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CELEBRITIES OF SCIENCE
GENERATION NEXT



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by Barbara J. Culliton

Medical research is one of the great success stories of the past fifty years, and the development of an astonishing array of lifesaving drugs for everything from heart disease to cancer to AIDS is the highlight of that success. "The quality of health care worldwide depends in large measure on advances in drug therapy," says Jan Leschly, chief executive of SmithKline Beecham and new chairman of the Pharmaceutical Research and Manufacturers of America (PhRMA) Foundation. The foundation's mission is to advance medicine by supporting cooperative research between industry and academia. Donna Moore, PhRMA Foundation president, reports that over the thirty-four years of its existence the foundation has sponsored research for more than 2,400 young scientists. "Eighty-six percent of them are still in academia—teaching the teachers and teaching the 'doers,'" she says with pride. "And we continue to jump-start the careers of the next generation of scientists."

Research is vital and it ultimately leads to new drugs. The PhRMA Foundation, which obtains its money from pharmaceutical company members who seek to foster cutting-edge research, has spent more than forty-three million dollars on young scientists since it was founded in 1965. The Bristol-Myers Squibb Foundation, one of the industry's largest, has contributed more than eighty million to unrestricted biomedical research since 1977. Many other large pharmaceutical companies have established charitable institutions through which they support the next generation of scientists—young lions preparing to solve basic questions about human health and disease.

Clockwise left to right: Surgeon General David Satcher (shown with President Clinton) received The Bayer Institute Outstanding Physician Communicator Award last month. Weekends, Nananda Col trades her lab coat for rollerblades. David Pompliano cycling through France along the Dordogne River. An avid traveler, Teresa Przytycka is pictured here vacationing in Olympia, Greece. Off duty, Maysel Kemp White completes the flight time required for her pilot's license. Martin Markowitz shown with mentor David Ho is busy pursuing leads in AIDS research.

UNDERSTANDING HIV

AIDS continues to confound medical science despite recent advances in drug therapy. Martin Markowitz, M.D., is a physician turned researcher who hopes to learn why the human immunodeficiency virus (HIV) persists even in patients who are taking the full cocktail of anti-AIDS drugs. He wants to know whether it is possible to rid patients of HIV once and for all.

"I was trained as a physician, specializing in oncology, and I originally set up a practice in New York City," says Markowitz, who graduated from Stanford University School of Medicine in 1978. During the eighties his practice grew to include many patients with AIDS. Markowitz witnessed an "explosion" in anti-AIDS drugs and helped to set up the first designated AIDS center in New York City at St. Clare's Hospital in midtown Manhattan.

"About seven years ago I decided I needed to switch my career to research," Markowitz recalls. It was a big step, made possible by an invitation to join the team of renowned AIDS researcher David Ho, M.D., at The Aaron Diamond AIDS Research Center in New York City. Ho is Markowitz' mentor in what Ho calls "studies of the dynamics of HIV. We're trying to understand the basics of HIV's capacity to destroy the immune system."

Working together for the past seven years, Markowitz and Ho have received strong support from a large number of pharmaceutical companies (including Bristol-Myers Squibb), which has allowed them to conduct novel clinical trials. They have made important discoveries that bring both bad news and good news. The bad news is that current drug therapy, no matter how intensive, does not completely eliminate

small reservoirs of HIV in the body. The good news, he says, is that "We have learned how the virus replicates and how a patient's immune system responds to it. Knowing this, we have potential leads about where to go next in research—leads that may eventually help us overcome the obstacles to discontinuing drug therapy without adverse consequences."

WEIGHING THE RISKS

Nananda Col, M.D. of Tufts University School of Medicine and the New England Medical Center in Boston, has her aim set squarely on a target of substantial importance—weighing the risks and benefits of drugs for disease prevention. Col is using mathematics to help menopausal women make important decisions about their health based on their individual lifestyles and history of disease, as well as the health histories of their relatives.

"The bulk of my research involves mathematical

The pharmaceutical industry has long played a critical but little heralded role in support of unrestricted biomedical research.

models to help women make treatment decisions about therapy to reduce the risk of heart disease, breast cancer, and osteoporosis," she says. Decisions must be based on multiple risk factors as they apply to a particular individual, not an 'average woman.' "It does not help women to learn that hormone replacement therapy (HRT) is generally considered to be a good thing after menopause," says Col. "What is important is that each woman has a way to decide whether it is good for her. The reality is that some women should take HRT. Others should probably just take drugs to prevent bone loss, and some should not take any drug therapy at all."

Col has devised a simple questionnaire for

menopausal women that permits her to use a computer model to weigh the combination of benefits and risks for each individual. It includes questions such as these: What is your cholesterol level? Have you (or a relative) had breast cancer? Do you frequently engage in exercise? Did your mother ever break any bones late in life?

Using mathematical models to assign numbers to each risk factor, Col can then generate a personalized benefit/risk profile for each woman to consider. The patient will be able to weigh the seriousness of one risk against another and to compare those risks to the health risks that accompany the therapy itself. Col's work is supported in part by a grant from the PhRMA Foundation.

MATH AND GENETICS THE NEXT REVOLUTION

Teresa Przytycka, Ph.D. dreams of using her talents in mathematics and computer science to understand basic features about the design and behavior of genes and proteins. She grew up in Poland and recalls, "One of the things that influenced me most was reading a biography of Marie Curie. Curie is a hero in Poland and when I read an account of her life, written by her own daughter, I knew I wanted to be like her." Przytycka already has numerous published reports in mathematics and computer science to her credit. Her current ambition is to become fluent in genetics so she can unravel some of the important health information that is locked in the human genome.

With a grant from the Burroughs Wellcome Fund, Przytycka is studying genes and proteins at The Johns Hopkins University School of Medicine in Baltimore. The fund has set aside twelve million dollars to foster the development and productivity of young researchers, and to help them make the critical transitions to become independent investigators.

"This grant was fundamental in helping me move into a new field" says Przytycka, who is using algorithms (mathematical descriptions of computational proce-

dures) to study the shape of proteins. "The way a protein looks is directly related to what the protein does in the body," she says. She wants to know why.

Przytycka's training will include a stint at The Institute for Genomic Research (TIGR) in nearby Rockville, Maryland, which has a collaborative relationship with Hopkins. TIGR is one of the world's leading genome centers. Genome sequencing requires the analysis of massive amounts of data and that, in turn, depends on advanced mathematics and supercomputers. Przytycka should be in her element.

OUTWITTING MUTANT GENES

DuPont, known worldwide as an innovative chemical company, is taking new initiatives in basic biology and drug discovery as it consolidates plans to be a major player in the pharmaceutical industry in the twenty-first century. Just within the past few months, DuPont Pharmaceuticals recruited thirty-eight-year-old David Pompliano, Ph.D. to lead research on new ways to disarm pathogenic microbes. "One of the big medical problems today is microbes that become resistant to antibiotics," Pompliano observes. "Infections that used to be readily cured now persist to produce a range of serious consequences." Genes encode proteins that are responsible for the survival of bacteria, and antibiotics target key proteins. But the genes are rapidly mutating all the time, and even a single, isolated mutation can lead to high-level resistance if the antibiotic only inactivates a single protein. To minimize the likelihood of such resistance, Pompliano will be targeting what he calls "families of related proteins," and then searching for drugs that will knock out multiple family members simultaneously.

Pompliano, whose professional interest in microbes is matched by experience in the behavior of tumors, will also lead new work at DuPont Pharmaceuticals in oncology. "Cancer drugs and antibacterials pose the same mutational challenge," he says, referring to the fact that highly mutable tumor cells develop resistance to chemotherapy just as microbial mutations lead to antibiotic resistance. Here, too, the challenge is to come up with a strategy

that will decrease the likelihood that resistance to drugs will occur.

Pompliano's research team will tackle cancer through research on angiogenesis—the process by which cells stimulate the growth of vessels that provide nourishment to the tumor. If its blood supply is cut off, a tumor will die. "Cells of the blood vessels are not themselves cancerous, and thus are not so unstable or mutagenic as the cancer cells are," says Pompliano. "By targeting these normal, genetically stable vascular cells, the chances are better that resistance to drugs can be avoided. The promise in this area is too great to let it slide."

IN PRAISE OF PATHOLOGISTS

Not long ago, several Olympus America executives from its Scientific Equipment Division were at the Memorial Sloan-Kettering Cancer Center in New York watching one of the hospital's pathologists at work in his clinical laboratory. The doctor was using an Olympus BX series microscope to investigate the status of a tumor that had just been removed from a patient's body. Says Daniel Biondi, senior vice-president, "The patient was still on the operating table, and already the pathologist was examining frozen sections of her ovarian tumor that had just come from the cryostat (a device that freezes and finely slices biopsied tissue). While the executives were present, the pathologist was able to call in a diagnosis that helped the surgeon decide how to complete the operation.

"It was stunning, and it was all live," says Biondi. "It brought home to us just how important pathologists are in medicine. These men and women—often called doctors' doctors because of their critical role in diagnosing diseases—are among the unsung heroes of medicine," Biondi says. Thus was born a new program, "Unsung Heroes," through which Olympus intends to honor these lesser-known diagnosticians. High-power microscopes are the pathologist's most important technical tool. Olympus, using cutting-edge technology, manufactures some of the finest scopes. And so, the company has decided to provide high-end Olympus BX40

clinical microscopes to deserving pathologists who will be identified in a nationwide search.

Unsung Heroes awards will go to pathologists who have made dramatic or key diagnoses or important research discoveries, as well as to those who have developed new tests or teaching methods. In addition, Olympus hopes to identify dedicated pathologists who are working with the poor and underserved in our society. State-of-the-art microscopes are very expensive but they can be lifesaving tools. The recipients of the first Unsung Heroes awards will be announced at the annual meeting of the College of American Pathologists in New Orleans this fall.

TALKING THE TALK

A physician may conduct 150,000 medical interviews in the course of a typical career and the information exchanged may be critical to the patient's health and prospects for recovery. Yet communicating effectively with patients has received short shrift in the nation's medical schools and training programs. The Bayer Institute for Health Care Communications aims to redress this imbalance in three ways: by advocating aggressively for the fundamental importance of doctor/patient communication; by sponsoring innovative research; and by offering "hands-on" communications workshops.

Most patients visit a doctor with a host of anxieties, but physicians tend to focus only on the presenting symptom or primary reason for the visit: an infection? a stomach disorder? a rapid heartbeat? "Doctors are not trained to see beyond the primary ailment," says Associate Director Maysel Kemp White, Ph.D. "We train doctors to not only ask 'Why are you here?' but also 'What else is the matter?' as many times as it takes to get to the end of a patient's concerns." The institute stresses that fruitful communication is both art and science. It is a skill that must be learned and mastered. More than a hundred medical centers, health maintenance organizations, and even the vast Department of Veterans Affairs apparently agree.

Since 1989, the nonprofit institute, founded and supported by the pharmaceutical division of the Bayer Corporation, has conducted more than 2,750 workshops for more than 40,000 clinicians in all stages of their careers. "Because research has shown that lectures seldom change communication behaviors, workshops are interactive and experiential rather than didactic," says White.

The Bayer Institute has contributed approximately \$600,000 since 1993 to attract new investigators and jump-start research studies in the burgeoning field of health-care communications. In addition, investigators at the institute also conduct original research if a topic piques their curiosity. Maysel Kemp White has recently completed a study focused on improving communication for women with breast disease. "Traditionally, doctors did not treat patients as partners," explains White. "But we now know that when there's a true partnership, patients have better health outcomes. Even in a situation where there's no hope for recovery, patients' quality of life will be improved," she says.

One of the nation's great communicators, former Surgeon General C. Everett Koop has cautioned that providing good primary care and prevention "calls for physicians with communication skills of the highest order." He added, "The Bayer Institute, through its education, research, and advocacy, is making a significant contribution to this endeavor."

LOOKING FORWARD

When Congress created Medicare in 1965, prescription drug benefits were not included because drugs played nowhere near the central role in the prevention and treatment of disease that they do today. But the development of useful drugs has been one of the most significant accomplishments in medicine during the past thirty or forty years, a fact brought home in the current debate about including prescription drugs in the Medicare program.

"I honor the research and development of new drugs by our pharmaceutical companies," said President

Clinton last month in Michigan, noting that "the government spends billions of dollars every year supporting such research, and we should." This topic is much on the President's mind as he debates with Congress over how to spend the nation's billions of dollars of budget surplus. Clinton ranks biomedical research right alongside education, defense, and the environment as a national priority that ought to receive a slice of the surplus pie. Long an advocate for health-related research, the President, in his 1998 State of the Union Address, proposed a "Twenty-first Century Research Fund for pathbreaking scientific inquiry—the largest funding increase in history for the National Institutes of Health, the National Science Foundation, the National Cancer Institute." Appealing directly to the American people, Clinton asked them to support his proposal so that, as he put it, "Ours will be the generation that finally wins the war against cancer, and begins a revolution in our fight against all deadly diseases."

AN OUNCE OF RESEARCH IS WORTH A POUND OF CURE

At a recent conference sponsored by the Funding First program of the Mary Woodard Lasker Trust—an initiative that seeks to stimulate the nation's financial commitment to medical research—distinguished scientists, budget analysts, and public policy experts engaged in a spirited debate about petitioning Congress to devote a fraction of the anticipated, multibillion dollar budget surplus to medical and health-related research.

Our congressional leaders propose using some of the surplus to save social security and Medicare and some to bolster our national defense. Lasker/Funding First thinks it is imperative to allocate a portion of the remaining surplus for research. The public apparently agrees. Recent polls indicate that there is broad support throughout the country for doubling the federal investment in medical research over the next five years. Funding First believes that good health stems from innovative research and that our lives may depend on it.

To read the conference report or for more information about Funding First, visit www.fundingfirst.org. Information about the Albert and Mary Lasker Foundation can be found at www.laskerfoundation.org.