 million to $246 million in 2003. Over the same period, the medical school's endowment shot up from $146 million to $651 million. Duke's physical plant has also grown substantially. In the past 15 years, more than 80 new facilities and major renovations relating to the medical center and health system have been completed, are near completion, or are being built—an investment totaling nearly $750 million.

THE DUKE CLINICAL RESEARCH INSTITUTE

In another life, Snyderman might have been a fortune teller, a mathematician, or perhaps an aggressive ice hockey forward. "I try to imagine where scientific and medical fields are going," he says. "I try to catch the currents of change. I try to imagine where the hockey puck is going. A general operating principle of my life has been to use leverage to find the area where maximum impact can be made."

With the Duke Clinical Research Institute (DCRI), Snyderman scored big. He was the first leader of an academic medical center to see that a university could turn the management of clinical trials into an academic strength while contributing to the societal good and generating substantial revenues.

"At the time, some thought our focus ought to be solely on individual bench research. Clinical trials were not considered cutting-edge. There's a grain of truth in that," Snyderman admits. "But that doesn't make trials any less creative or important. They are a critical part of the pipeline for the advancement of medical knowledge."

Today DCRI, established in 1996, is recognized as one of the world's most sophisticated clinical trials enterprises. Its 900 staffers provide data management, statistical analysis, technology assessment, outcomes assessment, site monitoring, and a host of other services—across a spectrum of medical fields—to researchers at Duke and around the world.

"DCRI is a model," says Holmes. "Few of us will be able to do something similar. Ralph jumped in early and put Duke way out ahead."

Snyderman's stint in the private sector had much to do with how DCRI got started. While at Genentech, he hired groups of researchers at various academic medical centers, including one headed by Duke cardiologist Robert Califf, MD, to conduct clinical trials of Genentech's clot-dissolving drug. After Snyderman's return to Duke, Genentech hired Califf to conduct a mega-trial—the first large-scale clinical trial ever done in America and one that set a new standard for clinical research. As a result, the Duke team knew more about conducting them than anyone in America.

Suddenly all eyes were on Duke. "It made us aware how much strength we'd developed in this area right under our noses," says Bill Donelan, executive vice president and chief operating officer for Duke University Health System. "Until then, clinical trials had been conducted as ad hoc operations. They hadn't been organized as a business unit." Realizing that he had to act quickly, Snyderman worked with management consultants McKinsey & Company, spun Califf's group out of the department of medicine, and turned it into an independent research entity. This was something unheard of: An academic clinical research organization that generated revenue and competed with

1994

DUMC responds to the changing health care market by creating the **Duke Health Network**. This network increased primary care through Duke University Affiliated Physicians, developed a managed care plan for Duke employees, and created an office to manage DUMC's managed care relationships.

Duke University Hospital moves to a **Clinical Service Unit structure**, creating the possibility for departments to work more closely together and provide better service to patients.

Duke researchers report early success in using laser beams to reshape pig corneas, demonstrating the potential of laser surgical techniques for eye problems such as far-sightedness and nearsightedness. **Duke Eye Center** is now a leader in LASIK eye surgery in the area.

Chancellor Ralph Snyderman is among academic health center leaders who meet with President and Mrs. Clinton to discuss the **need for universal health care coverage**.

Duke responds to the need for more primary care physicians by creating the new position of **Assistant Dean for Primary Care Education**. Duke also begins the first two-week clerkship in cost-consciousness for medical students.

The **Levine Science Research Center and Medical Science Research Building officially open**, providing more basic science and clinical science research space. The spiral staircase in the MSRB was designed to improve interdisciplinary work by removing barriers between floors.

private firms for corporate contracts while preserving its right to publish research results and other academic imperatives.

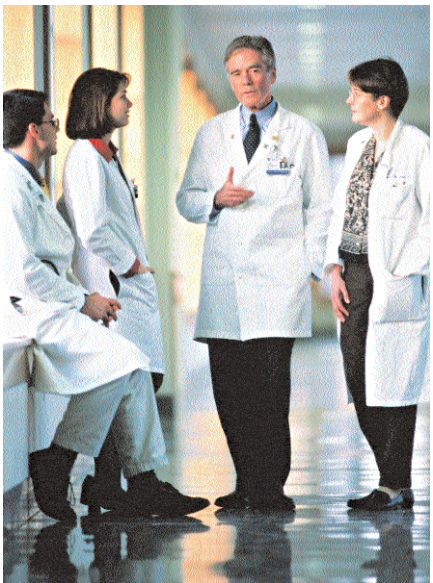
"Now everybody is playing catch-up," says Snyderman. "Nobody is close. All I did was open a door for some very bright people and say, 'Charge right through it'."

DUKE'S OFFICE OF SCIENCE AND TECHNOLOGY

Snyderman respects those with different views but he hasn't let opposition prevent him from turning his visions into reality. He needed a steel spine to start something as radical as the Office of Science and Technology (OST). To many at Duke, it was heresy; to the business-oriented part of his mind, it was a no-brainer.

Some faculty objected to tearing down the wall that traditionally separated the academic and business communities. Academic research considered itself concerned only with the pure, unfettered pursuit of knowledge, without fear or favor. Since the ultimate concern of industry was maximizing profits, many feared that marrying the two risked sullying the university's reputation.

Snyderman's instincts and experience told him that Duke could negotiate a middle path between these two extremes. At Genentech, he had a $26 million R&D budget. It yielded an annual profit of several hundred million dollars. But Duke's medical center was lavishing $120 million a year on R&D while generating no revenues—and at a time when the medical center's traditional income streams were evaporating. Established in 1991, OST today protects the university's objectivity and independence by providing one-stop shopping for commercial enterprises that want to leverage the intellectual and physical resources of Duke research. While preserving the right to control their research, publish their work, and own the intellectual property rights, Duke medical center faculty now lead the nation in corporate-sponsored research.



"It's done a very good job and has given an entrepreneurial flavor to Duke for those who want to play in that arena. It hasn't yet had any really big patents that have had big royalties, but if you look at the relationships it's created with industry, OST has been remarkable," says Robert Taber, PhD, vice chancellor for science and technology development. "Other medical centers—the good ones—get $35 million to $40 million a year in corporate funding. Our office got $130 million in 2003. In 2004, we'll sign 2,600 agreements, three times as many as anyone else."

CREATING THE HEALTH SYSTEM

There are two theories of history. One says that great forces shape people. The other holds that great people shape events. There's no question that Snyderman's indomitable willpower, which by his own description is at times "tenacious," steered Duke out of danger. The 1990s were a perilous time for U.S. medical centers facing the challenge of managed care. By masterminding the creation of the Duke University Health System, Snyderman helped prevent mass layoffs and put the institution's delivery of health care on an entirely new footing.

Chancellor Snyderman, shown chatting with medical residents in 1999, led Duke's transition from an outstanding medical center to one recognized internationally as a model for academic medicine.

1995

Duke researchers identify the **BRCA1 and BRCA2 genes** responsible for some forms of breast cancer.

Duke University Hospital's Operations Improvement project succeeds in reducing staff by 684 positions with just 24 layoffs, resulting in $40 million savings in labor costs.

1996

Reflecting DUMC's broadening from a tertiary care hospital to a fully integrated health system that covers a wide range of services, a **new logo is created for the Duke University Health System**. The new logo incorporates the "gothic towers" to symbolize Duke, and provides a sense of movement, reflecting DUHS's constant progress.

Duke establishes the **Duke Clinical Research Institute** as an independent entity within Duke University Medical Center.

Duke holds its first **Mind-Body-Spirit conference**. Over 600 people from across the nation come to hear physicians and researchers talk about how religion and attitude interact with the physical body. This galvanizes movement toward a Center for Integrative Medicine, which opened in 2000.

DUMC takes medicine out into the community with its **first school-based wellness clinic** at Southern High School.

"He guided the medical center through an enormously perilous time in American medicine," says Dale Purves, chairman of the Department of Neurobiology from 1990 to 2002. "He succeeded where other medical centers failed, and thanks to him, today Duke is in a very strong position financially, economically, and in terms of how it's respected in American medicine."

The next and larger battle, managed care, came relatively late to North Carolina. Snyderman knew that in California, where HMOs were deeply entrenched, physicians and hospitals had had their reimbursements slashed by more than 25 percent. In Minneapolis, where HMOs had also become dominant, the University of Minnesota had refused to participate in HMO contracts. It was one of the nation's premier public academic medical centers, and "their clinical program largely evaporated," Bill Donelan recalls. "It was astounding.

"We had the same issues here, but we had the benefit of being able to look at other, more highly developed managed-care markets that were temporarily ahead of us. Ralph led the strategic thinking to position Duke's clinical enterprise—its faculty practice, hospital,

A Chancellor Grows in Brooklyn

IN RALPH SNYDERMAN'S OFFICE with its elegant furniture and graceful artwork, a visitor finds something small and unusual on the wall: His father's yellowing peddler's license in a small, inconspicuous frame amid the handsome medical diplomas in their gleaming black frames.

Snyderman's parents instilled in their son the belief that he could live the American Dream, just as they had. Born in 1940, Snyderman is a first-generation American who grew up in the working class section of Bensonhurst, Brooklyn. His parents, Morris and Ida, were Russian immigrants who fled the pogroms. His father initially sold odds and ends out of a suitcase, then graduated to a pushcart. From the pushcart, his father saved enough to start his own store and ultimately became a successful retailer.

"He wasn't an intellectual who liked operas or weighty tomes," Snyderman says. "He was a solid, determined, proud, sharp guy."

His mother was the opposite—but equally influential. "She was more scholarly and artistic than my father," Snyderman recalls. "She read Flaubert. She always talked about the operas she saw. She had lived in abject poverty but would spend money to attend the opera."

Looking back, Snyderman says, "My father gave me toughness, integrity, a business sense, and the will to win. From my mother I got intellectualism, an appreciation of complexity, and most of all, a conscience. She advised me to always associate with people who are better than I was—people I could learn from. That was as profound as any lesson I learned from my father."

By high school graduation, Snyderman knew that he wanted to be a biomedical researcher, not just a physician. He wanted to apply leverage, a principle that Snyderman would rely on throughout his career. "I felt that being a doctor was the greatest thing, because you could help another human being," he recalls. "But it'd be even better to be a researcher and help thousands of people at once."

Snyderman admits he attended excellent but not prestigious schools: Washington College in Chestertown, Maryland, and Downstate Medical Center in Brooklyn. "I've always felt a little on the outside looking in," he says. "That feeling may relate to my whole modus operandi. Even when I'm running a race, I'd prefer to be several runners behind the leader and know what I have to do to win, rather than be in front."

1997

Duke Hospital physicians complete the **1,000th free vascularized fibular graft hip replacement**—a novel procedure pioneered at Duke that uses a patient's own bone and blood supply to arrest the degenerative process of osteonecrosis and prevent the need for a total hip replacement.

The National Institutes of Health and the Food and Drug Administration give approval for Duke to conduct **clinical trials testing the first RNA cancer vaccine**.

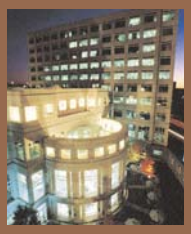
1998

The National Institutes of Health partner with Duke to offer a **joint master of health sciences degree in clinical research**. Using distance learning and televideo equipment, NIH fellows can earn a degree at Duke. This is the first graduate level degree partnership for NIH.

Recognizing that DUMC is an innovative leader in the competitive health care business, *Time Magazine* features Duke in its **"A Week in the Life of a Hospital"** issue.

The **Health System is formally created as a subsidiary of Duke University**, with its own Board of Directors. This arrangement allows the Health System to respond quickly to the changing health care environment without losing its ties to Duke University.

Duke takes the **first deposit in its Umbilical Cord Blood Bank**. Duke is a leader in using umbilical cord blood transplants to treat cancer.



DUMC opens the **Ambulatory Surgery Center** in the North Pavilion. This facility for same-day surgery now performs nearly 7,000 cases each year.

Duke University Health System and Durham County Hospital Corporation reach an agreement to have Duke manage **Durham Regional Hospital** for 20 years. Later in the year, DUHS purchases **Raleigh Community Hospital** (now renamed Duke Health Raleigh Hospital) and incorporates Triangle Hospice as part of the Health System.

Snyderman's Duke: Home and Away

INTELLECTUAL CURIOSITY, challenges and calculated risk-taking marked Snyderman's career before he became chancellor.

After he had completed his internship and residency at Duke and had trained to be a rheumatologist, he spent five years at the NIH researching inflammation, specifically chemotaxis—how certain cells respond to chemical signals and defend against invading microbes.

In the late 1960s, this new, ill-defined field wasn't considered a fast track to fame and fortune. "Many top scientists didn't consider what I was doing real science," Snyderman recalls. "'This is phenomenology!' they'd say. 'Big deal!'"

Convinced his research would pay off, he soldiered on, returning to Duke in 1972 as an assistant professor of immunology. In 1975, he was appointed chief of the Division of Rheumatic and Genetic Diseases.

Snyderman continued researching chemotaxis into the 1980s, but he was no longer outside the mainstream. It had become clear that his renegade field had major implications for treating infectious diseases, inflammatory diseases, and cancer. "Everything was peachy," he says. "My grants had been renewed. My work was going mainstream. I was in the limelight for the first time."

But after 15 years at Duke, Snyderman felt he was "maxing out relative to where I wanted to be." With other researchers now crowding the field and hot on his heels, "It was like a footrace, and it wasn't as much fun anymore."

"He's the kind of guy who can't sit still too long," says his colleague Robert Lefkowitz, MD. "He has to continuously challenge himself to reach new levels of mastery."

So when Genentech wooed him in 1987, Snyderman was eager to make the leap to the private sector. As VP of medical R&D, he was responsible for overseeing basic research and bringing drugs to market. The first big test for the ex-chief of a modest rheumatology division: Turn around the FDA's rejection, on the grounds of insufficient research, of Genentech's first major product, a drug designed to dissolve blood clots. He succeeded spectacularly: The drug was approved in a record five months and 13 days. "It's the fastest that a new therapeutic went from rejection to licensure in FDA history," he says. As a result, Snyderman was promoted to senior vice president, overseeing more than 300 researchers.

But when Lefkowitz called in 1988 about the chancellor's spot, Snyderman was open to change yet again. This time, for a very special reason, Snyderman's love for Duke and loyalty to the institution beckoned him in a powerful way when he was offered the Medical Center's top job. He was told that Duke needed him, and he felt he must respond.

and care delivery mechanisms—so that we could succeed in this new environment."

Snyderman and other Duke leaders recognized that the university would either be forced to join an outside HMO and lose control over quality, or control its own HMO. So in 1998, the Duke University Health System was born. It now includes a network of physicians, Durham Regional Hospital, Duke Health Raleigh Hospital, and Duke Health Community Care, along with Duke University Hospital.

DUKE INSTITUTE FOR GENOME SCIENCES AND POLICY

Ralph Snyderman hates losing, and he likes to doodle. Both came into play with the creation of the Duke Institute for Genome Sciences and Policy (IGSP). While at Genentech, he was saddened that Duke had "totally missed" the emerging biotech revolution. "When I became chancellor, I pledged that Duke would never again miss the leading edge of a major component of biomedical research and health. I decided that our focus was always going to be on the horizon."

The Duke IGSP, established in 2000, calls on medical center and university

1999

The federal government's Office for Protection from Research Risks (OPRR) closes down clinical trials at Duke for three days because of questions about documentation. The issue provides **opportunities for Duke to become a national model for improving human subject research**.

DUMC separates the role of the Dean of the School of Medicine and the Chancellor for Health Affairs. **Edward Holmes, MD**, is appointed as Dean of the School of Medicine. He is succeeded in 2001 by **R. Sanders Williams, MD**.

Duke completely **remodels the old Duke South clinic building**, adding a new reception building with new classrooms, clinic areas, and food court.

2000

DUMC begins **Promising Practices**, a program that uses nurse practitioners to bring health care to the homes of citizens of Durham in an effort to reduce the number of emergency room visits.

The **McGovern Davison Children's Health Center opens**, bringing all of Duke's pediatric specialties under one roof. The $32.5 million dollar facility is completely paid for through philanthropy.

Duke announces the creation of the **Institute for Genome Sciences and Policy**. The institute brings together scientists, engineers, physicians, and scholars in law, business, economics, public policy, ethics, religion, environmental studies, and other humanities and social sciences to consider the broad challenges of the genomics revolution.

2001

The **American College of Surgeons moves its Oncology Group**, which oversees the largest number of clinical trials investigating surgical approaches to treating cancer, from Chicago to the Duke University Medical Center.

DUMC develops a **$1 million human patient simulation facility** that allows students and faculty to hone medical skills without risk to patients.

faculty in law, philosophy, business and other schools and departments to collaborate in untraditional ways, exchanging ideas on different aspects of solving a single multi-faceted genomics problem.

"Ralph has been spectacular in grasping where genome research was taking medicine," says geneticist Huntington Willard, PhD, IGSP's director. "I give him bonus points for not only grasping it but realizing the need to develop a unique organization and assigning the resources to enable it to function. Many people in his position now realize they should have been doing this. But he's the only one who actually did."

Snyderman got the idea for IGSP in 1998. At a meeting of administrators and trustees, the discussion drifted to what Duke would do if a generous philanthropist gave the university an endowment of $200 million. At about the same time, a medical center faculty member suggested to Snyderman that Duke should develop a genetics clinic and become a leader testing people for their genetic susceptibility to disease. Duke was already capable of performing many of those tests, but Snyderman was fascinated by broader issues, such as the legal and ethical implications of such testing and what government policies should be.

"It was clear that the technical aspects of implementing the genome revolution, while challenging, would be less so than resolving the socio-political-ethical issues it raised," Snyderman recalls. "Putting those two ideas together, I conceived of an institute that would bring together the health system, the school of medicine, biomedical research, law, ethics, and policy, and have it be an overarching institution at Duke. I actually doodled all the structures interacting with each other on a napkin. It was like a daisy with IGSP at the center and all other schools arrayed around it," Snyderman recalls.

Today the multidisciplinary IGSP develops and implements novel approaches for genome analysis; fosters ethically responsible and socially beneficial uses of genome science; brings the products of genome research to the actual practice of medicine; analyzes genomic data to shed new light on specific diseases; and identifies the genes responsible for various diseases and deepens knowledge of disease processes.

Duke continues to outpace other schools in genome work. Willard recently attended an MIT meeting where the directors of other universities' new genomics institutes presented models of their work. "In terms of the breadth of activity that IGSP is conducting," Willard says, Duke was clearly in the lead. "Everyone else was focusing on the science alone. What we do here at Duke is science and beyond."

DUKE'S CENTER FOR INTEGRATIVE MEDICINE

Snyderman loves closing the gap between what is and what should be. That's how Duke's Center for Integrative Medicine came into being. Every year since taking office, Snyderman has made a presentation to the board of trustees in which he lists the top 10 medical discoveries that had been made at Duke during the past 12 months. One day it dawned on him that "these are tremendous advances, but they're not going to truly affect health care in my lifetime or possibly even during my son's lifetime. I realized that there's a discordance between what medicine is doing with science and technology and what people's health care needs are."

Duke is now a leader in integrative medicine, which combines the best conventional and non-conventional approaches to medicine to treat the whole patient, not just the disease.

Operational since 2000, the Duke Center for Integrative Medicine will break ground for its own separate facility this

2002

Duke Cardiovascular Magnetic Resonance Center opens, bringing the ability to produce high-quality, three-dimensional images of the heart non-invasively.

Duke and the Centers for Medicaid and Medicare Services (CMS) partner in a **pilot program for Prospective Health Care**. This novel method of delivering health care uses risk assessments and health care coaches to assist patients in creating a health plan for their future.

Nursing School begins the **Accelerated BSN degree**, the first undergraduate nursing degree offered at Duke since 1984.

2003

Duke announces a **partnership with Singapore** to create a medical school in Singapore based on Duke's curriculum.

Jesica Santillan's heart-lung transplant involving mis-matched organs raises the visibility of medical errors and patient safety across the nation. Duke responds by making immediate changes to its transplant procedures, changes which are subsequently largely adopted by United Network for Organ Sharing (UNOS), the national organization that administers the nation's only Organ Procurement and Transplantation Network.

Two new research buildings—**Genome Science Research Buildings I and II** provide space for the Institute for Genome Sciences and Policy.

Duke University School of Medicine ends the **"Keeping the Promise of Medicine" fund-raising campaign** (on Dec. 31, 2003), having raised over $700 million. These funds will be used to expand DUMC's faculty, facilities, and programs.

Duke University Hospital begins to implement **Computerized Physician Order Entry** to improve patient safety. The new system will first appear in the Heart Center, and gradually be introduced to all inpatient units.

Nannerl O. Keohane, president of Duke University, announces Victor J. Dzau, MD as **the next Chancellor for Health Affairs**. Dzau will begin his tenure on July 1, 2004.

2004

15 YEARS AT THE HELM

October. The center, like the Duke Clinical Research Institute and the Institute for Genome Sciences and Policy, is interdisciplinary. Specialists in obstetrics and gynecology, internal medicine, community and family medicine, psychiatry, and psychology see patients as a team. They then develop a personal health plan for patients that factors in healing-oriented medicine, nutrition, botanical medicine, meditation, spirituality, and other modalities.

"It's partly about botanicals and acupuncture," explains Tracy Gaudet, MD, director of the Center. "But it's broader than that. I may see you at our center and never talk to you about alternative medicine. But I would take a mind/body/spirit health history. Your personal health plan would consider not only the best that medicine and surgery have to offer but also such considerations as lifestyle, nutrition, stress reduction, and fitness."

Integrative medicine has been slow to develop in academic medical centers, but it's a growing trend: there are now formal Integrative Medicine programs in 20 universities.

What led to Snyderman's open-mindedness? As a practicing physician he has treated many patients suffering from rheumatoid arthritis, which is incurable. With one particular patient, he had developed a very close physician-patient relationship, he says. "I'd jiggle around her aspirin, but when she left, I'd think, 'You fraud. You haven't really helped her. Her disease will continue as though you weren't there.'"

Then he had an epiphany. "How foolish I was," Snyderman says. "This woman kept coming back because she wanted a caring relationship with a physician. I didn't understand the difference between curing and caring. While I couldn't always cure, I could always care and the latter could be as powerful as the former. Those two concepts need to be brought together in practice. That's what integrative medicine does. Its central feature is the patient's relationship to the physician and the health system and making that interaction more humane and effective."

In November 2003, Snyderman received the Bravewell Leadership Award. Sponsored by the Philanthropic Collaborative for Integrative Medicine in Minneapolis, this honor recognized Snyderman's pioneering leadership in restoring healing to health care and serving as a catalyst for change. Snyderman said he would apply the $100,000 award to use integrative medicine to improve approaches to prevention and early intervention for chronic diseases.

THE FUTURE: PROSPECTIVE HEALTH CARE

Snyderman's newest venture—prospective health care—may prove to be his most revolutionary and enduring contribution to health care. It's a common-sense strategy for shifting health care delivery from an interventional model, which is costly and inefficient, to a preventive one. If successful, it holds the potential to transform how health care is delivered around the world.

As Snyderman sees it, a prospective health care model uses rapidly evolving predictive tools to determine an individual's susceptibility to developing particular diseases. That information would then permit personalized health planning and interventions that could prevent or detect disease in its earliest stages, when treatments typically provide the maximum benefit. "Without such a shift in medical practice, skyrocketing costs can provide only marginal benefits in an inefficient way," Snyderman observes.

Virtually every major initiative achieved at Duke during Snyderman's tenure could potentially play a role in prospective health care. Gene researchers would develop the tests and tools needed to determine a person's risk for disease, and DCRI would run large-scale clinical trials to test the efficacy of such regimens. The Center for Integrative Medicine would apply the fruits of this research to involve patients in assuming more responsibility for their own care.

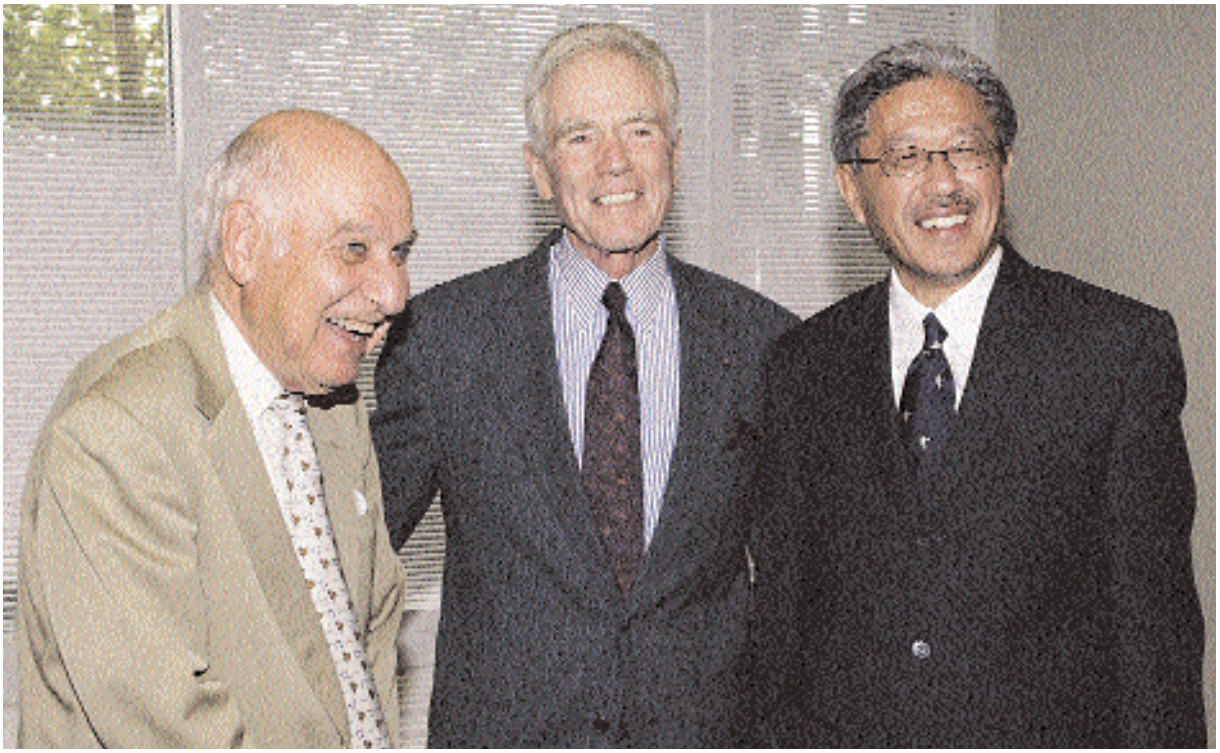
Today prospective medicine is mostly a gleam in Snyderman's eye. The Center for Integrative Medicine only recently completed a 10-month-long pilot study in which 160 patients took part. One group received the usual medical treatment. The center's staff worked with the other group to develop a personal health plan for each participant. The study's results are still being analyzed, but Gaudet notes that "the patients who received personalized health care are experiencing phenomenal life changes."

Last January, a more ambitious prospective-health planning initiative began. Thirty thousand Duke employees and their families with low health risks had the opportunity to visit a website that allowed them to create their own personal health plan emphasizing their health goals. Meanwhile, high-risk employees had the chance to enter a more intensive program, including health care coaching, support group reinforcement, and regimen oversight by a nurse manager.

Prospective health went international in 2003 when Duke Medical Center and the National University of Singapore formalized discussions to establish Singapore's first graduate school of medicine. "Duke is playing a key role in Singapore's impressive effort to reorient its educational and economic emphasis toward biomedicine," Snyderman says. Students will be taught the principles of prospective health care, and the model will be adopted by the country's health system, which serves 4.2 million people. Singapore's initiative is expected to serve as a paradigm for its region, one that will be eagerly watched by European and American physicians and legislators.

When Ralph Snyderman leaves Duke this summer, he won't be heading for a rocking chair. Instead, he'll be a visiting professor at the University of California–San Francisco. "I see this as a growth step in my career," he says. "I've done this job the best I could. Now I hope to move to an even larger playing field." He hopes to find as many "allies" as he can "to refine the risk-prediction model" that forms the basis for prospective health care, to get back up to speed on current developments in biotechnology, and "to work with the best and brightest to figure out how to roll out prospective health care. In the future, I'll try to have even more of an impact than I do now."

"It's a pretty amazing job that Ralph has done," says Ed Holmes. "He's a world-class biomedical investigator. He accomplished extraordinary things in industry. He built a health system at Duke that's one of the nation's best. He's had three careers that have been pretty darn successful. He must have a couple more left in him." □



Three chancellors: Chancellor Emeritus William Anlyan, MD; his successor, current chancellor Ralph Snyderman, MD; and incoming chancellor Victor Dzau, MD. For a brief history of leaders at Duke University Medical Center—plus more on the newest chancellor—visit www.dukehealth.org/newchancellor.

WHAT'S BRED IN THE BONE

THE NEW GENERATION OF TRANSPLANT THERAPIES IN THE FIGHT AGAINST CANCER

BY CATHERINE MACEK

Umbilical cord blood, innovative immunosuppression, and "mini-transplants" help maximize those saved by bone marrow and stem cell transplantation at Duke.

An oft-quoted line from the 1969 film "Butch Cassidy and the Sundance Kid" occurs when the pair, with lawmen in hot pursuit, find themselves perched on a high cliff over a stream—and the only way to escape is to jump. When Sundance balks because he can't swim, Butch says, "Why, you crazy? The fall will probably kill you!"

This scene brings to mind the situation facing the courageous cancer patients in the early '70s who took the plunge and underwent the first bone marrow transplant (a cure that can be as deadly as the disease). Before knowing whether they would sink or swim—if the treatment would rid them of their blood cancer—they first had to endure mega-dose chemotherapy and total-body irradiation to destroy the cancer cells and their bone marrow (which sometimes damaged vital organs in the process). After they received the salvage bone marrow transplant (which was not guaranteed to engraft), they spent weeks with no immunity against myriad opportunistic microorganisms that inhabit our environment. And then the donor's T cells might just turn against them, causing graft versus host disease (GvHD). At least one-quarter of these patients succumbed to a post-transplant complication within the first 100 days. But, like Butch and Sundance, these patients had no other option but to take this medical leap of faith, because they would have surely died without a transplant. Their willingness to participate in these early studies contributed a tremendous amount of knowledge that's valuable even today. More than 30 years later, bone marrow transplantation has evolved from a highly experimental procedure to a therapy that can dramatically change the prognosis for adults and children with blood cancers, some solid tumors, and certain nonmalignant and immunodeficiency diseases. Three decades of experience has helped to clarify which cancers are most likely to respond and to fine-tune post-transplant care so that much of it now occurs on an outpatient basis. Nowadays, the precious progenitors that reseed the bone

A new "mini-transplant" procedure is enabling Duke physicians to extend lifesaving stem-cell treatment to older and sicker patients, says Nelson Chao, MD.

marrow—adult stem cells—are as likely collected from a donor's blood or the umbilical cord of a newborn as from a quart of bone marrow. In fact, the procedure's now-preferred moniker, stem cell transplantation, reflects the increasing reliance on these other sources.

THE NEW MINI

Duke has busy stem cell transplantation programs for adults and children, performing around 200 adult and more than 100 pediatric transplants each year, says Nelson Chao, MD, medical director of the adult program and chief of the newly created Department of Medicine's Division of Cellular Therapeutics. More than 80 percent of adult patients have some type of hematological malignancy or myelodysplasia (bone marrow dysfunction); the rest have breast cancer, renal cell cancer, or melanoma. Both programs offer autologous transplants, meaning that the patient's own stem cells are harvested prior to high-dose chemotherapy and/or radiation therapy, as well as allogeneic transplants, using stem cells from siblings or unrelated individuals. Generally speaking, autologous transplants target lymphomas and myelomas, and allogeneic transplants treat diseases such as leukemia, aplastic anemia, and myelodysplastic syndrome.

Because the pretransplant chemo- and radiation conditioning regimen is so toxic, stem cell transplantation programs have historically restricted the procedure to adults younger than age 55 with no other major health problems. But a new procedure—called a nonmyeloablative or "mini" stem cell transplant—is extending this lifesaving treatment to older and sicker patients, Chao says. It's called nonmyeloablative because a less-intense pretransplant treatment intentionally does not wipe out the patient's bone marrow—but it doesn't kill all of the cancer cells, either. The second of a one-two punch comes from the donor's T lymphocytes, which seek out the patient's cancer cells and destroy them in a beneficial twist on GvHD. "It's a graft-versus-malignancy effect—the donor graft cells recognize the host tumor cells and reject them," Chao says.

Following infusion of donor stem cells, a state of "mixed chimerism" develops in which both donor and recipient immune systems coexist, thanks to immunosuppressive drugs that help keep the peace. The Duke immunosuppression protocol also includes giving the patient a monoclonal antibody called Campath-1H (alemtuzumab). This troop-reduction strategy depletes some of the recipient's T lymphocytes, thus preparing the patient to receive the new donor cells without rejecting them. At the same time, the antibody (which remains in the blood for about a month after infusion) weakens the donor cells so that they are less likely to cause GvHD.

"The next big thing is cellular therapy. It may be ten to twenty years in the future, but we will be correcting many diseases with cells."

—Joanne Kurtzberg, MD

Therapeutic Gold

Not long ago, the possibility that a blood cell could morph into a nerve cell seemed as likely as turning lead into gold—cellular alchemy. The long-held dogma about adult stem cells is that a handful of types exist, each committed to give rise to a limited number of specialized cells—so hematopoietic stem cells beget all blood cells, nerve stem cells differentiate into neurons and neuroglial cells, and so on. But the recent autopsy studies in Joanne Kurtzberg's lab add to the growing evidence that stem cells demonstrate far more plasticity than originally believed (see page 38).

Now, the cellular alchemists are turning fat into gold. Duke researchers have been able to reprogram cells taken from human liposuction procedures by culturing them in four cocktails of vitamins, growth factors, and steroids in vitro. Depending on what they imbibed, the cells were reprogrammed into either fat, bone, cartilage, or nerve cells. "We don't know exactly why body fat contains stem cells that can form bone or cartilage, but it does help dispel the dogma that adult stem cells can only be found in the bone marrow," says Farshid Guilak, PhD, director of orthopedic research and head of the three-year study.

On the clinical side, Duke cardiologists Christopher Granger, MD, and Eric Peterson, MD, are leading a pilot project involving injection of a patient's own bone marrow cells into the coronary vessels one to five days post-heart attack. Bone marrow stem cells have demonstrated sufficient plasticity to repair heart muscle in animal models, says cardiologist Pascal Goldschmidt, MD, chairman of medicine and one of the project's team members. "By providing the patient with bone marrow stem cells, we might limit the damage as a result of the heart attack, especially in a setting where the speed and capacity of heart tissue repair is usually limited," he says.

Based on research in mice occurring in Goldschmidt's lab, Goldschmidt and Peterson recently published a theory that the age-related loss of blood vessel-repairing stem cells leads to atherosclerosis and other diseases. "Augmentation of stem cell-mediated repair systems may provide a novel means of treating or preventing many age-related illnesses," they note in the article, published in the online *Science of Aging Knowledge Environment* (http://sageke.sciencemag.org/).

"The next big thing is cellular therapy," Kurtzberg says. "It may be ten to twenty years in the future, but we will be correcting many diseases with cells."

So far patients into their 70s have benefited from the nonmyeloablative transplants. "Right now it's a Phase I study in patients with late-stage disease, but we hope to move into a larger, phase II study soon," Chao says.

UNGRATEFUL GUESTS

The mini-transplant regimen reduces, but does not eliminate, the possibility of GvHD, and it remains the major problem with all allogeneic stem cell transplants, Chao notes. About 20 percent of these patients experience severe GvHD reactions, with many succumbing to the disease or its treatments. Along with the mainline immunosuppressive therapies—prednisone, cyclosporine, and antithymocyte globulin—newer drugs such as sirolimus and mycophenylate mofetil, already part of the solid-organ transplant armamentarium, may be employed. The same human leukocyte antigens (HLAs) that get matched for stem cell and solid-organ transplants are also involved in GvHD, and Chao's group is testing a peptide polymer derived from a Chinese herb that short-circuits GvHD by masking parts of the HLA molecules.

A stem cell transplant, or graft, is actually a mixed bag of blood cells at various stages of maturity, with the all-important stem cells comprising only a tiny fraction—much less than 1 percent. A sizable number in the bag are T cells of various subpopulations. A major focus of Chao's lab is to find ways to identify and remove from the graft those T cell subpopulations that ultimately cause GvHD. Their research in mice points to naïve T cells as the instigators. "And we find that without GvHD we see rapid engraftment, and the naïve cells come back very quickly," Chao says. "So the system seems to work well."

They are also experimenting with a photoactivation system that works on a principle similar to the PUVA (psoralen-UVA light) treatment used for psoriasis. Mouse donor cells pretreated with a psoralen compound are purposely exposed to recipient mouse cells in vitro, then exposed to UVA light. The light activates the psoralen, which inhibits DNA replication—so only those lymphocytes that have recognized recipient antigens as foreign and are undergoing cell division are destroyed. "This has worked well in the mouse model, and we're in the process of scaling it up to do in people," Chao says.

GOOD THINGS COME IN SMALL PACKAGES

Those willing to join the national marrow donor registry but who fear the donation process will be glad to know that peripheral blood has become the preferred source of stem cells, according to the International Bone Marrow Transplantation Registry. Although few stem cells can be found in the blood under normal circumstances, granulocyte colony stimulating factor (Neupogen) injections stimulate their production and mobilize them into circulation. A few days later they are collected along with blood leukocytes by apheresis, a process that separates whole blood by machine into its component parts. Data suggest that peripheral blood stem cells engraft more quickly than those harvested from bone marrow.

But the real stem cell champs seem to be those found in umbilical cord blood. Presumably because they are more immature, these neonatal stem cells are less likely to cause GvHD and require less rigorous tissue matching. "Although we typically try for a 4 in 6 HLA antigen match or better, we can go as low as 3 in 6," says Joanne Kurtzberg, MD, head of Duke's pediatric bone marrow and stem cell transplantation program and founder of the Carolinas Cord Blood Bank housed at Duke.

Cord blood stem cells do not engraft as quickly, however, possibly because there aren't very many of them. The typical cord blood sample contains a billion or so leukocytes, and it's estimated that less than 0.5 percent of them are stem cells. There are enough for a toddler, but for a 70-kg. man? Only about 15 percent of cord bloods have enough cells, Kurtzberg notes, although Duke's experience with nearly 60 adult patients supports it as a viable option (*Biology of Blood and Marrow Transplantation* 2003: 9, 772-780). Although combining units of cord blood for infusion into adults is being investigated elsewhere, there's no evidence of any advantage right now, she adds.

Encouraging stem cell growth prior to transplant is an obvious way to improve the odds, and Kurtzberg's lab has focused on ex vivo expansion of cord blood for several years. "We can increase the number of cells many-fold—100-fold—but when we infused them in the patient we didn't see any effect, so we don't think the cells that grew were actually stem cells," Kurtzberg says. "So now we are hoping to encourage stem cells to proliferate by growing them on the patient's own bone marrow stroma—the supporting structure of the bone marrow. We're about to start clinical trials with this ex vivo system."

About half of the pediatric stem cell transplants target malignancies—blood cancers, brain tumors, and certain solid tumors such as neuroblastoma and osteogenic sarcoma. Another 10 percent of the children have immunodeficiencies, and the rest have genetic diseases—"rare syndromes where they're missing an enzyme or protein needed for development of some part of the body," Kurtzberg says. The Duke program specializes in treating these otherwise fatal diseases, including Tay Sach's disease, Lesch-Nyhan syndrome, and Hurler syndrome (which causes mental retardation and cardiac abnormalities).

BEYOND LORENZO'S OIL

The leukodystrophies are a family of rare inherited disorders that affect myelin, the protective covering of nerve cells. The child depicted in the 1993 film "Lorenzo's Oil" has adrenoleukodystrophy (ALD), and Kurtzberg's team has transplanted several children with ALD and related disorders. "The diseases all cause severe neurologic damage and death, but they can be corrected if the child is transplanted before symptoms become apparent," Kurtzberg says. "But many of the kids we treat are identified because they had an older sibling who died of the disease. Sadly, by the time the child gets sick it may be too late."

The transplants don't necessarily produce a complete cure, but they have been able to stop disease progression, presumably because the transplanted stem cells morphed into other cell types. "It seems like stem cells know how to get to places where there's damage, and that may be because chemical signals are sent out by those areas," Kurtzberg says. "And we think cord blood stem cells work better than bone marrow in these patients because they're more flexible and more able to turn into other cells, and therefore do a better job at correcting the enzyme deficiency."

Kurtzberg's lab has autopsy evidence from two children who succumbed from complications of their transplants and who received stem cells of the opposite gender, making it easy to identify donor cells by their sex chromosomes. In one case, they researchers detected donor-derived heart cells (myocytes) in a child whose disease caused cardiac damage; in the other, about 40 percent of the brain cells in a girl who had neurologic damage clearly contained Y chromosomes. This is the first direct proof of donor stem cell differentiation on a molecular level in such recipients.

A ROOM OF ONE'S OWN

For stem cell transplant recipients, who can be some of the sickest patients in the hospital, Duke has separate adult and pediatric inpatient units with 16 beds each. Patient rooms on both units are equipped with HEPA (high-efficiency particulate air) filtration systems that remove potentially infection-causing microorganisms from the air. The hallways and exercise room on the newly renovated adult unit also receives HEPA-filtered air, giving patients more freedom to move about and strength-train.

Unlike the early days of bone marrow transplants, most adult recipients do not have to spend long months on the inpatient unit, Chao notes. Barring complications, even patients who underwent myeloablative treatment leave Duke after about a month and take up residence in nearby apartments with a designated caregiver. They receive follow-up care in the free-standing adult outpatient clinic, which is open every day and for extended hours. Besides eschewing fresh foods, "They lead the usual life, and they like it a whole lot better being out there," Chao says. Nonmyeloablative transplants are performed entirely on an outpatient basis.

> "The staff was wonderful. The doctors showed a lot of love and concern and care. I had never experienced that before with doctors."
>
> —former breast cancer patient

The cost of maintaining two households is yet another burden placed on the families whose loved ones face months of recovery after stem cell transplantation. Patients come to Duke from far and wide to enroll in novel cancer clinical trials, and some include stem cell transplantation as part of the protocol. And few programs in the world offer stem cell transplantation to children with inborn errors of metabolism, so about 10 percent of Kurtzberg's patients are from other countries. Some insurance companies provide a housing stipend, but it doesn't cover the loss of a salary, travel costs and myriad other expenses the families incur.

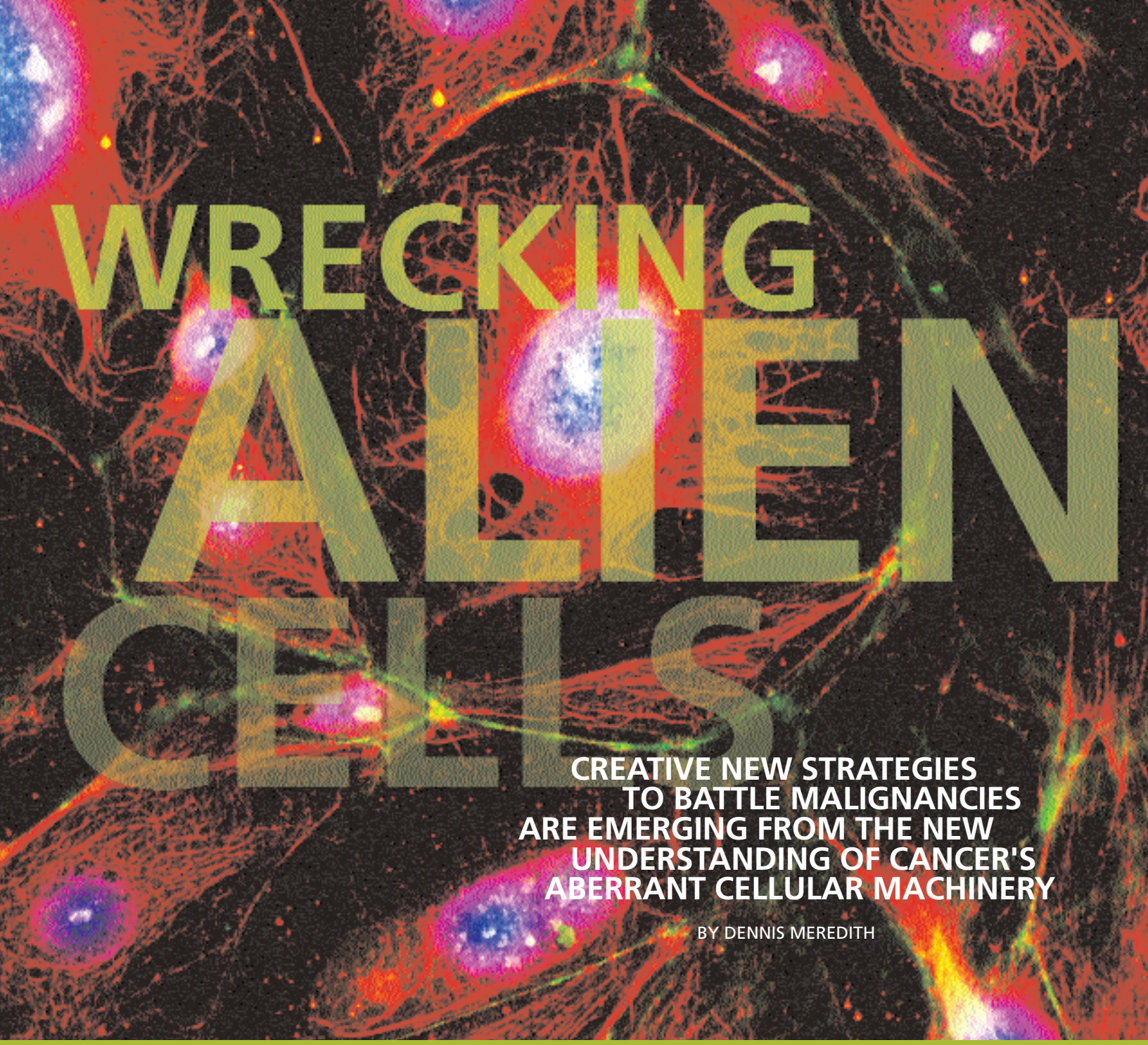
Hope Lodge will help lessen the burden for pediatric stem cell transplant patients and their families. Once funded, the American Cancer Society has pledged to build and run a 38-suite facility exclusively for these families, where they can stay for free. The ACS has established several adult Hope Lodges across the country, but this will be the first one dedicated to pediatric patients. "We're in the middle of a $10 million capital campaign right now," Kurtzberg says.

And although some vowed never to see the inside of a Durham hotel room again, former patients willingly return on the first Saturday in August to share the joy of life with others at the adult program's annual patient reunion. One of the most moving moments of the day occurs during patient and caregiver testimonials, when they share their memories about the transplant process and experiences at Duke.

"The staff was wonderful," says one former breast cancer patient. "The doctors showed a lot of love and concern and care. I had never experienced that before with doctors."

And she sums up the transplant process this way: "Out of difficulties grow miracles."□

Learn more about Duke's adult bone marrow and stem cell transplant program at bmt.mc.duke.edu and the pediatric bone marrow and stem cell transplant program at cancer.duke.edu/pbmt.



WRECKING ALIEN CELLS

CREATIVE NEW STRATEGIES TO BATTLE MALIGNANCIES ARE EMERGING FROM THE NEW UNDERSTANDING OF CANCER'S ABERRANT CELLULAR MACHINERY

BY DENNIS MEREDITH

THIS YEAR, THE PUBLIC HAS THRILLED TO A STUNNING FEAT OF SPACE SCIENCE— in which twin robotic spacecraft were hurled 35 million miles to Mars. After pinpoint landings, the robots precisely unfurled an array of instruments to probe the planet's alien geology.

Not as visible but every bit as dramatic have been the newest explorations by cancer researchers into the depths of the cancer cell—expeditions that are yielding promising new treatment strategies. And like the space scientists, the cancer researchers wield their own cadre of analytical instruments, computers and robotic manipulators to develop and test cancer-killing compounds.

However, there's a stark contrast between Mars and the cancer cell. While the robotic rovers scratch about for even the barest hints of Martian life, cancer researchers well know they face a malignant, alien life form—cancer. They also know that each new clue they glean about its lethal biology will ultimately save lives.

RUTHLESS TESTING IS YIELDING PROMISING TREATMENTS

Exemplifying such advances are new treatments being tested in the Experimental Cancer Therapeutics Program of Duke's Comprehensive Cancer Center. The scientists' strategies in their battle against cancer are ruthless. They are developing drugs to starve cancer cells of their blood supply, wreck their ability to repair damage by anticancer drugs, and even drive them to "suicide."

The scientists are also probing the genetics of cancer cells to understand their vulnerabilities, as well as studying genetic differences among patients that influence response to cancer treatments.

All these studies are yielding promising treatments for cancers of the brain, breast, colon, kidney, lung, and skin. Importantly, these treatments aim with far greater precision than ever before to kill the cancer cells themselves, sparing normal cells.

Says program co-director Michael Colvin, MD, "I think we're heading into a new era of cancer treatment, of understanding the molecular basis of cancer so that we can develop specific biological and chemical attacks on cancers. And, we'll produce an increasing number of cures without many of the devastating side effects characteristic of cancer therapy in the past."

Adds co-director Francis Ali-Osman, DSc, "Duke is uniquely positioned for leadership in this new era. Developing these new 'smart drugs' requires excellence in many disciplines. You need cell and structural biologists, biochemists, and computer modelers in order to understand the cellular defects and proteins involved in cancers, as well as to synthesize or identify compounds that affect those proteins. Duke has incredibly strong programs in all these areas.

"There's a great deal of science involved in the early stages of such drug discovery," says Ali-Osman. "And science is what we do best. We can identify the molecular defects underlying cancers, generate first-generation drugs, screen and optimize them, and then work with industry to bring them to clinical trials."

Ali-Osman's work exemplifies a major effort among cancer scientists to encourage cancer cells to commit "suicide." When normal cells are genetically damaged or no longer needed by the body, a death program called apoptosis is activated, ridding the body of the cells. However, the defects that drive cancer cells to proliferate often include defects that thwart this failsafe mechanism.

"THERE'S A GREAT DEAL OF SCIENCE INVOLVED IN THE EARLY STAGES OF DRUG DISCOVERY. AND SCIENCE IS WHAT WE DO BEST."

—Francis Ali-Osman, DSc

Ali-Osman and his colleagues are targeting a protein abbreviated as GSTP1 that many cancer cells overproduce. This GSTP1 overproduction both enables the cancer cells to break down anti-cancer drugs and interferes with the

CHANGING ATTITUDES TOWARD CLINICAL TRIALS

Cancer research is benefiting greatly from new attitudes toward clinical trials as a means to both advance science and offer patients new treatments, say Duke's cancer researchers

"There's been a major shift in the attitude of the oncologic community, in which oncologists are increasingly willing to refer their patients for clinical trials when they no longer have any medicines to offer them," says Michael Colvin, MD, co-director of the Duke cancer center's experimental therapeutics program. "There is a very positive attitude toward testing new drugs, which enables us to study experimental drugs earlier to determine their effectiveness or lack of effectiveness."

Major medical centers such as Duke can also offer advanced diagnostic tests that can aid treatment, adds co-director Francis Ali-Osman, DSc. "We now have a great deal of knowledge about the genes that drive cancer, so genotyping a patient will aid oncologists in choosing cancer therapies," he says.

Experimental studies of diagnostic cancer markers can significantly benefit patients, says Ali-Osman. "Previously, oncologists did a CT scan as a baseline and waited several months to get another, to tell whether their patients are responding to treatment," he says. "But these new advances in diagnostic testing are yielding surrogate markers that give a very early indication of tumor response. So, I think bringing such new technology to bear is going to raise the ability of oncologists to effectively treat their patients."


Michael Colvin, MD

The real heroes of clinical trials, emphasizes Colvin, are the patients. "During my twenty-five years of being involved with clinical trials, I've become more and more impressed with the remarkable courage of patients who are willing to participate in taking these new drugs," he says. "Despite the fact that they know the drugs may have side effects and that they are still unproven, these patients are not only interested in helping themselves but also the others who will come after them."

cell response to stress that would ultimately trigger apoptosis. Thus, drugs that block GSTP1 could offer a double-barreled attack on cancer cells.

In developing smart drugs to target GSTP1, the researchers use computer modeling to "test-fit" candidate drug molecules into the GSTP1 protein to inhibit its action. They are also using robotic systems to automate the testing of vast libraries of compounds for inhibitory activity against the enzyme. Over the next two years, these researchers hope to have drug candidates ready for clinical testing.

Ali-Osman is also working with Duke colleagues to develop ways to inhibit cancer cells' ability to repair their DNA after damage by chemotherapy treatments. The researchers have discovered a key protein switch in the DNA repair machinery and are designing drugs to jam that switch.

ON MELANOMAS AND RENAL CANCERS

Jared Gollob, MD, and his colleagues are testing drugs that encourage two particularly tenacious cancers—melanomas and renal cancers—to commit suicide. In particular, they aim to enhance the vulnerability of these cancers to other forms of therapy.

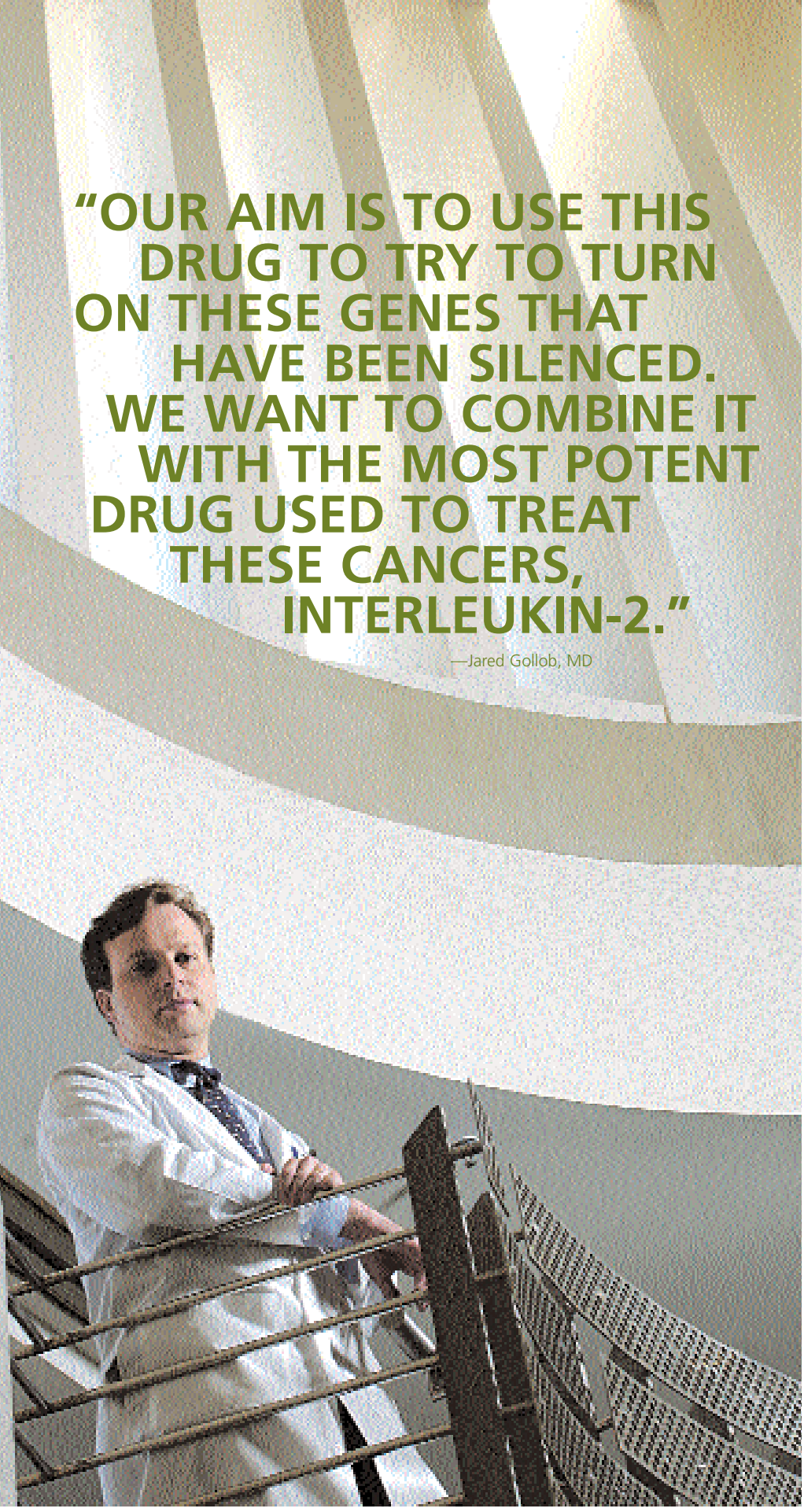
"Melanoma is notoriously resistant to chemotherapy, radiation, and immunotherapy," says Gollob. "The melanocytes in your skin are built to resist ultraviolet radiation, to survive, and produce melanin. So, they've evolved a mechanism to overcome cell death. The same goes for kidney cells, because they exist to take in poisons and detoxify them. So, when either of these cell types becomes malignant, that resistance to cell death is amplified."

Many melanomas and kidney cancers have switched off key genes involved in apoptosis—not because of mutations, but because of a chemical "silencing" mechanism called "methylation." Gollob and his colleagues are now clinically testing a drug, decitabine, which reactivates such genes.

"Our aim is to use this drug to try to turn on these genes that have been silenced," says Gollob. "And we want to combine it with the most potent drug used to treat these cancers, interleukin-2." While the immune-stimulating interleukin-2 alone has been only modestly successful, Gollob and his colleagues believe that also using decitabine to activate apoptosis will enhance its effectiveness. Indeed, in small Phase I clinical studies, they have seen evidence of such enhanced effectiveness.

In an effort to more effectively treat melanomas that invade the brain, the researchers are exploring the use of arsenic trioxide to render cancer cells more sensitive to apoptosis. In newly begun phase II studies, the researchers are combining arsenic trioxide with the widely used anticancer drug temozolomide.

Says Gollob, "This is really one of the first attempts to combine the pharmacologic inhibition of an apoptosis pathway with a drug like temozolomide. And it's also one of the very few studies that is addressing this big problem of brain metastases in patients with melanoma."



ON COLORECTAL CANCERS

Besides resistance to apoptosis, cancers also show an insidiously effective ability to induce the growth of blood vessels—called angiogenesis—to bring them oxygen and nutrients. Researcher Herbert Hurwitz, MD, and his colleagues are testing the drug bevacuzimab, trade name Avastin, as an antiangiogenic drug for colorectal cancers. The national phase II study that they led has found that, when combined with standard chemotherapy, Avastin can significantly improve survival in metastatic colorectal cancers.

"This study represents an important advance for patients with colorectal cancer," says Hurwitz. "It also represents an important proof of principle for our ability to develop targeted anti-cancer therapies with truly minimal toxicity; and proof of principle for the value of targeting this anti-angiogenesis approach in general."

Hurwitz and his colleagues are now conducting further clinical tests on patients with newly diagnosed colorectal cancers—with the hope that starving those cancers of their blood supply might also prove effective in enhancing traditional radiation therapy and chemotherapies.

Even cancers that appear identical might represent very different genetic abnormalities, researchers now realize. Such genetic differences mean that different patients might respond very differently to the same treatment. Thus, researchers such as Ali-Osman are now emphasizing a "pharmacogenomic" approach to studying and treating cancers.

"Until recently, it wasn't clear what drives the differences in responses among patients," he says. "But now we know that minor differences, or polymorphisms, in genes among patients are a major determining factor in variation of response to treatments and treatment toxicity."

Herbert Hurwitz, MD

Working with researchers in Duke's Institute for Genome Sciences and Policy, the program's researchers are developing ways to analyze such subtle genetic differences among cancer patients and to predict their clinical response to treatments. For example, Ali-Osman has found that cancer patients may have subtle differences in the enzyme he studies—GSTP1—that affects the ability to break down anti-cancer drugs, rendering them ineffective. Thus, he says, understanding those subtle differences can tell clinicians which patients will respond best to chemotherapy.

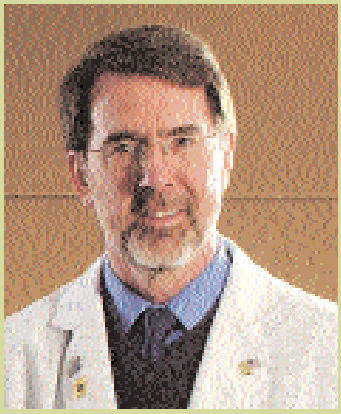
Similarly, Colvin and his colleagues are studying differences among breast cancer patients in one particular gene that determines the ability to activate a key chemotherapeutic drug, cyclophosamide.

Says Colvin of such differences, "We know that there is a fine line in cancer therapy between drug concentrations necessary to have an effect on the tumor and those that produce toxicity. And so, we are developing the ability to analyze a blood sample from a woman with breast cancer to see whether she has genetic differences in the genes for the enzymes that metabolize drugs. This allows us to dose-adjust the drugs so we can reduce toxicity while maintaining efficacy." Also, says Colvin, researchers are increasingly able to genetically distinguish cancers and thus to design treatments that are more effective and less toxic against a particular malignancy.

ON THE DEADLIEST CANCER

New strategies for treating lung cancer being tested at Duke exemplify how researchers are not only trying new drugs, but exploring the best way to apply existing treatment.

Says oncologist Jeffrey Crawford, "Lung cancer is the deadliest disease in oncology, due largely to the fact that we don't have ways to detect the disease early enough. So, the majority of patients present at an advanced, incurable stage."



Jeffrey Crawford, MD

To more strategically attack such cancers, Crawford and his colleagues are conducting an array of clinical studies in a range of patients, using both new and old chemotherapies, alone and in combination. New treatments include both drugs and antibodies that specifically target cancer cells. They are also studying the various combinations of chemotherapy with radiation or surgery.

The researchers are even exploring whether they can specifically reduce the pressure inside tumors using drugs, to make chemotherapy more effective. And, recognizing that quality of life is extremely important for cancer patients, they are also testing supportive-care strategies such as drugs that enhance blood cell function in patients undergoing treatments that suppress blood counts.

"Within the next five years, we hope to have an integrated systemic therapy for all patients with lung cancer," says Crawford. "This means we will have a strategy to offer all patients—from the earliest-stage patients to those with more advanced cancers—the full range of chemotherapies, radiation and surgery." Such a strategy also includes much earlier diagnosis of lung cancer with new imaging techniques and blood tests to detect telltale protein markers, says Hurwitz.

To Hurwitz, the real strength of Duke's experimental therapeutics program lies in the integration of rapidly advancing research on new treatment approaches and strategic use of traditional therapies. Such an approach of attacking cancers from many directions will lead to major advances in survival and quality of life, he believes.

"There's the old Samurai saying that to defeat your opponent first you need to understand him or her," says Hurwitz. "Cancer is complicated, and having these remarkable clinical and lab-based collaborations helps us think more deliberately about cancer and develop the most effective strategies for treating the many forms of cancer." □

To read more about cancer vaccine research at Duke, visit http://dukemedmag.duke.edu/article.php?id=414. To read more about experimental therapeutics in brain tumor research, visit http://dukemedmag.duke.edu/article.php?id=2029.

How can clinicians better support patients at the end of life?

The way we talk about it may be as important as what we say.

by James Tulsky, MD

PATIENTS UNDERGOING THE TRANSITION from fighting a potentially curable disease to focusing on palliative care face great challenges to their physical, emotional and spiritual integrity. Some patients cope by avoiding discussion of the issues, or even denying the severity of their illness.

Clinicians also struggle when caring for these patients. We may see ending curative treatment as a failure, or experience sadness at the anticipated loss of a dear patient. We may worry about taking away the patient's hope or even precipitating serious depression. In this situation physicians may withdraw from the terminally ill patient, avoid threatening topics, employ blocking behaviors that create distance, or convey an overly optimistic prognosis, thus creating unrealistic expectations.

Physicians' concerns about causing emotional distress and eliminating hope are generally ill-founded. A patient's psychological adjustment to bad news is related more to the quality of communication about that news than to the nature of the bad news itself. In fact, most patients with advanced disease have thought about end-of-life issues and wish to discuss them with a physician, but expect the doctor to raise the topic. Discussing the news openly allows patients to state their concerns and fears. By doing so, physicians can lessen patients' future anxiety and depression.

Furthermore, we can neither steal nor instill hope. Hope is defined, constructed and interpreted by the patient. In this situation, physicians can best provide an empathic, reflective presence that will help patients draw strength from their existing resources. By "planning for the worst while hoping for the best," the patient may be able to complete his affairs, accept a palliative approach to medical therapy, and even say goodbye to loved ones while still stating that he hopes to recover.

SENSING WHEN TO TALK

Patients facing terminal illness desire a physician who will talk in an honest and straightforward way, be willing to talk about dying, give bad news in a sensitive way, listen, encourage questions, and sense when they are ready to talk about death. They also wish for physicians to maintain hope while being truthful. Easier said than done.

An effective way to initiate discussions of end-of-life issues is by asking open-ended questions regarding the patient's understanding of the illness and prognosis before talking about specific clinical decisions. Don't presume to know your patient's agenda; physicians are not always good at predicting which patients want more and which want less information. Instead, consider this approach: "We've never really spoken about what you can expect from your illness over time. Some patients want to know everything about their illness. Others do not want as much information and want me to speak more generally. And some prefer I do not discuss bad news with them but want me to talk to their family. Have you thought about this?"

If the patient does not want to hear about his prognosis, ask him to say more about this and probe his fears or concerns. If the patient suggests that he would like to be told about his disease, the doctor should "ask before telling." That is, ask the patient about his understanding of his illness prior to educating him about the specifics of prognosis.

NURSE THE AFFECT

Attending to the patient's affect—the feelings and emotions associated with the content of the conversation—is equally important. Anger, guilt, frustration, sadness, and fear modify the ability to hear, to communicate and to make decisions. For example, after hearing bad news, most patients are so overwhelmed emotionally that they are unable to comprehend very much about the details of the illness or a treatment plan. Unfortunately, conversations between doctors and patients often transpire only in the cognitive realm, and

emotion is frequently not acknowledged or handled directly.

The primary goal when responding to affect is to convey a sense of empathy. This can be done through a variety of specific responses, organized below under the acronym NURSE—Name, Understand, Respect, Support, Explore.

Naming the emotion serves to acknowledge feelings and demonstrate that this is a legitimate area for discussion. Naming is best done in a quizzical fashion that does not presuppose the emotion: "Many people would feel angry if this happened to them. I wonder if you feel this way?"

Expressing a sense of understanding conveys your concern and normalizes the patient's emotion: "Although I've never shared your experience, I do understand that this has been a really hard time for you."

Respect reminds us to praise patients and families for managing a difficult situation. Offering respect defuses defensiveness and makes people feel good about themselves and more capable of handling the future: "I am so impressed with how you've continued to provide excellent care for your mother as her dementia has progressed."

Support is essential to helping those in distress feel that they are not alone. "I will be there with you throughout this illness" can be tremendously comforting. Offer follow-up support from others as well, such as nurses and chaplains.

Finally, patients frequently make statements that deserve further exploration: "After you gave me the results of the test, I thought that this is gonna be it." A simple response such as, "Tell me more" may help reveal the patient's fears and concerns about the disease that will be helpful in planning future treatment.

DREADED QUESTIONS

"How long do I have to live?" When faced with this most difficult question, the physician should not assume to know what the question is "really" about. The patient may be wondering if she is going to live until Christmas or ever leave the hospital. Acknowledge the question, but make sure you understand it before trying to answer: "That is a really tough question. What are you concerned about?"

Having anticipated replies to dreaded questions can be useful, and several examples follow:

PT: *How long do I have to live?*
MD: "I wonder if it's frightening not knowing what will happen next, or when." This answer allows the patient to speak about fears or worries.

If a more factual response is needed:
MD: "On average, a person in your situation lives three or four months, but some have much less time and others live more than a year. I would take care of any practical or family matters you wish to have completed before you die, but continue to hope that you are one of the lucky people who gets more time."

PT: *Are you telling me I'm going to die?*
MD: "I wish that were not the case, but it is likely in the near future. I am also asking, how would you want to spend the remaining time if it were limited?"

The "wish statement" helps the physician identify with the patient's loss and seeks to understand the patient's goals in light of new information. Creating new goals provides an outlet for the patient's hope.

PT: *Does this mean you're giving up on me?*
MD: "Absolutely not. But tell me, what do you mean by giving up?"

Suggesting that a patient receive palliative care risks conveying a sense of abandonment, so physicians must be emphatic that palliative care and hospice are indeed active forms of care.

Good communication skills provide the pathway to excellent care for patients facing their own mortality. Physicians should strive to talk with patients in an honest and straightforward way; be willing to talk about dying; give bad news in a sensitive way; listen and encourage questions from patients; be responsive to patients' readiness to talk about death; and achieve a balance between being honest and straightforward and not discouraging hope. Not only does good communication increase the likelihood that a patient's needs will be recognized and met, but the communication process itself is often therapeutic. We should not forget that every patient has a story to tell.

Dr. Tulsky is an associate professor of medicine at Duke and director of the Program on the Medical Encounter and Palliative Care at the Durham VA Medical Center.

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APPOINTMENTS

Willett named chair of Radiation Oncology

Christopher G. Willett, MD, a specialist in gastrointestinal cancers, has been named chair of the Department of Radiation Oncology at Duke University Medical Center (DUMC). He assumed the position in March.


Willett

Willett was clinical director of radiation oncology at Massachusetts General Hospital in Boston, MA, and a professor of radiation oncology at Harvard Medical School before coming to Duke.

Willett received his bachelor's and medical degrees from Tufts University in Boston. He completed a surgical internship at Vanderbilt University Medical Center and a residency in radiation medicine at Massachusetts General Hospital. He joined the faculty of Harvard in 1986, has held appointments as a radiation oncologist at Brigham and Women's Hospital and Dana-Farber Cancer Center in Boston, and had served as clinical director of radiation oncology at Massachusetts General Hospital since 1999.

Willett has served as the president of the International Society of Intraoperative Radiation Therapy (ISIORT) since 2000. He also was a founding member of the society in 1996. In addition, Willett has served as chair of the GI Committee of the Radiation Therapy Oncology Group, a national cooperative conducting clinical trials in cancer.

His research interests focus on the study of new therapies for treating rectal and pancreatic cancer, the use of intraoperative radiation therapy in treating gastrointestinal cancers, and conducting clinical trials in these malignancies.

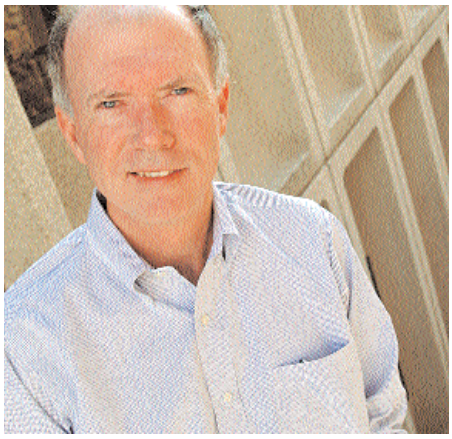
Nevins appointed to lead Center for Genome Technology

Joseph Nevins, PhD, a Howard Hughes Medical Institute investigator and James B. Duke Professor of Genetics at Duke, has been named director of the Center for Genome Technology (CGT), a center of the Duke Institute for Genome Sciences & Policy (IGSP).

Nevins investigates the genes that control normal cell growth and the genetic disruptions that lead to cancerous tumor development. His work incorporates DNA microarray, or gene chip, technology to simultaneously measure the activity of thousands of genes, thereby creating "genetic fingerprints" that can predict the future course of breast, ovarian, and brain cancers. He has been the interim director of the CGT since its inception in 1999.

CGT develops and applies novel approaches to the analysis of the genome—an organism's complete set of genetic instructions. Part of the center's mission is to provide support for investigators in applying these technologies in their research.

Nevins received his PhD in microbiology at Duke, where he studied viral gene regulation. He completed his postdoctoral studies as a Jane Coffin Childs fellow at the Rockefeller University, where he focused on the mechanisms by which DNA is transcribed into messenger RNA. He returned to Duke in 1987 as professor of microbiology and a Howard Hughes Medical Institute Investigator.


Nevins

Nevins became chair of the newly created Duke Department of Genetics in 1991 and continued as chair when the department was merged with the Department of Microbiology, creating the Department of Molecular Genetics and Microbiology. He will remain as chair of the department until a new chair is selected.

In his new role, Nevins will oversee the incorporation of genome technologies into research endeavors that span the university—both at the medical center and on the main campus.

For more information, visit www.genome.duke.edu.

Douglas selected as new cardiology division chief


Douglas

Pamela S. Douglas, MD, head of the Section of Cardiovascular Medicine at the University of Wisconsin, has been named the new chief of the Division of Cardiology at Duke University Medical Center.

Douglas, who specializes in non-invasive cardiovascular imaging with special interests in heart disease in athletes and women, officially begins her duties at Duke on August 16.

She also will serve as the Ursula Geller Professor for Research in Cardiovascular Diseases, as well as director of cardiovascular research strategies at the Duke Clinical Research Institute.

At Duke, Douglas will oversee the clinical enterprises and direct the research activities of one of the largest and most active cardiology divisions in the country. Douglas replaces Pascal Goldschmidt, MD, who was promoted to chairman of the Department of Medicine in March 2003.

Douglas has conducted pioneering research using echocardiography to better understand the function and dysfunction of the left ventricle, the main pumping chamber of the heart. She serves as the president of the American Society of Echocardiography and will serve as the president of the American College of Cardiology in 2005-06. She also is active on the national health-care scene advocating for more research into heart disease and women.

"Cardiology at Duke has had such a history of excellence," Douglas said. "Very few programs can match Duke's strengths in patient care, education, and research. Cardiovascular disease is the leading cause of death, and I am looking forward to working with my new Duke colleagues to better understand heart disease so we can be more successful in preventing and treating it."

Douglas received her undergraduate education at Princeton University and completed medical school at the Medical College of Virginia. She then completed a three-year residency in internal medicine and a three-year cardiology fellowship at the Hospital of the University of Pennsylvania.

From 1984 to 1990, Douglas served as assistant professor of medicine at the University of Pennsylvania, then spent the next 10 years on the faculty of Harvard Medical School. She started her current position as cardiology head and Dr. Herman & Ailene Tuchman Professor of Cardiovascular Medicine at the University of Wisconsin in 2000.

Diehl appointed new gastroenterology division chief

Anna Mae Diehl, MD, professor of medicine at Johns Hopkins University, has been named chief of the Division of Gastroenterology at Duke University Medical Center.

Diehl is a nationally-recognized expert in basic research and clinical treatment for chronic liver diseases. She will oversee clinical activities and research in the gastroenterology division and direct the Duke Liver Center.

Diehl began her duties April 5. She replaced Rodger Liddle, MD, who continues as a researcher and professor of medicine in the Division of Gastroenterology and a clinician at the Veterans Affairs Medical Center in Durham.

Diehl plans to grow the gastroenterology division through collaborations between basic researchers and clinicians, including research and treatment programs for diseases such as hepatitis infections, inflammatory bowel disease, pancreatitis, and colon cancer.


Diehl

One of Diehl's primary research interests is the cause and treatment of nonalcoholic fatty liver disease, frequently seen as a complication of obesity or diabetes.

"I'm excited about expanding the program of gastroenterology," Diehl said. "Duke has phenomenal faculty in this area, and they have contributed many advances to the field."

Diehl is the principal investigator of NASH (nonalcoholic steatohepatitis), a multi-center treatment trial for nonalcoholic fatty liver disease that will soon begin recruiting patients. She is involved in creating a national registry of patients with the disease and chairs the National Institutes of Health committee to develop an action plan on fatty liver disease.

Diehl's basic research focuses on mouse models of disease and the molecular regulation of liver injury and repair. In 2001, she received the Leon Schiff Prize for outstanding research in clinical liver disease from the American Association for the Study of Liver Diseases and was awarded the Hans Popper Prize for outstanding basic liver research from the International Association for the Study of Liver Diseases in 2002.

APPOINTMENTS

Payne to direct Care at End of Life Institute

Richard Payne, MD, an internationally known expert in the areas of pain relief, care for those near death, oncology, and neurology, has been named the Colliflower Director of Duke University's Institute on Care at the End of Life.

"Richard Payne is extraordinarily well-positioned to lead [the institute]," said Gregory Jones, dean of the Duke Divinity School. "He combines the stature, wisdom, creativity, passion, and leadership to build on the institute's current strengths and lead it in exciting new ways. He will continue the institute's focus on faith communities and on diverse populations, especially African-Americans, while also extending its reach in teaching, research, and outreach."


Payne

Educated at Yale University and Harvard Medical School, Payne has led the Memorial Sloan-Kettering program since 1998. "Dr. Payne is highly regarded as an international leader in pain management and palliative care," said R. Sanders Williams, MD, vice chancellor for academic affairs and dean of the Duke University School of Medicine. "His joint appointment in the Divinity School and the School of Medicine will inspire students and colleagues to examine more closely, and to understand more fully, the connections between the medical and spiritual dimensions of how patients and their families face this difficult, but inevitable, stage of human existence."

Based at Duke Divinity School, The Institute on Care at the End of Life was launched in 2000. Its members work to improve research, education, and practice in the care of those near death. The institute involves faculty and staff from the medical center, theologians, and ethicists from the divinity school, scholars from Duke's arts and sciences departments, and pastors and caregivers from across the nation.

Berger named director of Duke Interventional Catheterization Program

Peter Berger, MD, a cardiologist for 13 years at the Mayo Clinic in Rochester, MN, has been named director of the Interventional Catheterization Program at Duke University Medical Center.


Berger

Berger, who began his duties in January, will conduct clinical research as a member of the Duke Clinical Research Institute in addition to his clinical duties in the catheterization laboratory.

At Mayo, Berger served as professor of medicine at the Mayo Medical School and director of clinical research for the Cardiac Catheterization Laboratory and Interventional Databank Group.

"Dr. Berger is one of the premiere interventional cardiologists in the world who has conducted groundbreaking research into the role of invasive procedures in improving outcomes, and in the development of new devices to open blocked coronary arteries in patients with cardiovascular disease," said Pascal Goldschmidt, MD, chair of the Department of Medicine at Duke. "Duke is already particularly world-renowned for its research into the use of medications to make interventional cardiology safer and more effective for patients, and Dr. Berger brings an added dimension and expertise to our program."

Berger is currently chair of the catheterization and interventional cardiology committee of the American Heart Association, and serves on similar committees for the American College of Cardiology and Society of Coronary Angiography and Intervention.

"I am a big proponent of the role of the cath lab in improving patient outcomes," Berger said. "There has never been more data supporting the role of both diagnostic angiography and coronary interventions in improving the general well-being and life expectancies in patients with cardiovascular disease. I plan to bring my passion for interventional catheterization to complement the incredibly talented people already in the Duke cath labs. In my opinion, Duke is conducting some of the best cardiology research in the world, and my particular areas of interest should complement what Duke has already been doing very well."

Berger earned his medical degree in 1983 from the New York University School of Medicine, and then completed a three-year residency in internal medicine at Boston City Hospital. He then completed a two-year cardiology fellowship and a two-year interventional fellowship from Boston University Medical School before joining the Mayo faculty.

Brown selected as associate dean

Ann Brown, MD, assistant professor of medicine and obstetrics and gynecology at Duke, has been appointed associate dean for Women in Medicine and Science.

In this newly created position, Brown will spearhead initiatives to study and enhance the environment for success of female faculty, staff, and learners within the Duke University School of Medicine, and to fulfill the goals of the university-wide Women's Initiative.


Brown

"Her efforts will complement and coordinate with many excellent programs for faculty development already under way within individual departments and with other units of the School of Medicine, such as the Multicultural Resource Center and the new Office of Grant Support," said R. Sanders Williams, MD, vice chancellor for academic affairs and dean of the Duke University School of Medicine.

"Dr. Brown, an endocrinologist and clinical investigator, brings specialized expertise and experience to this role, having served as the director of the Duke Academic Program in Women's Health since 1996, as a member of President [Nannerl O.] Keohane's Women's Initiative Steering Committee in 2002-03, and now as a member of the University's Commission on the Status of Women," said Williams. "I look forward to working with Dr. Brown to strengthen support and opportunities for all women in the School of Medicine."

Norton tapped for council

John Norton, DVM, PhD, director of the Division of Laboratory Animal Resources at Duke University Medical Center (DUMC), has been appointed to the accreditation council of the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC).

Organizations that use animals in research, teaching, or testing may be accredited by AAALAC if their program conforms with standards as set forth by the Guide for the Care and Use of Laboratory Animals, NRC, 1996, and other applicable guidelines.

The accreditation process includes a thorough evaluation of the whole animal care and use program, including a site visit by a council member. Following a site visit, a program evaluation is prepared and submitted to the Council of Accreditation for review and approval.


Norton

Animal care and use programs must undergo evaluation every three years to maintain their accreditation status. Currently more than 650 organizations, including DUMC, have earned the accreditation.

Two boards elect Strand

Justine Strand, MPH, PA-C, chief of the Physician Assistant Division of the Duke Department of Community and Family Medicine, has been elected to the N.C. Medical Society Foundation Board of Trustees. She is the first physician assistant (PA) elected to the board.

She also was elected to a two-year term as director at large of the Association of Physician Assistant Programs (APAP) Board of Directors.

Established in 1972, the association is the national organization representing PA educational programs in the U.S. APAP's mission is to assist PA educational programs in the instruction of highly educated physician assistants. The association offers an array of services for PA programs, faculty, students, and the general public aimed at fulfilling this mission.

During her one-year term as secretary/treasurer with the N.C. Medical Society Foundation Board of Trustees, Strand hopes that her work will help improve access to health care for many North Carolinians.


Strand

"One of the things our board will do is be very active with the Community Practitioner Program. It provides loan repayment for physicians, PAs, and nurse practitioners who want to serve in medically underserved communities," said Strand. The program was started in 1989 with a grant from the Kate B. Reynolds Charitable Trust.

"Justine brings a breadth of knowledge to the Board of Trustees, and we welcome her into this leadership role," said Elizabeth P. Kanof, MD, president of the foundation. "Her dedication to improving healthcare access will undoubtedly make her a vital partner in continuing the foundation's work."

Jose M. Carmena, PhD

Michael D. Ehlers, MD, PhD

Duke honors distinguished professors

Duke University has awarded distinguished professorships to 25 faculty members, including 10 from the School of Medicine.

The School of Medicine recipients of chairs were:

- **Francis Ali-Osman, MD**—Margaret Harris and David Silverman Professor of Neuro-Oncology Research. He is a professor of surgery.
- **Haywood L. Brown, MD**—Roy T. Parker Professor of Obstetrics and Gynecology. He is a professor and chair of the Department of Obstetrics and Gynecology.
- **Joseph Heitman, MD**—James B. Duke Professor of Molecular Genetics and Microbiology. He is a professor of molecular genetics and microbiology, pharmacology and cancer biology, and medicine; an associate investigator of the Howard Hughes Medical Institute; and director of the Center for Microbial Pathogenesis.
- **H. Kim Lyerly, MD**—George Barth Geller Professor for Research in Cancer. He is the director of the Duke Comprehensive Cancer Center and a professor of surgery.
- **Mark F. Newman, MD**—Merel H. Harmel Professor of Anesthesiology. He is chair of the Department of Anesthesiology and a professor of medicine.
- **James A. Nunley, MD**—J. Leonard Goldner Professor of Orthopaedic Surgery. He is a professor and chief of orthopaedic surgery.
- **Edward F. Patz, Jr., MD**—James and Alice Chen Professor of Radiology. He is a professor of pathology, and a professor in pharmacology and cancer biology.
- **Jonathan S. Stamler, MD**—George Barth Geller Professor for Research in Cardiovascular Diseases. He is a professor of medicine and biochemistry and an associate investigator of the Howard Hughes Medical Institute.
- **William M. Thompson, MD**—Reed and Martha Rice Professor of radiology. He is a professor of radiology.
- **Huntington F. Willard, PhD**—Nanaline H. Duke Professor of Molecular Genetics and Microbiology. He is the director of the Institute for Genomic Sciences & Policy, and vice chancellor for Genome Sciences.

Carmena, Ehlers receive awards

Two Duke researchers were among 16 neuroscientists who were awarded grants from the Christopher Reeve Paralysis Foundation (CRPF).

Jose M. Carmena, PhD, a research associate in the Department of Neurobiology and the Duke Center for Neuroengineering, received a two-year, $120,000 grant for research into closed-loop brain-controlled prosthesis for recovery of upper-limb functionality in subjects with spinal cord injuries.

Michael D. Ehlers, MD, PhD, assistant professor of neurobiology and assistant professor in the Department of Cell Biology and the Department of Pharmacology and Cancer Biology, received a two-year, $150,000 grant for research into spatial regulation of endocytosis during growth cone migration and collapse. He also is the director of the Neuroproteomics Lab.

"CRPF's individual grants are catalytic," said Susan P. Howley, director of Research and executive vice president of CRPF. "They get a project or a new investigator started, and almost without exception lead to additional, more long-term support."

Snyderman receives first Bravewell Leadership Award

Ralph Snyderman, MD, chancellor for health affairs at Duke University Medical Center (DUMC) and president and CEO of Duke University Health System, has been named the inaugural recipient of the Bravewell Leadership Award.

The award, sponsored by the Minneapolis-based Philanthropic Collaborative for Integrative Medicine, confers a prize of $100,000. It was presented by Walter Cronkite at a ceremony held in New York on November 13, 2003.

The award recognizes innovators of integrative medicine for their efforts to transform the culture of health care by establishing better methods of treating the whole person—mind, body, and spirit.

"I am so honored to be the first recipient of the Bravewell Leadership Award," Snyderman said. "I was very pleased to be selected as a nominee and had outstanding company in my fellow nominees. The field of integrative medicine continues to grow rapidly, and I plan to continue my support of this important area of health care not only at Duke but at other centers throughout the U.S."

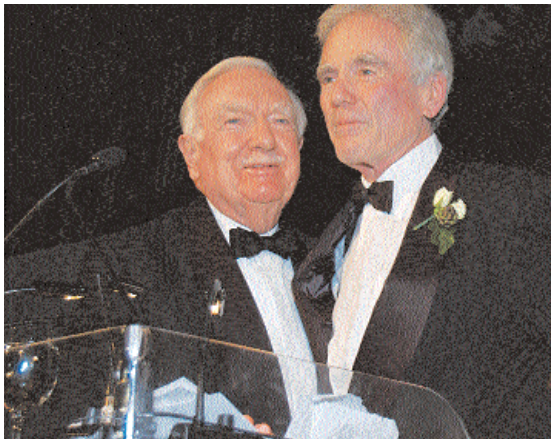
Snyderman donated the cash prize from the award to establish a new fund at Duke University to promote integrative medicine. The Bravewell Award Fund for Integrative Medicine at DUMC will be used to help develop new approaches to prospective health care and integrative medicine.

The chancellor has been a national leader in promoting the concept of "prospective health care," a personalized approach to health planning that would apply advances in genomics and other fields to promote health and prevent disease.

"A new model of prospective health care could provide individuals with their own personal health plans, identifying the diseases they are most likely to develop and providing the support they need to remain healthy and well," Snyderman said. "I am grateful to the Bravewell Committee and the Philanthropic Collaborative for Integrative Medicine for making these resources possible. It provides important support for my work at Duke so that it can provide continuing leadership in promoting an integrative approach that offers great promise for improving the health of people everywhere."

The Philanthropic Collaborative for Integrative Medicine develops and implements initiatives that are designed to strategically advance the field of integrative medicine. The Consortium of Academic Health Centers for Integrative Medicine, a group of 18 academic health centers in the U.S., including DUMC, is one of their largest benefactors.

For a detailed description of the power of integrative health care and Snyderman's views on its importance, see "Duke Leaders Propose Overhaul of Health Care and the Practice of Medicine" at www.dukemednews.org.



Walter Cronkite (left) presented the Bravewell Leadership Award to Ralph Snyderman, MD.

V Foundation recognizes Blobe

Gerard Blobe, MD, assistant professor of medical oncology, pharmacology, and cancer biology and a member of the Duke Comprehensive Cancer Center, has been named as one of 15 recipients of the 2003 V Scholar Research Grants from The V Foundation. The foundation is named for the late N.C. State University men's basketball coach Jim Valvano.

The $100,000 award will support Blobe's research into how the tumor suppressor protein, TGF-beta, functions during breast cancer tumor formation.

The latest finding by Blobe and his collaborators, reported in the September 5, 2003 issue of *Science*, is another step toward identifying the mechanisms that cause TGF-beta resistance in cancer cells. Blobe said their ultimate goal is to target the TGF-beta pathway with new drugs that can help prevent or treat breast cancer.

Gerard Blobe, MD

Susan M. Schneider, PhD, RN, CS, AOCN

Dennis Rickman, PhD
and Natalie Afshari, MD

Brooks W. McCuen, II, MD

Paul P. Lee, MD, JD

Nursing society honors Schneider with award

Susan M. Schneider, PhD, RN, CS, AOCN, director of the Graduate Oncology Nursing Program at the Duke University School of Nursing and an assistant professor of nursing, was named the recipient of the 2003 Oncology Nursing Society Mary Nowotny Excellence in Cancer Nursing Education Award.

Schneider received a plaque and a $2,000 educational stipend. The award is given each year to recognize and support excellence in cancer nursing education.

The Oncology Nursing Society (ONS) is a professional organization of more than 30,000 registered nurses and other healthcare providers dedicated to excellence in patient care, education, research, and administration in oncology nursing. It's also the largest professional oncology association in the world.

Bruzga wins National Physical Therapy Award

Bob Bruzga, PT, OCS, SCS, ATC/L, has been awarded the 2004 Sports Physical Therapy Section Academic Education Award by the Sports Physical Therapy Section of the American Physical Therapy Association (APTA). He is the manager of the Sports Medicine Division of the Department of Physical Therapy and Occupational Therapy at Duke.

The award is given annually to recognize a member of the Sports Section who has made significant contributions in the area of teaching.

"This is a great honor, and Bob's contributions to the education of students has been truly outstanding," said Daniel V. Dore, PT, MPA, director of the Department of Physical Therapy and Occupation Therapy.

The APTA is a national professional organization representing more than 63,000 members. Its goal is to foster advancements in physical therapy practice, research, and education.

Research grants for Eye Center faculty

Duke University Eye Center faculty **Natalie Afshari, MD**, and **Dennis Rickman, PhD**, have each received a distinguished grant from the Research to Prevent Blindness (RPB) organization.

Afshari, an assistant professor in the Department of Ophthalmology, has been awarded the RPB Career Development Award to further her career as a clinician-scientist and facilitate her research in corneal disease. Established in 1990, the award helps attract young physicians and basic scientists to eye research.

Rickman, an assistant research professor in Ophthalmology and in Neurobiology, was awarded the RPB Lew R. Wasserman Merit Award. Established in 1995, the award provides unrestricted support to mid-career MD and PhD scientists who are actively engaged in eye research within departments of ophthalmology at medical institutions in the U.S. The award will support Rickman's work on neural stem cell transplantation to treat neurodegenerative diseases of the retina and optic nerve.

Eye Center faculty selected for professorships

Duke University Eye Center has selected two members of the Department of Ophthalmology to receive a named chair. This distinguished professorship is the highest honor Duke can confer upon a faculty member.

Brooks W. McCuen, II, MD, has been awarded the Robert Machemer Professor of Ophthalmology in the School of Medicine. He is the vice chair of the Department of Ophthalmology and director of Vitreoretinal Surgery.

Paul P. Lee, MD, JD, has been awarded the James Pitzer Gills, III, MD, and Joy Gills Professor of Ophthalmology in the School of Medicine. The former medical director of the Duke Department of Ophthalmology, he is a senior fellow at the Duke Center on Aging and part of the Health Services Program at RAND, in Santa Monica, CA.

MEDICINE

Amy P. Abernethy, MD
919-668-0647
Particular Clinical Interests and Skills: Palliative care, cancer pain management, symptom control, supportive oncology, and general hematology/oncology
Faculty Rank: Assistant Professor
Division: Medical Oncology
MD Degree: Duke University School of Medicine, 1994
Residency: Internal Medicine, Duke University Medical Center, 1997
Fellowship: Hematology-Oncology, Duke University Medical Center, 2001
Palliative Care: Flinders University of South Australia, 2003

Stephen Y. Chui, MD
919-684-3877
Particular Clinical Interests and Skills: Breast cancer prevention and treatment, novel therapeutics, breast cancer biology, immunity and immunotherapy, gene therapy
Faculty Rank: Associate in Medicine
Division: Medical Oncology
MD Degree: Duke University School of Medicine, 1996
Residency: Internal Medicine, Duke University Medical Center, 1996-1999
Fellowship: Medical Oncology, The Princess Margaret Hospital, Canada, 2000
Hematology and Medical Oncology, Duke University Medical Center, 2001-2003

Wolfgang B. Liedtke, MD, PhD
919-684-0058
Particular Clinical Interests and Skills: Multiple sclerosis and demyelinating diseases, epilepsy and convulsive disorders, pain including headache syndromes, sleep and circadian medicine, and neurological intensive care
Faculty Rank: Assistant Professor
Division: Neurology
MD Degree: University of Colgne, Germany, 1989
PhD Degree: Clinical Medical Sciences/ Medical Virology, University of Bochum, Germany, 1990
Residency: Neurology, University of Tuebingen, Germany, 1989-1991, Neurology, University of Essen, Germany, 1991-1993, Psychiatry, University of Essen, Germany, 1993-1994
Fellowship: Neuropathology, Albert Einstein College of Medicine of Yeshiva University, New York, 1994-1997
Fellow of the Alexander von Humboldt Foundation, Feodor Lynen Fellow, Mentor Dr. Cedric S. Raine, Germany

John P. Middleton, MD
919-660-6860
Particular Clinical Interests and Skills: Hypertension, general nephrology, progressive renal diseases, ESRD
Faculty Rank: Associate Professor
Division: Nephrology
MD Degree: Medical College of Virginia, 1983
Residency: Internal Medicine, University of Texas Medical Branch, 1986
Fellowship: Nephrology, Duke University Medical Center, 1989

Momen M. Wahidi, MD
Director, Interventional Pulmonology
919-668-0340
Particular Clinical Interests and Skills: Interventional pulmonology, thoracic oncology, pleural diseases, advanced diagnostic and therapeutic flexible bronchoscopy, rigid bronchoscopy, airway stent placement, cryotherapy, argon plasma coagulation, photodynamic therapy, autofluorescense bronchoscopy, medical pleuroscopy
Faculty Rank: Assistant Professor
Division: Pulmonary, Allergy and Critical Care
MD Degree: University of Damascus, Syria, 1992
Residency: Internal Medicine, Indiana University Medical Center, 1995-1999
Fellowship: Pulmonary and Critical Care, Duke University Medical Center, 1999-2002
Interventional Pulmonology, Beth Israel Deaconess Medical Center, Harvard Medical School, Massachusetts, 2002-2003

OB/GYN

Jeffrey P. Wilkinson, MD
919-783-4299 or
919-684-4647
Particular Clinical Interests and Skills: Urinary and fecal incontinence, pelvic organ prolapse, fistulae, and pelvic floor dysfunction
Faculty Rank: Assistant Clinical Professor
Division: Gynecologic Specialties
MD Degree: Johns Hopkins University School of Medicine, Maryland, 1993
Residency: OB/GYN, University of North Carolina at Chapel Hill, 1993-1997
Fellowship: Urogynecology, University of North Carolina at Chapel Hill, 1997-1999

Frank G. Gress, MD
919-684-1817
Particular Clinical Interests and Skills: Gastrointestinal tumors, pancreatitis, pancreatic cancer, Barrett's esophagus
Faculty Rank: Associate Professor
Division: Gastroenterology
MD Degree: Mount Sinai School of Medicine, 5th Pathway Program, New York, 1988
Residency: Internal Medicine, Montefiore Medical Center, New York, 1988-1991
Fellowship: Gastroenterology Fellowship, State University of New York at Downstate/Brooklyn Hospital Center, 1991-1993
Advanced Therapeutic Endoscopy, Indiana University, 1993-1994

ON THE SPOT

Q. What drew you to study palliative care and how has your study influenced your practice?

A. "I particularly enjoy being in an area of medicine that is evolving. Palliative care focuses on helping the patient and their loved ones live life to fullest, regardless of how many days are left. Over the years we have moved from an either/or model of curative treatments versus terminal care, to an integrated model where the proportion of treatments concentrating on curative or palliative therapies changes as disease progresses and the patient's needs change. The focus is on maximizing quality of life and relieving suffering. I am constantly balancing the opportunities and appropriateness of disease-directed therapy with the need for prompt attention to function, pain, existential concerns, psychological well-being, and other issues."

–Amy P. Abernethy, MD

OPHTHALMOLOGY

Lawrence M. Buono, MD
919-681-9191
Particular Clinical Interests and Skills: Diagnosis and management of diseases of the optic nerve, visual pathway in the brain, orbit and the ocular motor system; research interest in giant cell arteritis, ischemic optic neuropathy, optic neuritis, and hereditary optic neuropathies
Faculty Rank: Assistant Professor
Division: Comprehensive Ophthalmology, Neuro-Ophthalmology
MD Degree: Thomas Jefferson Medical College, Pennsylvania, 1997
Residency: Ophthalmology, New York Medical College, 2001
Fellowship: Neuro-Ophthalmology, Wills Eye Hospital, Pennsylvania, 2002

Terry Semchyshyn, MD
336-768-3240
Particular Clinical Interests and Skills: Cataract surgery, laser refractive surgery (LASIK, PRK, and LASEK), corneal transplantation, combined corneal transplant and cataract surgery, Fuch's endothelial dystrophy
Division: Cornea and External Diseases
MD Degree: Vanderbilt University School of Medicine, Tennessee, 1998
Residency: Ophthalmology, Vanderbilt University Department of Ophthalmology and Visual Sciences, Tennessee, 1999-2002
Fellowship: Cornea, External Disease, and Refractive Surgery, Duke University Medical Center, 2002-2003

Christine E. Speer, MD
919-684-4417
Particular Clinical Interests and Skills: Cataract surgery, intraocular lens implantation, general and urgent eye care, dry eye, contact lens-related problems, glaucoma, diabetic eye disease
Division: Comprehensive Ophthalmology Service
MD Degree: University of Arkansas for Medical Services, 1999
Residency: Georgetown University/The Fairfax Hospital, Washington, D.C., 2000
Wills Eye Hospital, Pennsylvania, 2003

PEDIATRICS

Coleen K. Cunningham, MD
Chief, Pediatric Infectious Diseases
919-416-3457
Particular Clinical Interests and Skills: Infections, unexplained fevers, meningitis, pneumonia, bone and joint infections, viral disease
Faculty Rank: Associate Professor
Division: Infectious Diseases
MD Degree: State University of New York Health Science Center at Syracuse, 1985
Residency: Pediatrics, State University of New York Health Science Center at Syracuse, 1985-1988
Fellowship: Pediatric Infectious Diseases, State University of New York Health Science Center at Syracuse, 1988-1991
Other Degrees: B.S., Biochemistry, State University of New York at Binghamton, 1981

PSYCHIATRY

Katherine L. Applegate, PhD
Director, Psychological Services for Bariatric Surgery Program
919-660-2229
Particular Clinical Interests and Skills: Assessment/treatment of depression, anxiety, chronic pain, sexual dysfunction, eating disorders, smoking cessation, stress management, individual and group cognitive-behavioral psychotherapy, biofeedback
Faculty Rank: Assistant Clinical Professor
Division: Medical Psychology
Degree: PhD, The Ohio State University, 2000
Residency: Medical Psychology, Duke University Medical Center, 1999-2000
Fellowship: Aging Center Fellowship, Duke University Medical Center, 2000-2002
Behavioral Medicine Research Center, Duke University Medical Center, 2002-2003

Barbara Crockett, MD
919-681-2918
Particular Clinical Interests and Skills: Clinic practice of adult psychiatry with fellowship training in psychopharmacology; special interest in mood disorders, anxiety disorders, PTSD, and pharmacological management issues
Faculty Rank: Associate Clinical Professor
Division: Outpatient Psychiatry
MD Degree: Hahnemann Medical College, Pennsylvania, 1968
Residency: Adult Psychiatry, Institute of Pennsylvania Hospital, 1969-1972
Fellowship: Psychopharmacology, Duke University Medical Center, 1997-1999

Maria Marta Gazzola, MD
919-416-2405
Particular Clinical Interests and Skills: General adult, child and adolescent psychiatry, cross-cultural psychiatry, dual diagnosis, research interest in clinical trials, internalizing disorders
Faculty Rank: Clinical Associate
Division: Child and Adolescent Psychiatry
MD Degree: Medical School of the Federal University of Minas Gerais, Brazil, 1983
Residency: Psychiatry, Columbia University, St Luke's - Roosevelt Hospital Center, New York, 1996-1999
Fellowship: Child and Adolescent Psychiatry, Columbia University, New York State Psychiatric Institute, 2001-2003
Diplomas: Diploma of Advanced Studies in Psychoanalysis, University of Paris, France, 1988-1990
Diploma of General Psychiatry, University of Paris, France, 1990-1992

RADIATION ONCOLGY

Christopher G. Willett, MD
Chair, Radiation Oncology
919-668-5640
Particular Clinical Interests and Skills: Clinical interest in multimodality management of GI cancer and clinical trials in GI cancer
Faculty Rank: Professor
Division: Radiation Oncology
MD Degree: Tufts Medical School, Massachusetts, 1981
Residency: Surgery, Vanderbilt Medical Center, Tennessee, 1981-1982
Radiation Oncology, Massachusetts General Hospital, 1982-1985
Fellowship: Radiation Oncology, Massachusetts General Hospital, 1985-1986

SURGERY

Louis C. Almekinders, MD
919-471-9622
Particular Clinical Interests and Skills: Arthroscopic treatment of knee, shoulder, ankle and elbow problems, cartilage restoration procedure through arthroscopic methods
Faculty Rank: Clinical Professor
Division: Orthopaedic Surgery
MD Degree: Erasmus University Medical Faculty, Netherlands, 1982
Residency: Orthopaedic Surgery, University of North Carolina, 1989
Fellowship: Orthopaedic Research, Duke University Medical Center, 1983

Philipp Dahm, MD
919-684-9949
Particular Clinical Interests and Skills: Urologic oncology with emphasis on prostate and renal cancer, radical perineal prostatectomy, immunotherapy trials
Faculty Rank: Assistant Professor
Division: Urology
MD Degree: University of Heidelberg School of Medicine, Germany, 1994
Residency: Dresden University Medical Center, Germany, 1994 Tubingen University Medical Center, Germany, 1995-1996
Duke University Medical Center, 1996-2002

Dev M. Desai, MD, PhD
919-668-2279
Particular Clinical Interests and Skills: Adult and pediatric liver, kidney, and pancreas transplant, hepatobiliary surgery
Faculty Rank: Assistant Professor
Division: General Surgery
MD Degree: University of California San Francisco, 1995
Residency: General Surgery, Stanford University Hospital, California, 2001
Fellowship: Tranplant/Hepatobiliary Surgery, Stanford University Hospital, California, 2003
PhD: Immunology, University of California San Francisco, 1994

Scott S. Kelley, MD
919-479-7954
Particular Clinical Interests and Skills: Adult hip and knee reconstructive surgery
Faculty Rank: Clinical Professor
Division: Orthopaedic Surgery
MD Degree: University of Iowa, 1982
Residency: Orthopaedics, State University of New York, Upstate Medical Center, 1983-1987
Fellowship: Adult Reconstructive Surgery, Mayo Clinic, Minnesota, 1987-1988

Mark H. Moriarty, MD
919-989-6535
Particular Clinical Interests and Skills: All facets of orthopaedics with special interest in sports medicine, athletic injuries, arthroscopy, and adult reconstructive procedures
Faculty Rank: Assistant Clinical Professor
Division: Orthopaedic Surgery
MD Degree: Georgetown University School of Medicine, Washington, DC, 1981
Residency: General Surgery, Monmouth Medical Center, New Jersey, 1981-1982 Orthopaedic Surgery, Monmouth Medical Center, New Jersey, 1982-1986

David A. Thompson, MD
919-471-9622
Particular Clinical Interests and Skills: Hand, microvascular and upper extremity surgery
Faculty Rank: Assistant Clinical Professor
Division: Orthopaedic Surgery
MD Degree: University of North Carolina at Chapel Hill, 1996
Residency: Orthopaedic Surgery, UNC Hospitals, Chapel Hill, 1996-2001
Fellowship: Hand, Microvascular and Upper Extremity Surgery, Duke University Medical Center, 2002-2003

ON THE SPOT

Q: Is tendonitis purely an overuse injury or are other factors involved?

A: "It is a common misconception that tendonitis is an inflamed tendon as a result of repetitive overuse. Our research indicates that many forms of tendonitis are the result of age-related changes in the tendon, weakening due to disuse, and only occasional overuse. Inflammation is rarely found in tendonitis. Traditional treatments have focused on anti-inflammatory measures, whereas newer treatments are aimed at reversing degenerative changes and stimulating tendon metabolism."

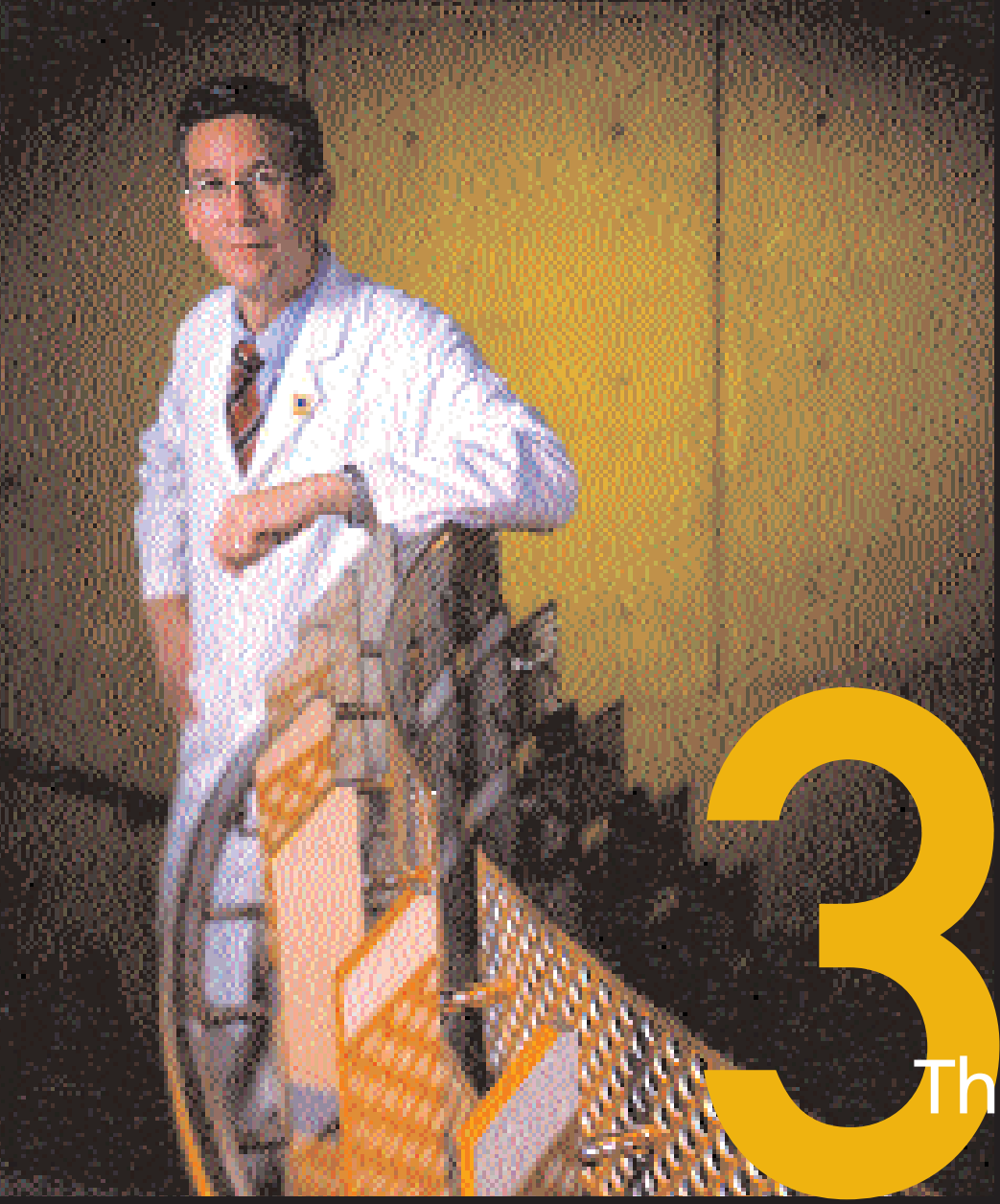
—**Louis C. Almekinders, MD**

Thomas Y. L. Hung, MD
919-668-5240
Particular Clinical Interests and Skills: Facial cosmetic and reconstructive surgery, craniomaxillofacial trauma, reconstruction of local skin cancers, endoscopic sinus surgery
Faculty Rank: Assistant Clinical Professor
Division: Otolaryngology-Head and Neck Surgery
MD Degree: University of Massachusetts Medical School, 1996
Residency: General Surgery, Massachusetts General Hospital, Harvard Medical School, 1996-1997 Otolaryngology, Duke University Medical Center, 1997-2001
Fellowship: Facial Plastics and Reconstructive Surgery, Duke University Medical Center, 2001-2002

Joe T. Minchew, MD
919-471-9622
Particular Clinical Interests and Skills: Disorders of the spine
Faculty Rank: Associate Clinical Professor
Division: Orthopaedic Surgery
MD Degree: Johns Hopkins University School of Medicine, Maryland, 1988
Residency: Surgery, UCLA School of Medicine, California, 1988-1989 Orthopaedics, UCLA School of Medicine, California, 1989-1993
Fellowship: Fellowship, Disorders and Surgery of the Spine, UCLA School of Medicine, California, 1993-1994
Other Degrees: BS, Chemistry and Biochemistry, University of Georgia, 1984

Paul J.W. Tawney, MD
919-479-7940
Particular Clinical Interests and Skills: Musculosketal medicine, non-operative orthopaedics, spinal cord injury
Faculty Rank: Assistant Clinical Professor
Division: Orthopaedic Surgery
MD Degree: University of New Mexico, 1989
Residency: Physical Medicine and Rehabilitation, University of Virginia, 1993

Traci L. Thoureen, MD
919-684-5537
Particular Clinical Interests and Skills: Human simulation and resident education
Faculty Rank: Assistant Clinical Professor
Division: Emergency Medicine
MD Degree: St. George's University School of Medicine, Grenada, 1998
Residency: Emergency Medicine, Yale University, Connecticut, 2002



3 Three questions

H. Kim Lyerly, MD, director of the Duke Comprehensive Cancer Center, on the war on cancer.

So how is the war on cancer progressing and what are the key breakthroughs we can anticipate in the future?

We have made progress. In the early 1970s, when the "War on Cancer" was started, newly diagnosed cancer patients had a 50 percent chance of surviving five years. Today, over 62 percent of newly diagnosed cancer patients will survive at least five years. In pediatric cancers, the trends are even more promising, as newly diagnosed patients have over an 80 percent chance of surviving five years. Nonetheless, for many common cancers, the effectiveness of treatments has not met our expectations, and dramatic changes are needed to deliver to society the benefits of the exceptional cancer discovery research that has occurred over the past 30 years.

In 2002, National Cancer Institute (NCI) Director Andrew von Eschenbach proclaimed a goal to eliminate suffering and death from cancer by 2015. This goal challenges us to completely reevaluate how we develop and deliver new therapies to prevent and treat cancer. This will be done by exploiting the major advances in genomic technology and informatics to profile patients and their cancers, designing treatments tailored to an individual, and monitoring treatment responses using validated biomarkers.

What do you see as Duke's greatest strength in delivering cancer care?

Duke is uniquely positioned to be a world leader in cancer care. On the one hand, we have one of the nation's largest cancer centers, caring for over 10 percent of all cancer patients in North Carolina. On the other hand, we have one of the nation's largest cancer research enterprises, with over 360 investigators and an annual research budget of over $180 million. One of the most promising areas of cancer research is in developing new agents to inhibit signaling processes in cells, and Duke's Pharmacology and Cancer Biology Department is one of the best in the world in signaling research. Duke is also unique in developing programs and activities that span the entire enterprise, and we have strong collaborations with groups as diverse as the Institute for Genome Sciences and Policy, the Stedman Nutrition and Metabolism Center, and the Pratt School of Engineering. The atmosphere is ripe for collaborations and synergies. Finally, Duke is home to some of the premier clinical research enterprises in the country, such as the Duke Clinical Research Institute, the American College of Surgeons Oncology Group, and the statistical and data center of the Cancer and Leukemia Group B. These three elements—world-class basic researchers, large volumes of cancer patients, and the infrastructure and expertise to conduct first-rate clinical research—have Duke poised to be the premier institution to develop and deliver new therapies to patients.

How is Duke cancer research benefiting patients directly?

We are continually searching for new and effective ways to prevent cancer, to diagnose cancer earlier, to provide emotional as well as physical support to our patients, and to treat each patient with the most effective treatment regiment for them. As an example, Duke oncologist Dr. Herb Hurwitz was the lead investigator on a national study that extended the lives of patients with metastatic colon cancer with a new class of drugs called angiogenesis inhibitors. We are excited about this treatment as we believe it can be used to treat many other types of cancer as well. In addition to new therapies, we continue to discover innovative new diagnostic and treatment tools like the breast "Pap smear." Dr. Victoria Seewaldt and her team have developed this procedure which allows physicians to survey cells from the entire breast and test for early changes to the breast that precede cancer. These are just two of the discoveries that our investigators are working on every day to provide patients with more choices and to improve and extend their lives. Clearly, that's our number one goal.

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9:45 a.m.	Check out new features at **dukehealth.org**

Sarah works hard, plays hard, and wants to keep it that way. So she checks in often at the new **dukehealth.org**. It's where the Southeast's most trusted medical facility—Duke University Health System—offers vital health resources including:

- Dynamic health information portals
- Disease, symptom, and treatment encyclopedia
- Drug and herb libraries
- Informative feature articles
- Searchable health news database

…Plus everything she needs to know about getting care at Duke, from clinical specialties to community education offerings, physician directories to detailed maps.

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Site-seeing for people who love to live well.

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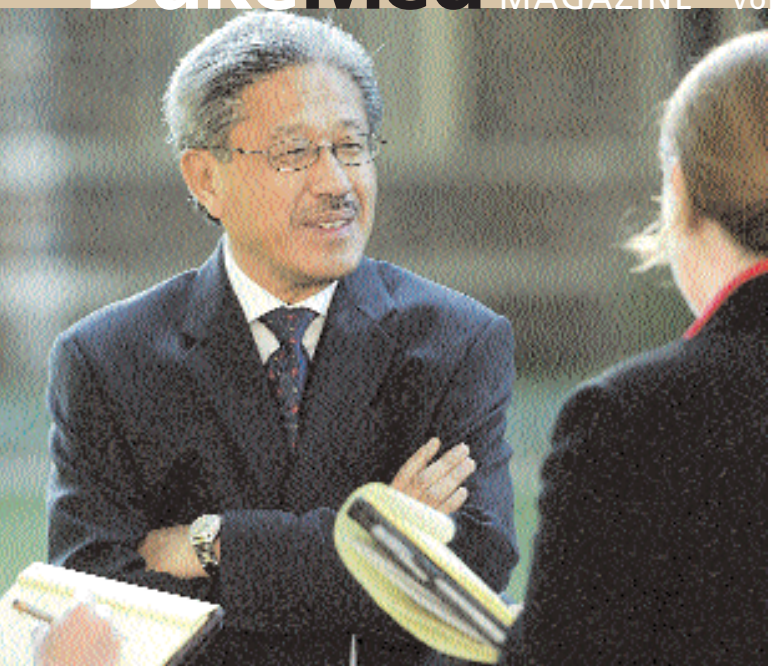

MEET THE NEW CHANCELLOR.

"I am honored to be chosen to lead the Duke University Medical Center and Health System at this challenging yet exciting time for academic medicine and biomedical research," says Victor J. Dzau, MD, who becomes Duke University's next chancellor for health affairs July 1. "Duke has a reputation for excellence and innovation in medical care and research that is envied across the nation and around the world. The Schools of Medicine and Nursing are strong and have been well led, and they provide an excellent foundation on which to build even greater strength. It will be a privilege to work with my Health System and University colleagues and to lead this strong medical enterprise."

Read more on p. 4.

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