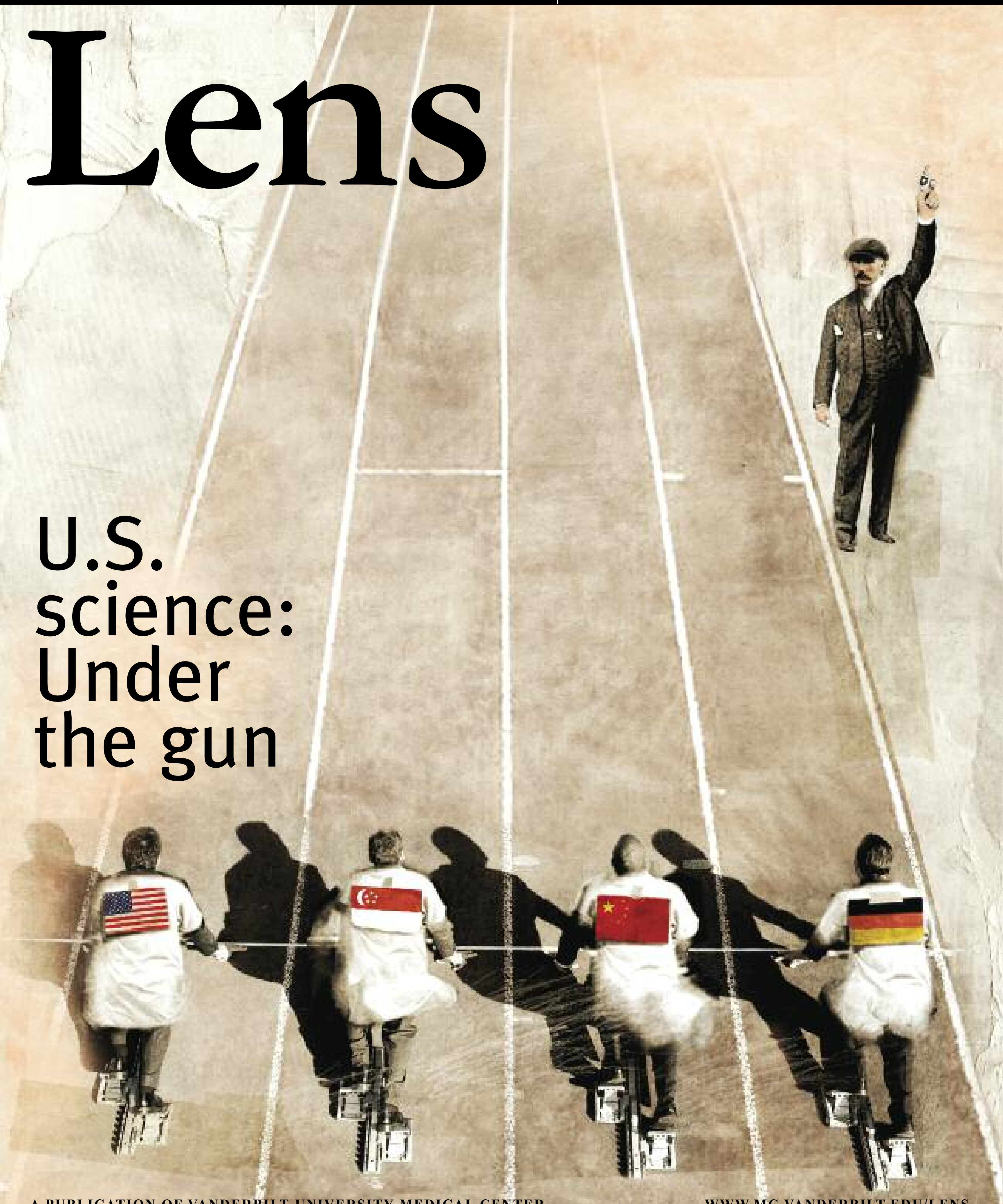
WINTER 09

Lens



U.S. science: Under the gun

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Lens –
A New Way of Looking at Science

WINTER 2009

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Cover: New competitors emerge in the race for discovery.
Illustration by Antonello Silverini (http://antonellosilverini.myblog.it).

The true worth of an experimenter consists in his pursuing not only what he seeks in his experiment, but also what he did not seek.

–CLAUDE BERNARD

Lens is published twice a year by Vanderbilt University Medical Center in cooperation with the VUMC Office of News and Public Affairs and the Office of Research. *Lens*® is a registered mark of Vanderbilt University.

Our goal: to explore the frontiers of biomedical research, and the social and ethical dimensions of the revolution that is occurring in our understanding of health and disease. Through our *Lens*, we hope to provide for our readers – scientists and those who watch science alike – different perspectives on the course of discovery, and a greater appreciation of the technological, economic, political and social forces that guide it.

Lens
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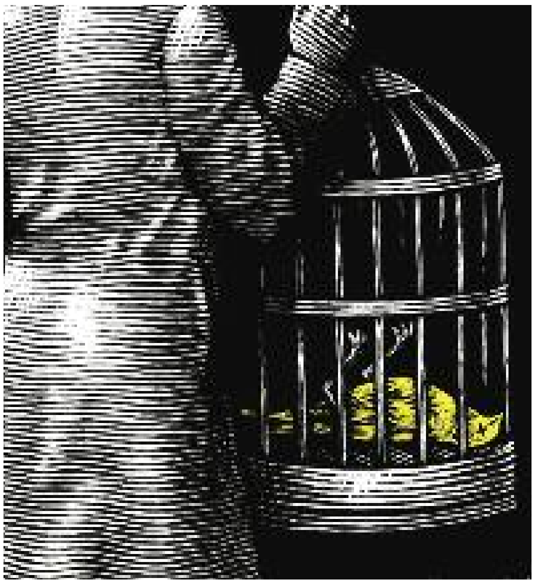

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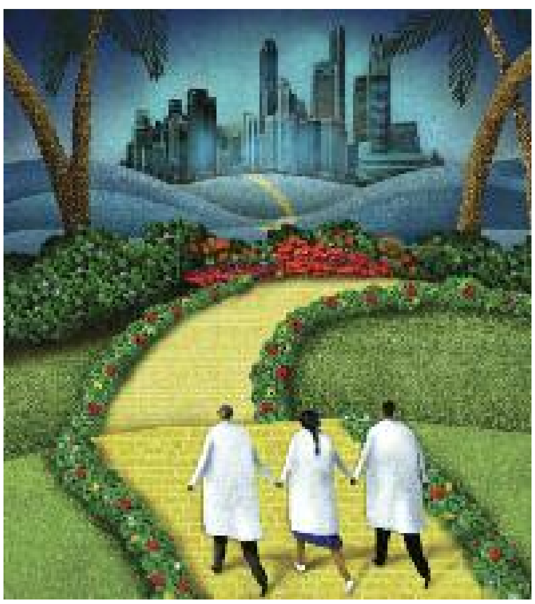


page 18 It's a beautiful place to work

Challenge and opportunity

How academic medical centers can help reverse disturbing trends

By Jeff Balser, M.D., Ph.D.

Dean, Vanderbilt University School of Medicine
Associate Vice Chancellor for Health Affairs

"In the middle of every difficulty lies opportunity."

– Albert Einstein

The nation's biomedical research community is indisputably experiencing challenging times. The budget of the National Institutes of Health (NIH), the primary source of biomedical research dollars, has not increased for several years; when adjusted for inflation, NIH funding has actually declined by 13 percent over the last five years. This, combined with a decline in U.S. students choosing academic research careers[1] ultimately may have a negative impact on worldwide health and could lead to the erosion of biomedical science as a fundamental pillar of the U.S. economy.

In short, we are sowing the seeds of attrition in a magnificent edifice: our nation's biomedical research enterprise.

This issue of *Lens* magazine examines this unprecedented challenge to our future, and explores ways that we – the research community at Vanderbilt University Medical Center with our colleagues throughout the country – can advocate responsibly and effectively for progress.

Why is Vanderbilt raising its voice?

We are among the fortunate academic medical centers that are seamlessly connected to a leading research university, and we have leveraged that overall strength and connectivity to invest in programs that will greatly accelerate the realization of individualized and cost-

It is our responsibility to clearly articulate why expanding biomedical research – even at a time of economic adversity – will allow us to leap forward.

effective drug discovery, diagnostic testing and healthcare delivery. It is therefore our responsibility to clearly articulate why expanding biomedical research – even at a time of economic adversity – will allow us to leap forward and dramatically improve both our economy and the treatment and prevention of human disease, while reducing the cost of health care for our nation.

Here's why. The science funded by NIH has a far broader economic impact than in the long-term improvements in health care and quality of life; broader even than the direct effect of dollars invested across our campuses. Every $1 of NIH money spent results in about $2.30 in economic output (increased goods and services) in the local and state-wide economy, according to a June 2008 report by Families USA.[2] In fiscal year 2008, for example, Vanderbilt University Medical Center received over $420 million in funds from outside agencies, the majority from the NIH and other government sources. This resulted in more than $1 billion of new business activity that created and supported more than 7,000 jobs at wages that greatly exceed that national average.

For the next fiscal year (2009), the national research community is calling for a budget increase of 6.7 percent for NIH, which would keep pace with inflation plus provide an additional 3 percent to begin to make up for recent years in which funding has fallen relative to inflation. Such an increase ($1.4 billion) would translate into approximately $60 million in business activity gains in Tennessee alone, and more than 200 new jobs with more than $20 million in wages.

Nationwide, we would see approximately $3 billion in new business activity and over 9,000 additional jobs with $1.1 billion in new wages, according to the Families USA report. This is a minimum economic return of three-to-one even if NO health care benefits resulted from our investment in biomedical science!

But of course the health benefit of biomedical research also can yield an impressive return on investment.

In 2006, University of Chicago economists Kevin Murphy, Ph.D., and Robert Topel, Ph.D., estimated that increases in life expectancy between 1970 and 2000 "added about $3.2 trillion per year to national wealth, with half of these gains due to progress against heart disease alone."[3] While it is difficult to determine exactly how much of this progress can be attributed to medical research, it is well accepted that the dramatic drop in heart disease mortality in recent decades is due to improved understanding of the role of cholesterol, and resultant changes in diet, interventional procedures and new pharmaceuticals.

Currently there are more than 500 potential drugs for complex diseases in clinical trials in the United States, yet only about 50 percent of the patients enrolled in these trials will experience a positive result, and fewer than 20 new drugs make it to the marketplace every year.

Why is the success rate so low? One reason is that genetic variation has a huge impact on our individual responses to medications. Because of this variability, pharmaceutical trials must be conducted in very large patient populations, at considerable cost (approximately $1 billion per drug), and over a long period of time (it can take a decade to complete some studies). As a result, few novel therapeutic agents make it through the pharmaceutical pipeline. If one could define, in advance, which individuals or populations would be most likely to benefit from a specific therapy, smaller studies at substantially less cost would be required, and the constricted pipeline of new drugs would literally burst open.

VUMC is investing heavily in personalized medicine – that is, identifying and characterizing the molecular diversity among individuals through test results, tissue samples, and an electronic database of health and genetic information. Our "DNA databank" now contains over 60,000 samples, and is among the fastest growing DNA repositories worldwide. Thanks to large-scale, global investments in biomedical informatics over the past decade, information gleaned from samples can be stripped of identifying information to protect patient privacy. This work is laying the foundation for the identification of biomarkers that will dramatically improve the output of new diagnostics and drugs, and at a fraction of the cost.

Vanderbilt also recognizes that in order to maintain and grow a vibrant research enterprise, we need a renewable talent pool entering our institution to innovate and solve big questions about health and disease. Yet the national statistics are disturbing: U.S. students continue to lag behind their peers in other countries in science achievement scores, college completion rates are low, and fewer choose academic research as a career.

It becomes our challenge and opportunity as an institution of higher education to help reverse those trends by supporting programs that provide enhanced, accelerated and engaging science curricula to students in high school and even earlier. Several of these programs are described in this issue.

These are but a small fraction of the many novel initiatives that we and our colleagues in biomedical science across the nation and around the world are undertaking to advance human health. We must commit ourselves to making the case, clear and strong, for increasing our nation's investment in biomedical research. Together we can turn these uniquely challenging times into ones of great opportunity – for our academic medical centers, our local communities, and for the nation and global community we are privileged to serve. **LENS**

[1] Karen Hede, "The Job Outlook for Physician Scientists," *Science*; Dec 5, 2008

[2] "In Your Own Backyard: How NIH Funding Helps Your State's Economy," a report by Families USA's Global Health Initiative, June, 2008

[3] Murphy, K.M., and Topel, R.H., "The Value of Health and Longevity," *Journal of Political Economy*, 114: 871-904, October 2006

UNCLE SAM: SCIENTIST

BY LISA A. DUBOIS
ILLUSTRATION BY NORMAN ROCKWELL

During the last century, America soared to the top of the world in science and technology. The United States outstripped all other countries in the number of science-related Nobel prizes awarded, in bringing new biotechnical products to the market, and in the amount of money spent on basic research. ☆ ☆ ☆ Here, at the beginning of the 21st century, however, Uncle Sam's position of strength is in peril, hamstrung by the triple-whammy of reduced federal funding for basic research, a flagging biotech industry, and a public education system so rife with inadequacies that it is failing to turn on young people to careers in the sciences.

IRONICALLY,

at the same time that the United States is trying to hold on to its frontrunner status, countries like China and Singapore, among others, are muscling up and making massive federal commitments to support research and technology. These nations are banking on a concept that some now see as the backbone of economic wealth in the new century: innovation. Investment in innovation creates new industry, strengthens the national education system and improves the well being of the citizenry at large.

Competition from foreign countries for innovative discovery should be a healthy phenomenon. The problem is that America seems to be on the verge of conceding the race. "America is losing its innovation edge with profound implications for our security and prosperity as a nation," corporate consultant and author John Kao, M.D., M.B.A., told *The Huffington Post* last year.

"The genius of the American system is the ability to create new things based on new knowledge," adds Ellen Wright Clayton, M.D., J.D., professor of Pediatrics and Law at Vanderbilt University. "And if we don't have that, then I think it really affects the vitality of the country. I think that it really is based on creativity, and without that, the heart's gone."

J. Michael Bishop, M.D., chancellor of the University of California, San Francisco (UCSF), is optimistic that, given its past, the nation will rise to the challenge of its future – in biomedicine as well as the equally competitive areas of engineering and computer science.

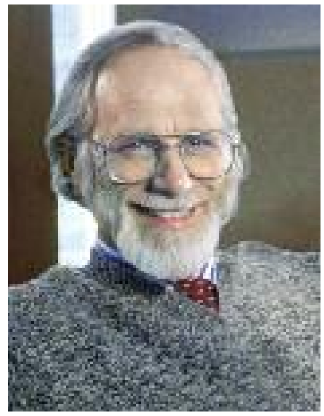
"For the moment, we still have the front rank in the world in biomedical science," says Bishop, who shared the 1989 Nobel Prize in medicine with Harold Varmus, M.D., for their discovery of oncogenes. "What has distinguished our science in the world has been its extraordinary breadth of diversity. We've taken on just about every accessible challenge that exists in biomedicine."

NEIL BRAKE

ELLEN WRIGHT CLAYTON, M.D., J.D., DIRECTOR OF THE VANDERBILT CENTER FOR BIOMEDICAL ETHICS AND SOCIETY, CITES CREATIVITY.

In addition, Americans have shown unique insight by forging alliances between academicians and businesspeople, translating fundamental research findings into products that are useful at the bedside and in the marketplace. Plus, the United States has fostered an enclave of venture capitalists who helped create a thriving trade in biotechnology.

"No other country has had a community of investors that even vaguely resembles the biotech venture capitalists in the U.S.," Bishop says. "We've dominated the scene."



COURTESY UCSF

J. MICHAEL BISHOP, M.D., CHANCELLOR OF THE UNIVERSITY OF CALIFORNIA, SAN FRANCISCO (UCSF), REMAINS OPTIMISTIC.

Americans tend to be a practical people, and their scientific history reflects that. Prior to the 19th century, American science was famously empirical, unlike the science going on in most of Europe, which was largely based on theory and experimentation.

People in the United States applied their ingenuity to the high-tech endeavors of the day, such as the steel industry, in building bridges, roads and canals, in solving health problems caused by contaminated water systems. Yet while the physical and engineering sciences were booming, Americans lagged behind their European colleagues in the medical sciences, such as biology and physiology. Medical schools served as certificate factories, requiring only four months of study or less, and most were unaffiliated with universities or hospitals.

In the early 20th century, Abraham Flexner, Ph.D., changed that scenario. Charged by the Rockefeller Foundation to evaluate all the medical school programs in the country, in 1910 he issued the "Flexner Report," demanding that medical education require a rigorous course of study in the basic sciences and classical languages.

In response, the Rockefeller and other philanthropic foundations donated $154 million to improve the quality of American medical education. These unprecedented dollars from the private sector spurred states to begin channeling money into universities, launching an era of governmental, institutional and foundational support for biomedical science that remains in effect today.

Also in the early 1900s, the agency that was the precursor to the National Institutes of Health (NIH) moved from strictly focusing on infectious and contagious scourges like cholera and yellow fever, to developing vaccines and antitoxins, and then to investigating noncontagious problems, like pellagra, that were caused by dietary deficiencies.

IMMIGRANT SPIRIT

Some of these needs arose as immigrants, escaping wars, oppression and poverty overseas, poured onto American shores, causing

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WE LEARNED THAT FEDERAL INVESTMENTS IN BASIC RESEARCH CAN SHORE UP A STRUGGLING ECONOMY.

public health issues to bubble up to the surface of the American consciousness. Many of these immigrants also brought with them something else – a background based in scientific theory.

"During the 1920s and '30s," explains Cyrus Mody, Ph.D., an assistant professor at Rice University who teaches about the history of innovation and technology, "some of those immigrants – and especially the children of immigrants – really started to penetrate into the American scientific elite."

For example, the three American physician-researchers who were primarily responsible for the polio vaccine were of immigrant Jewish stock: Albert Sabin was born in Russia, Hilary Koprowski was from Poland, and Jonas Salk was born in America to Russian immigrant parents. Spanish-American biochemist Severo Ochoa won the 1959 Nobel Prize for his work on the synthesis of RNA. French-born Nobel laureate Andre Cournand came to the United States in 1930 and later helped develop cardiac catheterization, a technique that revolutionized treatment of heart disease.

Essentially, as a new pool of intellectuals began establishing laboratories in the U.S., the quality of biomedical science quickly vaulted to the top of the chain.

The Depression almost destroyed this progress when the endowments for many foundations supporting research crashed with the stock market. Thanks to the efforts of Louisiana Senator Joseph E. Randall, Alabama Senator (Joseph) Lister Hill and others, the U.S. government stepped in and began funneling money into the NIH to support basic scientists working on fundamental medical research, and to prevent America from losing its edge in this arena.

The aftermath of World War II solidly established the NIH as the major player in American biomedicine. For the first time, leaders realized that federal investments in basic research could actually shore up a struggling economy. Largely under the directorship of James A. Shannon, M.D., Ph.D., the NIH budget expanded from $8 million in 1947 to more than $1 billion in 1966. What's more, those dollars had a direct impact on state revenues, because they were spread to 128 academic medical centers scattered across the country.

"Research dollars flow back into the local community with a fivefold multiplier effect," notes Heidi Hamm, Ph.D., chair of Vanderbilt's Department of Pharmacology. "There is a real economic benefit of doing research."

DEAN DIXON

★ ★ ★

VANDERBILT PHARMACOLOGY CHAIR HEIDI HAMM, PH.D., BELIEVES RESEARCH HAS A "FIVEFOLD MULTIPLIER EFFECT" ON THE LOCAL COMMUNITY.

For the next 35 years, various presidents and legislators continued to grow the NIH budget, convinced of the parallels between personal health and economic health, between innovative research and international leadership.

The hallmarks of American research have been its lack of hierarchy and its encouragement of independence. Grants submitted by young investigators are evaluated on a level playing field with grants submitted by senior scientists, even by Nobel laureates. Researchers are allowed to pursue their personal areas of interest, and even to change course if they so choose.

Also, they are not limited to government funding, as a number of private foundations, notably the Howard Hughes Medical Institute (HHMI), provide substantial support for basic biomedical research. The career trajectory of Harvard's Douglas Melton, Ph.D., illustrates this distinction.

An HHMI investigator, Melton was studying the developmental biology of frogs, when his infant son was diagnosed with type 1 diabetes. Anxious to address the needs of his child, Melton turned his attention to stem cell research. He later approached the scientific review team at HHMI, explaining why and how he wanted to switch directions and study pancreatic beta cells. The reviewers examined his proposal and agreed to continue his funding. Melton is now one of the leading stem cell researchers in the world.

The advantage to this system, which is fairly unique worldwide, is that it's a tremendous motivator to young scientists, says Steven McKnight, Ph.D., professor and chair of biochemistry at the University of Texas Southwestern Medical School. "If they succeed, they get all the credit for their discoveries," McKnight says. "The flip side is that if they fail during four, six or eight years in the lab, they don't get tenure and they lose their jobs. Job security depends upon success."

Based on any number of measurements, this system of rewards has tended to breed excellence. Americans have surpassed their European and Asian counterparts in the number of breakthrough discoveries, an advantage that continued throughout the George H.W. Bush and Bill Clinton presidencies.

ECONOMIC DRAIN

The trend of increased federal support came to an abrupt halt, however, during the George W. Bush administration, which funded the NIH at a flat level, amounting to a negative sum gain in research grants when factoring in the inflation rate.

Scientists complain that the flat NIH budget is squelching

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"IF WE DON'T INVEST IN SCIENCE AND EDUCATION, WE WILL BECOME A SECOND-RATE COUNTRY."

innovation and slowing progress. In the neurosciences, for example, the funding crunch has essentially squandered momentum that was blazing new inroads in the 1990s, the "decade of the brain," asserts Randy Blakely, Ph.D., director of the Vanderbilt Center for Molecular Neuroscience.

During this period, "we saw the convergence of the disciplines of molecular biology, genetics, biochemistry, brain imaging, developmental biology and translational work," Blakely says. "We got up to speed to really tackle most, if not all of the major brain diseases. Then we geared down."

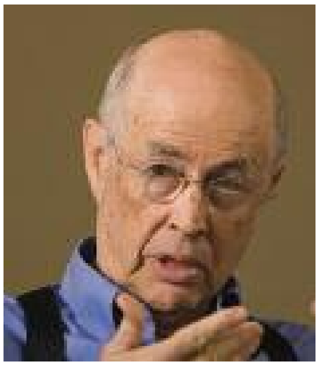
This has happened at a most inopportune time, he continues. The American population is aging, which automatically puts more people at risk for neurological diseases of the elderly, like Alzheimer's and Parkinson's. Also, soldiers returning from the wars in Iraq and Afghanistan with neurological problems and traumatic brain injuries are taxing the boundaries of current medical knowledge.

Inadequate funding of research ultimately is a drain on the economy, scientists insist.

"Biomedical science is a huge part of the economic engine of this country," says Jeff Balser, M.D., Ph.D., dean of the Vanderbilt University School of Medicine and associate vice chancellor for Health Affairs. "Science is fueling start-up companies and industry because it's discovered, published. It's information available that those companies use to do their next thing."

One reason Congress agreed to double the NIH budget, from $13.6 billion in 1998 to $27.3 billion in 2003, was to preserve the preeminence of the country's pharmaceutical industry, says John Oates, M.D., founding director of Vanderbilt's Division of Clinical Pharmacology.

JOE HOWELL



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JOHN OATES, M.D., BELIEVES FEDERAL SUPPORT IS KEY TO MAINTAINING THE NATION'S PHARMACEUTICAL PIPELINE.

NIH is the powerhouse for the discoveries necessary for the development of new drugs. "If we lose our superiority in that area, it's going to be one more area that we're not exporting in," Oates argues. "We'll have to go back to making shoes and sending them to China."

Jack Dixon, Ph.D., HHMI's chief scientific officer and former dean for Scientific Affairs at the University of California, San Diego, agrees.

"I think it's essential to be on the front-end of discovery," Dixon says. "The molecular biology revolution, if you want to call it that, is based upon discoveries that happened in academic labs across the country. We have dozens and dozens of drugs and compounds on the market today that wouldn't have happened if we hadn't had those early discoveries taking place in the United States."

This view is not universally shared. Slipping in science should not affect the nation's bottom line, some observers argue, because we can simply exploit discoveries made by others.

According to Christopher Hill, Ph.D., professor of public policy and technology at George Mason University, companies as diverse as Google and Wal-Mart have become wealthy not by applying research conducted in the United States, but "by structuring human work and organizational practices in radical new ways."

In an article published in the policy journal *Issues in Science and Technology* in March 2007, Hill maintained that the United States has already begun to move into what he calls a "post-scientific society," one in which "the leading edge of innovation … whether for business, industrial, consumer, or public purposes, will move from the workshop, the laboratory, and the office to the studio, the think tank, the atelier, and cyberspace."

Harvard economist Richard Freeman, Ph.D., agrees. He told *The New York Times* in April 2008 that Americans should worry less about their nation's research status and more about "developing new ways of benefiting from scientific advances made in other countries."

While it is true that, especially in this age of ubiquitous electronic communications, scientific advances made in one country are almost-instantaneously shared with the rest of the world, there still are strong arguments in favor of retaining a leadership position in research.

For one thing, a lively and well-supported scientific enterprise has characterized countries, dating back to ancient Greece, that have had a transformative impact on the world. "It's not a prediction," says Melton, "it's sort of a fact, based on history, that if we don't invest in science and education, we will become a second-rate country."

For another, "homegrown" biomedical research can be more readily applied to solving the unique health challenges that emerge from the nation's ethnic and genetic melting pot.

STRENGTH IN DIVERSITY

The recent revolution now driving our understanding of the genetic underpinnings of disease means that for the first time we may be able to solve some of the age-old riddles confronting portions of our population: why cystic fibrosis, for example, occurs more commonly among people of Northern European descent, why Pima Indians have such a high rate of diabetes and obesity, and why African-American women are more likely to die of breast cancer than their white counterparts.

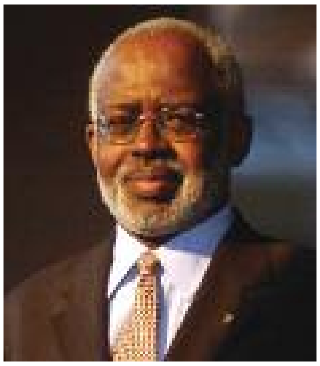
Studies of diverse minority groups also can advance an entire field of inquiry. For example, the BRCA1 and BRCA2 cancer genes were identified by researchers trying to find out why Ashkenazi Jews had a higher risk of developing certain breast and ovarian cancers. By isolating the genetic, environmental and dietary variations among America's ethnic subsets, scientists can better understand how certain diseases progress in the greater population.

"The idea that fundamental research can go on elsewhere, and then we can optimally translate it into our health care system I think is an illusion," argues Clayton, who directs the Vanderbilt Center for Biomedical Ethics and Society.

"It's like the way most people use a computer … They more or less can get stuff done, but because they don't have a clue how it works, they don't maximize the extent to which they use it."

George Hill, Ph.D., Vanderbilt's associate dean for Diversity in Medical Education, agrees that the United States has scarcely scratched the surface of the scientific opportunities provided by its heterogeneous population. Only he would go further: America's strength lies in the diversity of its scientists, as well as its population.

"When you have individuals who have been affected by these diseases in our educational pipeline, when you have people of color, Asian-Americans, African-Americans, Hispanics, etc., some of them are going to be interested in conducting research in these areas," Hill argues. "When bright, inquisitive men and women from a wide variety of backgrounds attack these problems, we have a much better chance of getting to the answers that much faster."



DANA JOHNSON

AMERICA'S STRENGTH LIES IN THE DIVERSITY OF ITS SCIENTISTS, SAYS VANDERBILT'S GEORGE HILL, PH.D.

As powerful as these arguments may be, they may not persuade, given all of the other economic and security challenges facing the country. But wouldn't it be interesting if the answers to our current flailing economy and inroads to world peace were found not in the halls of Congress or on the floors of Wall Street, but rather in the basic science laboratories of the United States?

"I'm hopeful that the collapse of the U.S. financial industry will make it clear to the leadership and to the American public that science and technology have been and must be the source of our future economic health," says Bruce Alberts, Ph.D., professor of biochemistry and biophysics at UCSF and past president of the National Academy of Sciences (NAS).

TOM KOCHEL

BRUCE ALBERTS, PH.D., IS HOPEFUL THAT THE GLOBAL COMMUNITY OF SCIENTISTS CAN BE THE CATALYST FOR "PEACE AMONG NATIONS."

During his tenure at the NAS, Alberts joined a chorus of scientific voices that called for raw data from the newly sequenced human genome to be released into the public domain. The data "should be made freely available to scientists everywhere in order to promote discoveries that will reduce the burden of disease, improve health around the world, and enhance the quality of life for all humankind," he said at the time.

Alberts and others realized that they could best serve the greater good by sharing the newfound information rather than hoarding it. And such has been the case. Releasing the human genome map to the world has launched new exploration into human genetics and into targeted therapies for treating individual patients.

"The scientific community may still be the only truly global community," says Bishop, UCSF's chancellor. "And one of the greatest satisfactions for me is being a part of that community – a community that is by and large unselfish, by and large sharing. One where we're working toward a common purpose across nations, one in which we're speaking the same language, not only linguistically, but in terms of ethos and ambition."

Bishop concedes that his view is optimistic. "But (we) believe that since science is the strongest and most cohesive global community in the world, it can be the catalyst for international cooperation and peace among nations." **LENS**

The case for serendipity

Progress in biomedical science owes much to serendipity. Basic research, the simple curiosity about how things work, has led to many of the discoveries that have transformed health, medicine, and our understanding of human disease. Here is *Lens* magazine's list of the "top 10" discoveries in biomedical science in the 20th century.

BY GARY KUHLMANN

Penicillium mold in a Petri dish.
Image provided by Visuals Unlimited.

1910
Genetics

EXPERIMENTING WITH THE common fruit fly, *Drosophila melanogaster*, Columbia University embryologist Thomas Hunt Morgan demonstrates that genes are the mechanical basis of heredity, thereby launching the modern science of genetics. ¶ Morgan reportedly tells colleagues about experiments that lead to unexpected results: "They [the flies] will fool you every time." His first attempts to find tractable mutations fail, but Morgan perseveres and discovers the white-eyed fly, which leads to his discovery of sex-linked inheritance.

1913
Cholesterol

A RUSSIAN FINDING – that cholesterol is the main dietary culprit in atherosclerosis – languishes for decades until researchers at the University of California, Berkeley, establish in a landmark 1950 paper the role of lipoproteins in the disease. ¶ In the early 1970s, Michael Brown and Joseph Goldstein at the University of Texas Southwestern Medical School in Dallas discover cholesterol receptors and the mechanism by which blood cholesterol is regulated. After a National Institutes of Health study establishes that lowering cholesterol lowers the risk of heart attack, the stage is set for the introduction of the first cholesterol-lowering statin drugs in 1987.

1928
Penicillin

SCOTTISH BACTERIOLOGIST Alexander Fleming accidentally grows a culture of penicillin in a dirty Petri dish. At the outbreak of World War II, scientists at Oxford University, working with scant wartime resources, show penicillin can clear a range of infections without the toxic effects of sulfa drugs. ¶ To keep the precious culture out of the hands of Nazis, it's smuggled into the United States, and the mold thrives in the corn steep liquor (the syrupy byproduct of corn starch production) in a federal fermentation research lab in Peoria, Ill. By 1943, penicillin makes it to the battlefields, where it saves the lives of thousands of wounded Allied soldiers.

A 3-year-old boy before, and several weeks after receiving insulin in 1922. Photos courtesy of Eli Lilly and Company Archives.

1921
Insulin

WHEN CANADIAN SURGEON Frederick Banting gives up his struggling practice, he goes into the research laboratory to follow a nagging hunch about a cure for diabetes. In 1921, he and his assistant Charles Best reverse diabetes in a dog by injecting a concoction of pancreatic extracts. ¶ John J.R. McLeod and James Collip at the University of Toronto help them purify the extract, and in 1922, insulin saves the life of 14-year-old Leonard Thompson. Within a year, the manufactured protein becomes available worldwide.

1950 Psychotropic drugs

AN OBSERVATION by French naval surgeon Henri Laborit that the antihistamine promethazine promotes "euphoric quietude" in patients being treated for shock leads to development of one of the first psychotropic drugs, chlorpromazine. By the early 1950s, the drug, marketed in the United States under the trade name Thorazine, has become a mainstay in the treatment of schizophrenia. ¶ About the same time, two doctors in Staten Island, N.Y., Irving Selikoff and Edward Robitzek, observe that new anti-tuberculosis drugs appear to lift patients' moods. One of the drugs, iproniazid, is found to block the enzyme monamine oxidase, thereby increasing brain levels of neurotransmitters, and is championed by flamboyant New York psychiatrist Nathan Kline for the treatment of depression. ¶ Thus begins what has been called the "pharmacologic revolution of psychiatry."

1953 Double Helix

THE DISCOVERY of the double helix, the twisted-ladder structure of deoxyribonucleic acid (DNA), by American James Watson and his British colleague Francis Crick gives rise to modern molecular biology. Watson and Crick come to their pursuit with complementary backgrounds in physics and X-ray crystallography (Crick) and viral and bacterial genetics (Watson), but they act on the advice of Caltech chemist Jerry Donahue – and the first X-ray pictures of DNA taken by British chemist Rosalind Franklin – to arrive at a correct DNA model. ¶ In short order, their discovery yields groundbreaking insights into the genetic code and protein synthesis, and a few decades later, helps produce new and powerful scientific techniques, specifically recombinant DNA research, genetic engineering, rapid gene sequencing, and monoclonal antibodies.

Jonas Salk, M.D., inoculates a child against polio in 1954. Courtesy of the March of Dimes Foundation

1954 Polio vaccine

U.S. PHYSICIAN Jonas Salk defies conventional wisdom to develop the vaccine that helps eradicate polio. Contrary to the widely held view at the time that immunity develops only after the body survives infection by live virus, Salk observes that the body can acquire immunity through contact with inactivated (killed) virus. ¶ Salk tests injections of inactivated polio virus on himself and his family. Within two years of its widespread introduction in 1954, Salk's vaccine nearly eliminates polio in the United States, but a live oral vaccine developed by another American physician, Albert Sabin, later becomes the preferred alternative.

1970 Reverse transcriptase

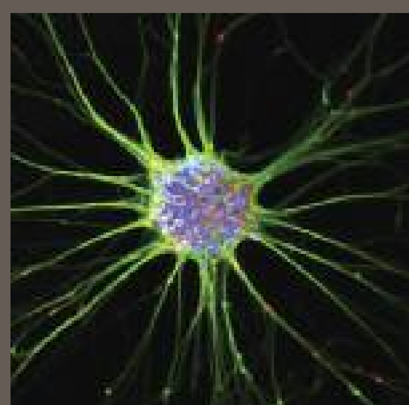
WORKING INDEPENDENTLY, David Baltimore of MIT and Howard Temin of the University of Wisconsin-Madison discover an enzyme used by certain tumor viruses to "transform" the cells they infect into cancer cells. ¶ The enzyme, called reverse transcriptase, allows these viruses to convert their RNA into DNA copies that can slip into – and alter – the cell's genetic instructions. This finding leads, in 1984, to the discovery of the human immunodeficiency virus (HIV). ¶ In recognition of their discovery, Baltimore and Temin share the 1975 Nobel Prize in medicine with Renato Dulbecco.

1970 Gene splicing

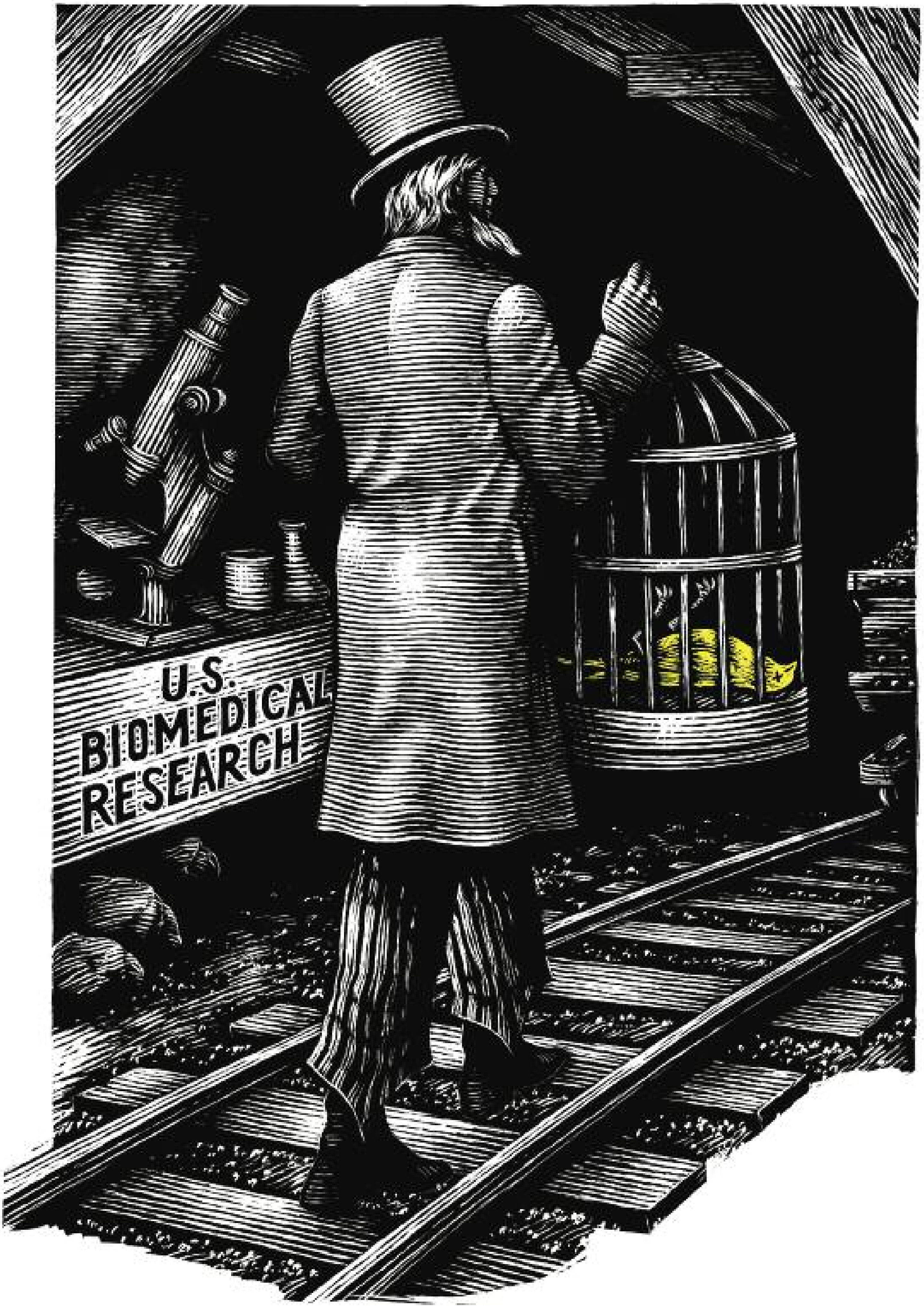
JOHN HOPKINS University microbiologist Hamilton Smith sparks a revolution in genetic research when he discovers the first restriction enzyme that cuts DNA. After this comes a flurry of follow-up discoveries: the first recombinant DNA molecule in 1972; DNA cloning in 1973; rapid DNA sequencing in 1977; DNA copying in 1983; and the first automated gene sequencing machine in 1986. ¶ Understanding DNA has paved the way to gene therapy, DNA fingerprinting, a cloned sheep named Dolly, genetically engineered crops, and efforts to sequence the human genome – a feat accomplished in 2000 by Celera Genomics and the federally funded Human Genome Project.

1981 Stem cells

RESEARCHERS IN BRITAIN and the United States, working independently, isolate cell lines from mouse blastocysts that are pluripotent. These so-called embryonic stem cells can be grown into all types of cells in tissue culture. ¶ In 1988, James Thomson and co-workers at the University of Wisconsin-Madison extract the first human embryonic stem cell line – and in 2007, the same team, simultaneously with an independent team in Japan, reports that they have successfully restored pluripotency in human connective tissues cells. ¶ The newly induced pluripotent stem (iPS) cells, as they're dubbed, reproduce steadily, meaning scientists should be able to produce an unlimited supply, and with the same chameleon-like characteristics as embryonic stem cells. The discovery gives new hope to medical scientists who have been investigating how stem cells might help treat age-related diseases such as Parkinson's and Alzheimer's, as well as stroke and diabetes.



Neurons derived from human embryonic stem cells project from a neurosphere in this confocal microscopy image taken by Sharona Even-Ram, Ph.D., of Hadassah University Hospital's Goldyne Savad Institute of Gene Therapy in Jerusalem.


U.S.
BIOMEDICAL
RESEARCH

Canary in the research lab

There are ominous signs that all is not well in the nation's biomedical research enterprise.

Thanks to five years of flat budgets at the National Institutes of Health, which supports the bulk of basic biomedical research in the United States, only about one in 10 research proposals is funded on the first submission, down from 30 percent a decade ago. As a result, young scientists increasingly are leaving university research labs, taking jobs in other countries like Singapore that have more robust research budgets, or are leaving science altogether. Perhaps most ominous: U.S. students rank below their peers in other – mostly Asian – countries when it comes to mastery of math and science.

As Microsoft founder Bill Gates put it to the House Committee on Science and Technology last March, "Too many of our students fail to graduate from high school with the basic skills they will need to succeed in the 21st century economy … Although our top universities continue to rank among the best in the world, too few American students are pursuing degrees in science and technology."

"My fear is we're going to lose a generation of young investigators," adds William Lawson, M.D., assistant professor of Medicine at Vanderbilt University Medical Center. Lawson contributed to a March 2008 report by a consortium of academic health centers, including Vanderbilt, which warned that the nation's research "pipeline" may be "broken."

BY BILL SNYDER

ILLUSTRATION BY KEN PERKINS

Some observers dispute this "sky is falling" reaction.

By many measures, from R&D spending to the annual number of highly cited publications, from the reputation of its universities, to the lion's share of Nobel laureates who work here, "the United States still leads the world in science and technology," conclude RAND Corporation scientists Titus Galama, Ph.D., M.B.A., and James Hosek, Ph.D., in a 2008 report, "U.S. Competitiveness in Science and Technology."

That may be true, but these statistics are, in a sense, "historical," replies Lawrence Marnett, Ph.D., director of the Vanderbilt Institute of Chemical Biology.

"This (report) reflects that you've got people who have been around a long time … who are in the prime of their careers and well supported for a long time and are doing a great job," Marnett says. "Looking at the future, it's very clear to me that we can't even judge how many … young people are turned off on the whole notion of going into science."

There may be, as yet, few signs of calamity in the research lab, but there certainly are no lack of voices sounding the alarm.

"It's very discouraging to hear that many of our best young scientists are 41 or 43 years old when they receive their first grant," says Douglas Melton, Ph.D., co-director of the Harvard Stem Cell Institute who is searching for a cure for type 1 diabetes. "It's just unreasonable for society to expect that people would devote 10 to 15 years to their education and then not be given real independence until they were in their 40s."

"For young people, these are the most productive, innovative and exciting times in their careers," adds Jack Dixon, Ph.D., chief scientific officer of the Howard Hughes Medical Institute and former dean for Scientific Affairs at the University of California, San Diego. "If they're spending a lot of their time on the treadmill of writing and submitting and rewriting and resubmitting, then they're not spending their time doing experiments that will lead to breakthroughs in innovation.

"You can't let talented young scientists go unfunded for five to eight years. They will end up washing out of the system. You are basically burning up talent that took many years to develop. In the Midwest," says Dixon, who formerly taught at Purdue, Indiana University and the University of Michigan, "we call that 'eating your seed corn.'"

Inadequate funding squelches creativity, especially for young investigators, Lawson continues.

"When we put a grant in, one of our biggest criticisms is 'you are being too ambitious' or 'you're being too creative,'" he says. "This isn't just a matter of losing people. We run the risk of stifling or slowing down our discoveries because investigators are being told to avoid riskier ideas and pursue more predictable avenues with their research. Essentially, at times we have been told that, 'You need to back off. You need to make this a safe research plan.'"

Despite its limitations, the NIH has tried mightily to support innovative research.

In 2004, under then-NIH Director Elias Zerhouni, M.D., it launched the Pioneer Awards – $500,000, five-year grants to selected recipients, which gave them the rare chance to conduct high-risk, high-impact, high-potential biomedical research.

Steven McKnight, Ph.D., professor and chair of biochemistry at the University of Texas Southwestern Medical School, was one of the first Pioneer awardees. He used the funds to investigate the metabolic cycle of yeast, later transferring those discoveries to the brain in hopes of laying the groundwork for understanding what biochemical reactions drive sleep and exhaustion in living organisms, and what molecular processes are restored by the act of sleeping.

This kind of research, McKnight says, might not be "sexy," but it may be extremely important.

Zerhouni also implemented the Young Innovators Award, based on the concept that the NIH should expand beyond its standard policy to promote higher-risk research projects.

Survival of the fittest?

Marnett calls the NIH the "the crown jewel" of the U.S. government in terms of its effectiveness. Adds his colleague, Mark Magnuson, M.D., who directs the Vanderbilt Center for Stem Cell Biology, it's "probably the most successful agency that the United States government ever created in terms of its impact and how well it spends money."

And yet because its purchasing power has dropped by 13 percent due to inflation since 2003, the NIH is less able to do what it used to do so well. The scarcity of funding is particularly troublesome for young scientists.

"It's been said that in the past we raised physician-scientists like guppies

PAUL FETTERS FOR HHMI

Jack Dixon, Ph.D., HHMI's chief scientific officer, warns against "burning up talent."

JOE HOWELL

Vanderbilt's Mark Magnuson, M.D., says NIH is the "most successful agency."

where you gave birth to thousands of them and a few survived," says Nancy Brown, M.D., chief of the Division of Clinical Pharmacology at Vanderbilt.

"But when you have limited resources, it's harder for those guppies to survive," Brown says. "There are more predators. What we really need is a model like raising mammals, where you nurture people along."

It's an apt analogy. Not only is the next generation of scientists at risk, but so is the next generation of their ideas – and the potential breakthroughs that could result.

"What the lack of funding always does in any ecosystem is halt innovation," argues Jeff Balser, M.D., Ph.D., dean of the Vanderbilt University School of Medicine and associate vice chancellor for Health Affairs.

"If the NIH isn't funding the less innovative sciences, the universities can, but they can only do that for so long because there's only so much money," Balser says. "At the end of the day, the impact of a declining NIH budget is less money for pursuing highly innovative ideas."

In May 2005, U.S. Senators Lamar Alexander (R-Tennessee) and Jeff Bingaman, (D-New Mexico), asked the National Academies, which include the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine, to assess the nation's "ability to compete and prosper in the 21st century."

In response, the academies formed a blue-ribbon committee of experts in a wide range of fields, from engineering to genetics.

The committee's report, "Rising Above the Gathering Storm: Energizing and Employing America for a Brighter Economic Future," was submitted to Congress five months later. It called for, among other things, recruiting 10,000 science and math teachers each year, encouraging young people to earn college degrees in science by providing scholarships, and increasing federal investment in long-term basic research.

"The most important barrier that must be surmounted is the poor science knowledge of the teachers who are responsible for teaching science to our students," says Roy Vagelos, M.D., retired chairman and CEO of Merck & Co. who served on the committee that produced the report.

"Many of the secondary school teachers of biology, physics and chemistry have not majored in those subjects; some have never had a major course in the subject they are teaching," says Vagelos, a member of the board of the National Math and Science Initiative. "The same can be said for all of the sciences."

The report led to passage in 2007 of the America COMPETES Act, which among other things would increase recruitment and scholarship funding for future K-12 science and math teachers, advance the knowledge base of existing teachers through continuing education programs, and provide more science and research opportunities to middle and high school students. As yet, however, the law has not been fully funded.

Another challenge to the nation's research enterprise cited in the 2005 report: visa laws that restrict foreign-born, American-trained scientists from taking jobs in the United States.

Given that immigrants have long infused lifeblood into American science – in 2008, for instance, the Nobel Prize for Chemistry went to Chinese-American Roger Tsien, Ph.D., and the Nobel Prize for Physics to Japanese-American Yoichiro Nambu, D.Sc. – the report questioned the wisdom of rewarding brilliance in the laboratory by sending scientists back to their home countries, many of which don't have the resources to support high-level research.

"There are lots of ways that we in the United States are shooting ourselves in the foot," says Bruce Alberts, Ph.D., professor of biochemistry and biophysics at the University of California, San Francisco, and past president of the National Academy of Sciences.

30 to 1 return

Why does it seem so hard to make a case for investing in biomedical science?

After all, notes John Oates, M.D., founding director of Vanderbilt's Division of Clinical Pharmacology, thanks to basic biomedical research, rheumatic heart disease "almost doesn't exist in the United States today because of antibiotics." The iron lung, which enabled victims of polio to breathe, has been retired.

Among the most dramatic success stories is the treatment of cardiovascular disease, which, in the past 20 years, has reduced the annual heart disease death rate by 600,000 – and all for a research investment of $30 per American, Hamm says.

Writing in the 2003 book, "Measuring the gains from medical research," Harvard economics professor David Cutler, Ph.D., and graduate student Srikanth Kadiyala estimated a 30 to 1

JOE HOWELL

Vanderbilt's Nancy Brown, M.D., says scientists must tell their story better.

return on that investment. "Our unambiguous conclusion is that medical research on cardiovascular disease is clearly worth the cost," they concluded.

New cancer diagnoses and cancer death rates also have fallen in recent years. However, the collection of diseases known as cancer still kills 560,000 Americans annually, and there are increasing calls for revamping the entire research enterprise in order to achieve faster progress against them.

This issue was raised last May during the annual Forum on Science and Technology Policy in Washington, D.C., organized by the American Association for the Advancement of Science.

As quoted by *Chemical and Engineering News,* Christopher Hill, Ph.D., professor of public policy and technology at George Mason University, said the public's inability to understand what scientists are doing and a growing frustration with the "failure" of science and technology to solve the world's major problems will "make the public less likely to remain convinced that expenditures on science and technology are an unalloyed good thing."

That frustration may result in a shifting of funds to "problem-solving research," Hill predicted.

One reason basic biomedical research is such a hard sell is that innovations may take many years to come to fruition.

They are characterized by years and years of painstakingly derived results, before progress begins to accelerate, eventually leading to leaps in knowledge, and finally into life-saving treatments and cures. Plus, they are often difficult to instantly visualize. It's much easier to spot innovative technology in cars, computers and cell phones.

For example, the life scientists deliberately stayed in the background while the physical scientists initially – and successfully – pitched the National Nanotechnology Initiative to Congress as a potential boon to the microelectronics industry, "because," says Cyrus Mody, Ph.D., an assistant professor at Rice University who teaches about the history of innovation and technology, "that's an industry where talk about competitiveness is always on the table."

The Human Genome Project similarly required a hard sell by scientists and a multi-billion dollar leap of faith by the government. Many politicians and academicians had doubts about the rationale for such a costly venture. Originally proposed as a way to study mutations caused by nuclear exposures, then cancer, and later genetic diseases, the Human Genome Project called upon a swarm of researchers from various disciplines to create a genetic map of the human chromosomes, identifying all the 20,000 to 25,000 genes in human DNA.

The project, completed in 2003, didn't give scientists any answers to cancer or diabetes or birth defects – but it did offer them high-resolution navigation tools and clues for where they should begin looking.

Such a sell would be more difficult today, scientists admit, given the current state of the economy and the equally urgent challenges facing the nation's health care delivery system. "In the public's mind, they see that we're 40th in health or wherever we are nationally," Brown says. "I think the public conflates the mission of the NIH with other social issues and other health outcome issues that we need to fix as well.

"We need to be very specific about the positive outcomes of NIH dollars because they're so far downstream with health outcomes and they may not understand that there are many steps in between."

"Honestly, if we don't talk about what we're doing, and if we don't sell what we're doing and point out the benefits that accrue from it, we have nobody to blame but ourselves," adds Ellen Wright Clayton, M.D., J.D., who directs the Vanderbilt Center for Biomedical Ethics and Society.

"We exist at the sufferance of the people, and so we're accountable to them and we just have to tell the story," Clayton says. "It's a great story. But that's what we have to tell them." LENS

Lisa A. DuBois and Nicole Garbarini contributed to this story

One reason why legislators and the public are not up in arms insisting upon robust support of biomedical science is because innovations in this area take many years to come to fruition.

It's not all about science

BY BILL SNYDER

Bill Stead, M.D., does a lot of thinking about connections.

As director of Vanderbilt University Medical Center's Informatics Center, he's in charge of managing an information technology infrastructure that supports Vanderbilt's patient care, research and educational programs.

As chairman of the Vanderbilt Center for Better Health, he also oversees efforts designed to help transform the nation's health care system and accelerate improvements in health care outcomes.

But although he describes himself as an optimist, Stead worries that the United States is "drifting toward … a whole series of national-scale crises," not only in health care, but in education, infrastructure, energy and the environment.

"We've now had a decade of one bubble after another," he explains. "We're getting people who are experts at making money out of chaos … (but) I think as a society we've really lost our ability to do anything important.

"We did take on high performance computing as a challenge a number of years ago. We did take on the human genome. (But) I'm not aware that we've done anything since then that has been taken on as a national grand challenge.

"It's not all about science. I believe it's a much broader cultural problem.

"We should each feel responsible for the fact that (last fall) our children (were) sitting in gas lines a generation after we did. And we've done nothing about it."

In health care, "historically we've been superb in discovering new things," Stead continues. Yet Vanderbilt, for example, is located in a state that has among the nation's worst health indicators in such areas as obesity, diabetes and low birth weight.

"Producing the best science and providing the best service isn't enough," he argues. "How do we actually get the benefit in terms of health in society? What is the transformative model that generates a major difference in results?"

Through an ambitious exercise called "Vision 2020," Vanderbilt hopes to develop such a model – one that transforms clinical practice and professional education through the rapid and efficient application of fundamental discoveries.

"We've now got 40 years of people trying to fix this (health care) system from the outside," Stead says. "I think we've actually got to fix this system from the inside."

There is concern that such targeted, "translational" research diverts funds from basic research that can lead to paradigm-shifting discoveries.

Stead believes they are not mutually exclusive. In fact, he says, "we've got to come up with new approaches for supporting fundamental research."

"What would have happened if we'd had the emergence of HIV in the '80s, and we hadn't had the previous 20 years of basic virology research? Look at how fast we grabbed that."

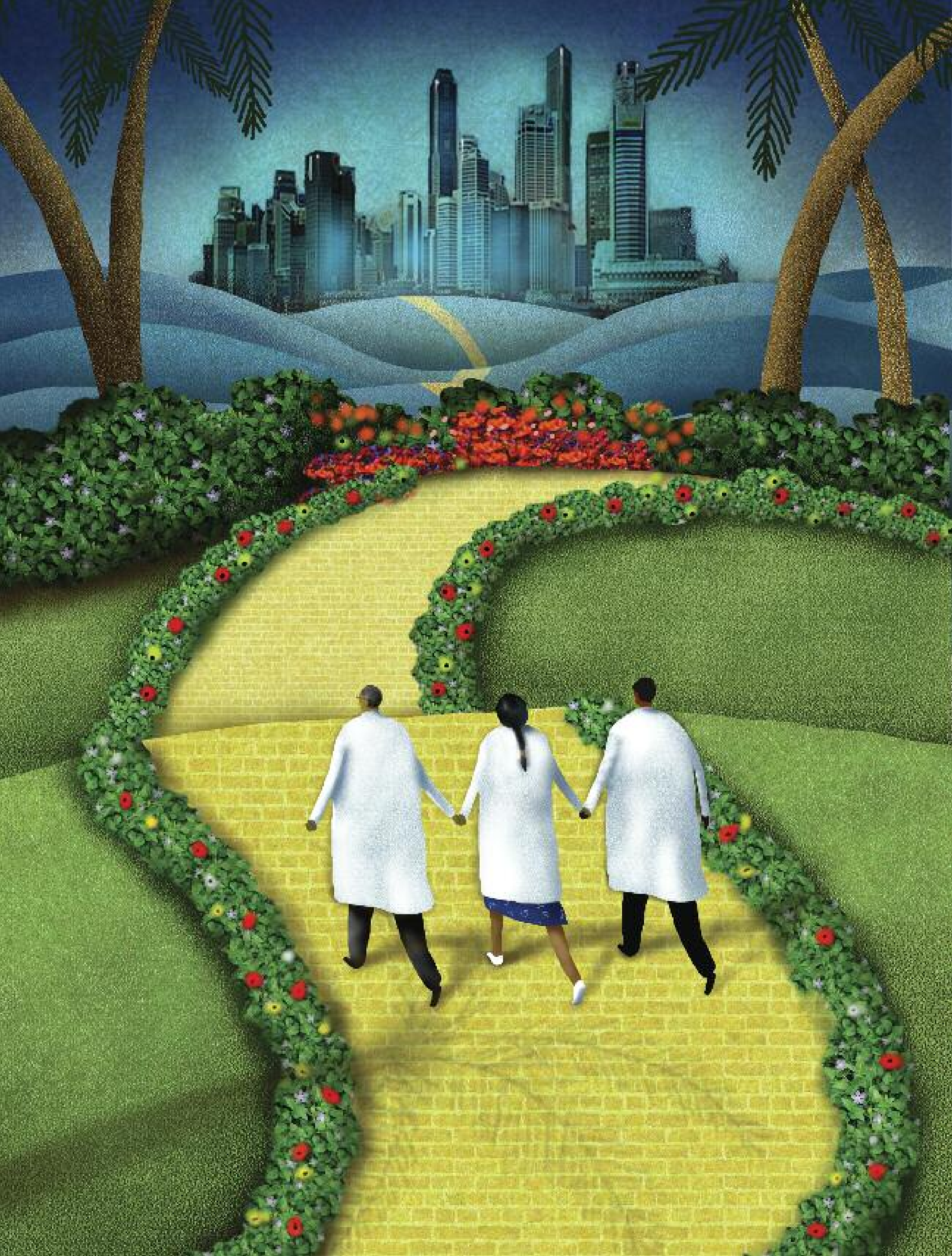
In today's world, the Internet has become as important a driver of communication and collaboration as was the printing press nearly six centuries ago. Yet Stead worries that many Americans are "coming out of school with extraordinarily limited skills."

And while it is true that the United States can benefit from lessons learned elsewhere, "I don't think we can depend on other countries to give our people the skills to solve problems," he says.

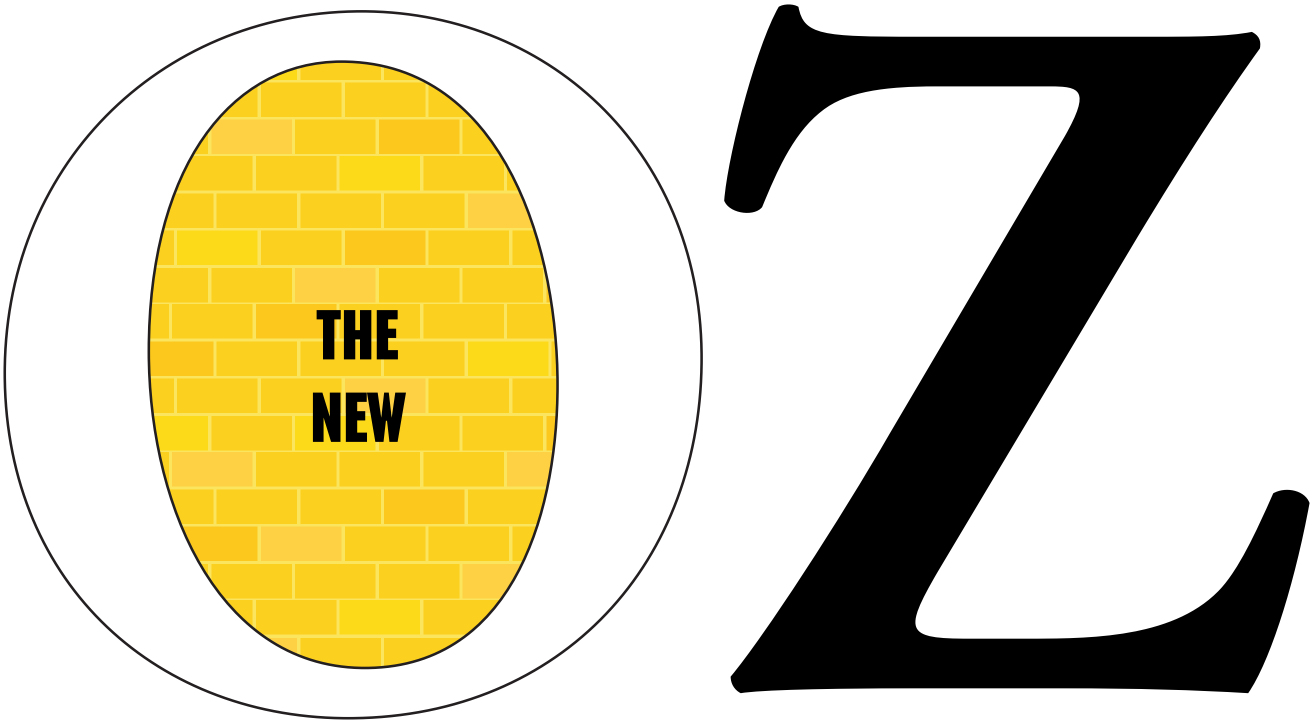
"We need to be working on the ideas we think are most important for the problems we have," Stead says. "We need to be doing things to get other people to work on those problems … (to) create the connections between the problems and the ideas … in a way that make light bulbs go off." **LENS**

JOE HOWELL

Bill Stead, M.D., leads a discussion in the Vanderbilt Innovation Center. The "scribing" on the white board was drawn by the center's production manager, Kelly Adams.



BY LEIGH MACMILLAN
ILLUSTRATION BY DAVE CUTLER



U.S. scientists follow yellow brick roads overseas

In a southern corner of Singapore, there is a biomedical research metropolis – fittingly named Biopolis – that wasn't there 10 years ago. *Science* magazine dubbed the complex a "scientific Emerald City," conjuring images of the sparkling city in "The Wonderful Wizard of Oz." Biopolis appears to offer that same sense of promise. Scientists from around the globe are following the yellow brick road to Singapore, where they are finding modern research space, excellent shared resources and secure funding.

Neal Copeland, Ph.D., laughs at the Emerald City image. "That might be a little strong," he says, "but it's certainly a beautiful place to work."

Copeland directs the Institute of Molecular and Cell Biology – one of Singapore's research institutes, similar to the National Institutes of Health in the United States. He and his wife and research partner Nancy Jenkins, Ph.D., moved their program to Biopolis in 2006, after 22 years at the National Cancer Institute.

What lured them away?

It was a number of things, Copeland says, perhaps chief among them the growing frustration of dealing with the government bureaucracy at the NCI.

"It seemed to be getting worse every year," he says. And added to that were the uncertainties of the annual budget cycle.

"We had an operating budget that didn't mean anything, and all of a sudden – six months into the fiscal year – we'd get a budget that included cuts," Copeland says. "That's not a way to run anything."

In Singapore – an island nation the size of Chicago – Copeland and Jenkins found a place where biomedical research is buzzing. The government has a vision, and the funding to back it, for vaulting Singapore into the upper echelon of biomedical research performers in one generation.

R&D spending as a share of the economy (relative to gross domestic product, GDP) is expected to reach 3 percent by 2010 (the United States spent 2.57 percent of its GDP on R&D in 2006).

"Singapore is building and growing (its research enterprise), while the United States is flat or headed down," Copeland says.

One component of the government's vision is Biopolis – a complex of (so far) nine modern buildings interlinked by sky bridges. The buildings, with names like Centros, Genome, Matrix and Proteos, house the biomedical research institutes of the Agency of Science, Technology, and Research (A*STAR) – the Singaporean equivalent to the intramural NIH campus – alongside research labs of pharmaceutical and biotech companies.

Built in two phases since 2003, Biopolis now boasts more than 2 million square feet of research space and amenities like food outlets, retail shops, and exercise and childcare facilities.

As of early 2007, Singapore had spent about $1.3 billion building and staffing Biopolis, which is part of a master plan for a 500-acre science and technology development that will include shops and homes.

"It's beautiful infrastructure," Copeland says. "It's really quite amazing what they've done in such a short period of time."

To jumpstart its ascendance as a biomedical research power, Singapore knew that it would need to import scientific talent. It has been wildly successful in its recruiting efforts. Along with Copeland and Jenkins, other prominent transplants include Edison Liu, M.D., former director of the NCI's Division of Clinical Sciences; Jackie Ying, Ph.D., formerly of MIT; Alan Colman, Ph.D., who ran the Roslin Institute where Dolly the sheep was cloned; Edward Holmes, M.D., former dean of the School of Medicine at the University of California, San Diego; and Judith Swain, M.D., former dean for Translational Medicine at UCSD.

"They're trying to do in 10 years what other places would take 25 years or more to do," Copeland says. (San Diego's transformation into a biomedical research hub took 40 years.)

"It's a very international place," he says. Among the 450 or so researchers in the Institute of Molecular and Cell Biology, "about 50 different nationalities (are) represented."

Eighty to 90 percent of the leadership of the various A*STAR institutes is foreign born, Copeland estimates. But the government has programs in place to increase the number of Singaporeans in the leadership ranks and to move the overall mix of institute researchers closer to a 50-50 balance.

It is paying the way for about 1,000 students to earn Ph.D. degrees at foreign universities by 2015, with the requirement that they return to Biopolis for five years of postdoctoral training. The government hopes that half or more will stay on.

American brain drain

In the last century, many research roads blazed a one-way path toward the United States. Increasingly, they now offer more attractive passage in other directions.

Along with top U.S. scientists heading to other lands like Singapore – an "American brain drain," writes leading innovation expert John Kao in "Innovation Nation" – foreign students and scientists who come to U.S. shores are more apt to leave.

Jeffrey Conn, Ph.D., the Lee E. Limbird Professor of Pharmacology and director of the Vanderbilt Program in Drug Discovery, notes that the best graduate student he's had since he joined the Vanderbilt faculty in 2003 intends to return to his native China to pursue academic research.

"That was unheard of 15 years ago," Conn says. "Students and scientists would come here with a desire to stay – now the best come with a desire to go back (to their home countries). It's anecdotal, but it's so pervasive that everyone sees it in their own students and experience."

Lin Mei, M.D., Ph.D., agrees. Mei is a program chief in the Medical College of Georgia's Institute of Molecular Medicine and Genetics who has watched students and research fellows return to China.

Two of his recent postdoctoral fellows, both of whom had published papers in the high-profile journals *Neuron* and *Nature Neuroscience*, have taken positions in China – one at the Institute of Neuroscience in Shanghai that Mei helped found, and the other at one of China's top five universities.

It's a sign of the times, Mei says. "China is becoming an exciting place to do research. When I was a master's student in China (23 years ago), the research opportunities were very limited; there was not much you could do. Nowadays, the

Shares of Total World R&D, 2007

Sources: American Association for the Advancement of Science (AAAS) R&D Budget Policy Program; Organization for Economic Cooperation and Development (OECD), Main Science and Technology Indicators, 2008. Data: 2007 or latest year available.

World = OECD members plus Argentina, China, Romania, Israel, Russia, Singapore, Slovenia, South Africa and Taiwan.

* – calculated in U.S. dollars using purchasing power parities.

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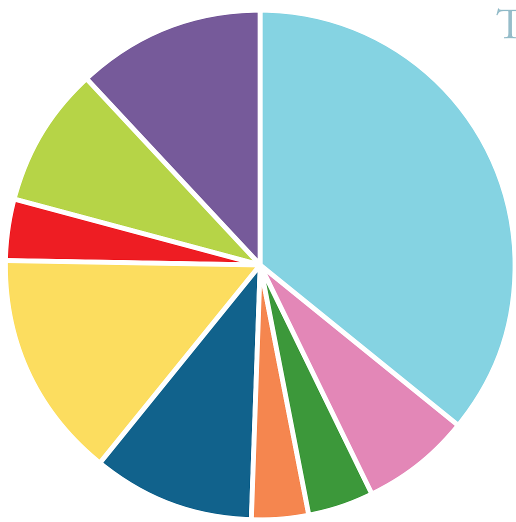
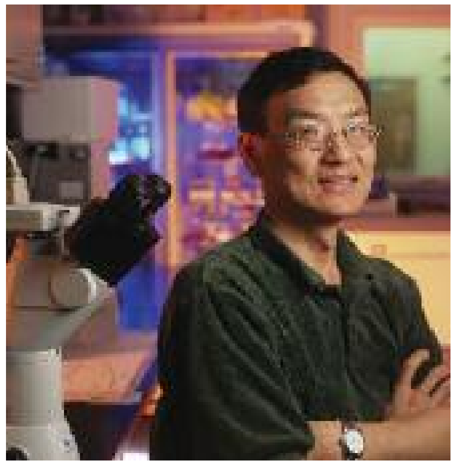


Total World R&D = $962 billion*

- US **$344**
- GERMANY **$67**
- FRANCE **$41**
- UK **$36**
- OTHER EU **$99**
- JAPAN **$138**
- KOREA **$36**
- CHINA **$87**
- ALL OTHER **$114**

At right, Neal Copeland, Ph.D., in Biopolis, and, far right, Lin Mei, M.D., Ph.D.

COURTESY NEAL COPELAND, PH.D.



BILLY HOWELL, GEORGIA RESEARCH ALLIANCE

government is investing lots of money in research."

In 2006, China announced plans to nearly double its R&D spending as a proportion of GDP within 15 years; the proportion – 2.5 percent – will be similar to that of the United States. Expenditures will grow from $30 billion in 2005 to $112 billion in 2020. (The United States currently spends about $300 billion.)

Also troubling are the foreign-born students who are no longer coming to the United States in the first place.

U.S. graduate school applications from foreign students fell 28 percent in 2004, and dropped another 5 percent in 2005, Kao writes. Among the reasons: attractive graduate programs all over the world – often at lower cost compared to American programs – and greater difficulties in obtaining student visas.

More restrictive post-9/11 immigration policies are making it difficult to attract not just students and trainees, but also foreign-born scientists.

In the 1990s, 195,000 H-1B visas (valid for up to six years) were available annually for people with technical skills and an employment sponsor. That number dropped to 65,000 in 2003. For fiscal year 2008, the limit of H-1B visas was reached on the first day that applications were accepted, according to "Science and Engineering Indicators 2008," published by the National Science Board.

"The United States has been at the cutting edge of science for the past 100 years," says Mei. "One driving force for America's global position has been an influx of highly talented immigrants. If foreign students and postdocs are not encouraged to come, if there is no effort to keep them, I see a huge problem in the future.

"How can the United States stay at the cutting edge?"

View from the Titanic

Competition for the global talent pool isn't threatening the United States' preeminence in biomedical research. Yet.

By many measures, America is on top of its game. The Council on Competitiveness wrote in its 2007 report, "Competitiveness Index: Where America Stands," that "with only 5 percent of the world's population, America employs nearly one-third of the world's science and engineering researchers, accounts for 40 percent of global research and development spending, and publishes 30 percent of all scientific articles."

But, says Richard Caprioli, Ph.D., director of Vanderbilt's Mass Spectrometry Research Center, "these numbers are where we are now. That's not what we're interested in. Where are we going to be?

"We're going to have to do better, not just stay the same. We're in a very competitive world. This business of 'Oh, we're not doing too badly' is kind of what the captain of the Titanic thought: 'Gee, so far we haven't hit an iceberg. We're OK.'"

And even though the United States does indeed sit at the number one position in rankings of countries by dollars spent on R&D and number of scientific papers published, the trends tell a different story.

Over the last 40 years, the United States has been shifting research and development spending to the private sector. In the 1960s, U.S. government dollars funded about two-thirds of the country's total R&D spending. By 2006, the government's share had shrunk to just 28 percent. Even though the private sector has stepped up to keep the United States spending about 2.5 percent of GDP on R&D, these resources "are directed more toward applied rather than innovation-generating basic research," Kao writes.

China and South Korea, by contrast, are upping their government R&D spending by 10 percent or more per year.

In terms of R&D spending as a share of GDP, America trails Israel, Sweden, Finland, and Japan, a group of countries that spend more than 3 percent of GDP annually. The United States – the country with the world's largest economy – comes in eighth, part of what Kao calls a "second tier" for R&D spending.

The trend in scientific papers published follows the same pattern. While the United States published 29 percent of the world's science and engineering papers in 2005 – more than any other country – that percentage represented a drop from 34 percent in 1995. The average annual increase in papers published by researchers in the United States was only 0.6 percent over those 10 years.

During the same time period, China and South Korea's outputs of scientific articles increased at annual rates of 16.5 percent and 15.7 percent, respectively.

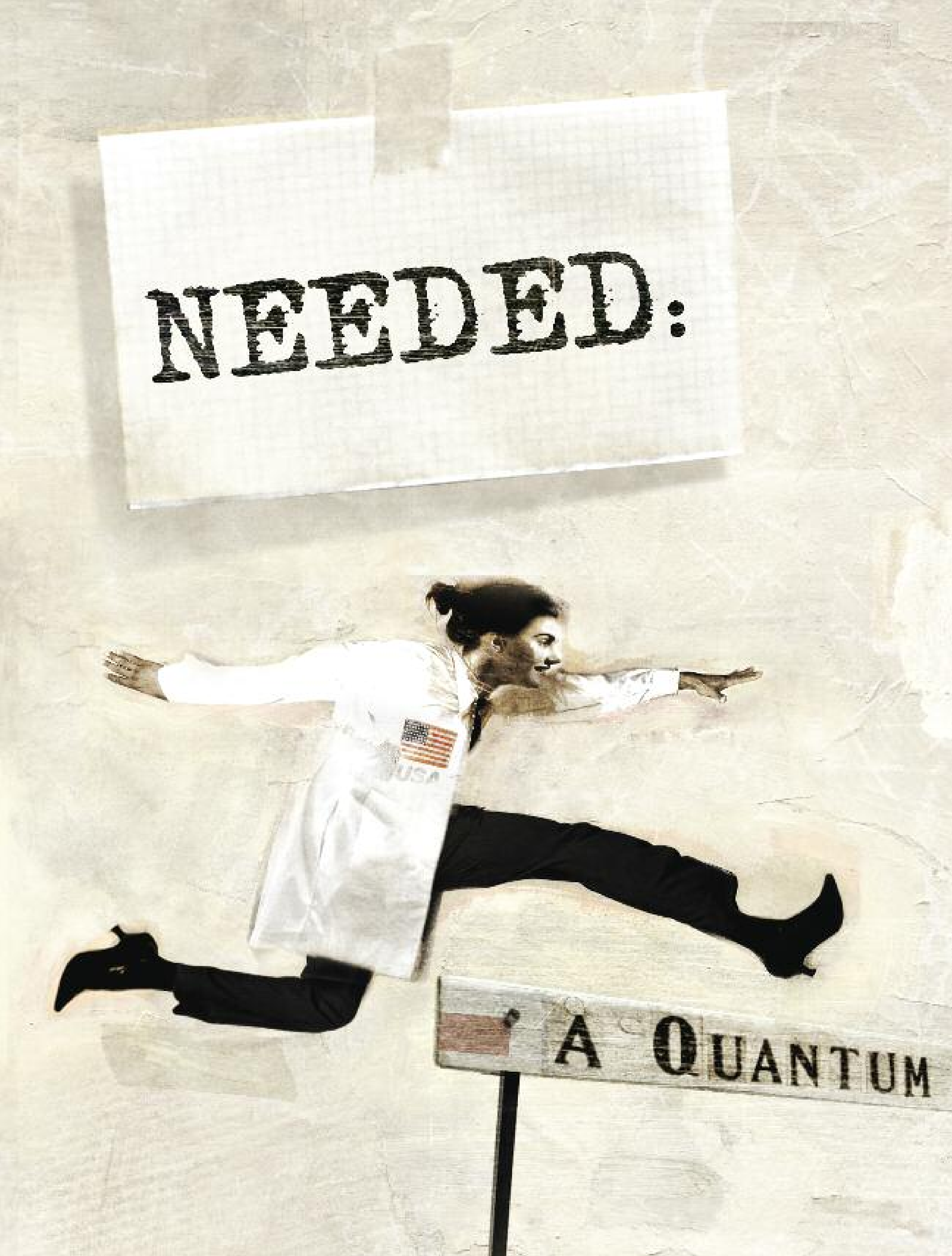
Together, the flat funding of research in the United States, failure to attract and retain scientists, and modest performance in scientific publishing signal that now is not the time for America to rest on its laurels.

The United States needs to "recognize the seriousness of the situation," wrote William Haseltine, Ph.D., chairman of Haseltine Global Health and founder and former CEO of Human Genome Sciences, in the October 2007 issue of *Discover* magazine.

"We have not yet killed the goose that lays the golden eggs of science and technology, but we have placed it on a starvation diet."

What America needs, Kao argues, is a national innovation agenda.

There's no wizard to show us the way. But with coordinated efforts, we can boost our research and development funding, grow our own talent pool through improved science education, and create our own "Emerald Cities" of discovery that attract and retain the world's most talented researchers. **LENS**


NEEDED:
USA
A QUANTUM

One of the great transformational moments in biomedical science is happening **right now.**

It's the shift from gene to cell.

"I think what we're seeing in this century now is a renewed appreciation for not DNA … but cells as being the secret to life," says Harvard stem cell researcher Douglas Melton, Ph.D. "We'll see what I might call a more synthetic biology, using information obtained from DNA to think about how cells work, about physiology and how our bodies work."

Richard Caprioli, Ph.D., who directs Vanderbilt's Mass Spectrometry Research Center, thinks a lot about the cell, too. But for him, it's metaphorical.

"I don't think we as scientists are really going to make huge innovations in understanding until we integrate just like the cell does," Caprioli says.

Some of U.S. science today is "too highly focused," he says. "We all have our own expertise, jargon and acronyms generally not understood by non-experts in a particular field. We need to work much closer together to achieve a quantum leap from where we are."

This transformation must include the entire scientific enterprise, Caprioli asserts, from the university research lab to the National Institutes of Health (NIH) and even to industry.

Lens magazine asked Caprioli and other scientists at Vanderbilt and throughout the country to brainstorm ideas for revitalizing the nation's biomedical research enterprise.

Their suggestions may surprise you.

BY BILL SNYDER
ILLUSTRATION BY ANTONELLO SILVERINI

Stop yo-yo funding

Continued support of the NIH is essential, but simply increasing its budget will not solve the problems facing U.S. science. What's needed instead is stable funding, a budget that does not wobble up and down in response to the vagaries of the political system.

"The budget of the NIH should not be an annual legislated amount of money," argues Jeff Balser, M.D., Ph.D., dean of the Vanderbilt University School of Medicine and associate vice chancellor for Health Affairs. Instead, it should have a "fixed adjusted-for-inflation increase over a 10-or-so-year period like many programs in government."

If the National Cancer Institute, for example, "knew what its budget was going to be five years from now, imagine how effective and efficient they could be in planning programs," he says.

Yo-yo'ing funding is not only a problem for NIH, it can be crushing to the individual investigator, and it ends up wasting tax dollars, adds Scott Hiebert, Ph.D., associate director for basic science programs at the Vanderbilt-Ingram Cancer Center.

"The vast majority of researchers across the country have one or two grants, and when their grant doesn't get renewed for two cycles the research stops, and then it gets funded and they have nobody in the lab to do it," Hiebert says.

"It takes a couple of years to get going. And we're doing this and it's killing us. We're wasting tax dollars doing this because we're losing the momentum."

"This thing of going up a lot and then going down a lot is just devastating to the continuity of laboratories (that) are trying to … make a breakthrough," agrees Heidi Hamm, Ph.D., chair of Vanderbilt's Department of Pharmacology. "You lose trained people in your laboratory. You start all over. It's a wasteful system."

Funding a program is not unlike flying a plane, adds Dan Masys, M.D., chair of Biomedical Informatics at Vanderbilt and a licensed pilot. Repeatedly climbing and descending instead of keeping to a steady altitude can increase fuel consumption by 60 percent while actually lengthening the time to reach a destination, Masys says.

Partner with industry

Academic medical centers also need to be innovative in their acquisition and use of research dollars, Vanderbilt scientists say.

One of the reasons that Vanderbilt University Medical Center has had a successful research enterprise is that it has invested in "elements of 21st century success," Masys continues. These include information technology and other systems approaches aimed at squeezing waste and inefficiency out of its delivery of health care, while improving quality and outcomes.

"It's vision; it's core facilities; it's a lot of different strategic moves we've made over the years," adds Mark Magnuson, M.D., who directs the Vanderbilt Center for Stem Cell Biology.

Another avenue of innovation can be found in collaborations with industry.

"We're in the place in our biomedical research history and the history of the pharmaceutical industry especially where companies are desperate for new models and opportunities to invest," says Jeffrey Conn, Ph.D., director of the Vanderbilt Program in Drug Discovery.

Drug companies are reluctant to invest in university-based research "for the sake of research," Conn says, "but when they see research that can impact the company's viability, those opportunities are there."

An example is Vanderbilt's partnership with the Boston-based biotech firm Seaside Therapeutics to find potential treatments for fragile X syndrome, the most common inherited form of mental retardation and the most common genetic cause of autism. The goal is to reduce or eliminate the neurological and psychiatric consequences of the condition by chemically modulating the aberrant signaling of a neurotransmitter in the brain.

"If it works, it could be transformative," says Conn, who led the neuroscience program at Merck for several years. "It could totally change the way people view developmental disorders."

As academic medical centers do a better job matching their needs with those of pharmaceutical companies, he continues, "I think we increase the productivity of the companies that rely on (that) science … and then we increase the support of the public. The reason that we're having such a crisis right now with public support is that they see this investment, and they're looking for what's coming out of it."

Yo-yo'ing funding of research can be crushing to investigators and ends up wasting tax dollars.

Diversify research support

Innovation also must extend to the pursuit of a diverse portfolio of research support.

Toward that end, VUMC has created a program focused on helping investigators find the support that they need. Many of these foundations "have a strong interest in developing the careers of junior faculty members, coupled with a mission to fund basic, translational and clinical research," says Vanderbilt's director of Development for Biomedical Research, Julie Koh, Ph.D.

For example, the Howard Hughes Medical Institute (HHMI) recently created 70 Early Career Scientist positions as an investment for the future. The institute also is granting new funds through its newly established Collaborative Innovator Award project. Here the principal investigator (PI) must be an HHMI researcher, but the research team must include others from outside his or her discipline, from outside the institute or even from outside the United States.

Says Jack Dixon, Ph.D., HHMI's chief scientific officer and former dean for Scientific Affairs at the University of California, San Diego: "The strategy is to develop teams of people to tackle important problems that couldn't be tackled as effectively by an individual laboratory. It's something of an experiment for us."

Grassroots movements like ACT-UP, which promotes AIDS research, and private foundations like the Michael J. Fox Foundation for Parkinson's Research, which supports research and drug development, are among the increasingly powerful funders of biomedical research.

The recently formed Stand Up to Cancer, which raised more than $100 million during a televised celebrity fundraising event last fall, directs its donations to "interdisciplinary, multi-institutional translational and clinical research Dream Teams" in order to speed progress and "achieve a paradigm shift in clinical cancer research," according to its Web site, www.standup2cancer.org.

Similarly, the Multiple Myeloma

Wonder Drake, M.D.
assistant professor of Medicine

Vanderbilt researchers brainstorm ideas

In October 2008, *Lens* magazine assembled two groups of researchers at Vanderbilt University Medical Center to examine the challenges facing U.S. biomedical research, and to suggest possible solutions. This special issue of *Lens* emerged from discussions with members of the *Lens* editorial board, particularly Peter Buerhaus, Ph.D., R.N., Lawrence Marnett, Ph.D., Richard Caprioli, Ph.D., Randy Blakely, Ph.D., Joel Lee, associate vice chancellor for Medical Center Communications, and former Associate Vice Chancellor for Research Lee Limbird, Ph.D.

Richard Caprioli, Ph.D.
director, Mass Spectrometry Research Center

Julie Koh, Ph.D.
director of Development for Biomedical Research

Peter Buerhaus, Ph.D., R.N.
Institute for Medicine and Public Health

Dan Masys, M.D.
chair, Department of Biomedical Informatics

Jeffrey Conn, Ph.D.
director, Program in Drug Discovery

Lawrence Marnett, Ph.D.
director, Institute of Chemical Biology

Scott Hiebert, Ph.D.
professor of Biochemistry

Research Foundation has used a "pay-for-results" funding model that, in the words of *Time Magazine's* Bill Saporito, "has more to do with Silicon Valley than Big Pharma."

Foundations also can provide "support for controversial or unpopular topics where government is reluctant to tread, and nurturing of ideas early in their inception prior to broader acceptance," said Susan Fitzpatrick, Ph.D., vice president of the St. Louis-based James S. McDonnell Foundation.

"Having a large number of funding organizations with diverse decision-makers helps ensure flourishing of alternative models and approaches that may depart from the common wisdom or challenge the status quo," Fitzpatrick said in remarks prepared for a forum on science and technology policy hosted by the American Association for the Advancement of Science last May.

"Driving cures requires investing in high-risk science," adds Brian Fiske, Ph.D., an associate director of research programs at the Michael J. Fox Foundation, which committed more than $30 million in new Parkinson's disease research in 2008. "It's all about testing hypotheses that may very well fail, and betting on technologies that may fall apart or become obsolete in a few years. But if we don't take that risk, others won't."

The foundation is currently funding clinical trials of several novel therapeutic approaches to Parkinson's disease that otherwise would likely not yet have advanced to testing in patients.

"When the foundation was launched in 2000, we didn't necessarily anticipate that we would have to go this far before someone else would take the lead," Fiske says. "But we can't stand by as potentially promising drugs sit on the shelf and never go to definitive clinical trials, and no one ever knows if they will work or not."

Private efforts, however, do not come close to matching the $28-billion-a-year NIH "engine" that drives the nation's biomedical discovery enterprise. Notes Conn: "I think the entire system would implode if you didn't have that strong national investment."

Invest in education

Nurturing the spirit of discovery ultimately must begin with the next generation.

That's why an increasing number of scientists and universities around the country are partnering with public schools to bring more of the joy and excitement of discovery into the classroom. VUMC, for example, has provided summer science workshops for teachers for more than a decade.

"These science teachers out there are highly motivated. They just need … access to mentoring from us," Balser says. "And so creating a really direct linkage between the science teachers in this community and university faculty so that we're all part of a community, and we're all engaged in this together – that's really where the solution lies."

Individual faculty members and students from Vanderbilt also are investing their time and talents to help capture the imagination and talent of public school students.

Last year, for example, Vanderbilt Student Volunteers in Science (www.vanderbilt.edu/vsvs), a 15-year-old organization of undergraduate, graduate and medical students, brought hands-on science lessons to more than 120 middle school classrooms in Nashville.

In 2007, Billy Hudson, Ph.D., director of the Vanderbilt Center for Matrix Biology, launched the "Aspirnaut Initiative" (www.aspirnaut.org) to provide laptop computers to middle and high school students in rural Arkansas, where he grew up, so they can access accelerated math and science programs during long bus rides to and from school.

Wonder Drake, M.D., assistant professor of Medicine, brings young people from her church into her lab for summer research experiences. Some of them are at risk of being turned off by school. But the lab experience challenges them.

"We mentored 10 kids over a five-year period in my lab, and six of (them) are in graduate school right now, either an M.D., Ph.D., or M.D./Ph.D. program," she says. "One reason for their success is that they found translational research very exciting; it provided them an opportunity to see how stimulating the life of a scientist can be."

Improving science education also benefits the broader society, argues Bruce Alberts, Ph.D., former president of the National Academy of Sciences and current editor-in-chief of the journal *Science*.

"If we made the kind of investments in teacher education and teacher support that we need to make as a nation, we could create a citizenry that would be

"BIG SCIENCE" IN THE BALANCE

While the federal government funds the lion's share of biomedical research in the United States, there is concern that a predilection for "big science" projects may actually weaken rather than strengthen the potential for discovery.

"I agree that we need better integrated science, but not the type of 'big science' that we've seen from NIH in the past decade," says Lawrence Marnett, Ph.D., director of the Vanderbilt Institute of Chemical Biology. "The Genome Project was a big science project that has paid dividends and will pay dividends over the long run, but many of the other projects that came about in the afterglow of its success are poor shadows.

"What we need is more communication between people doing complementary work so that they focus on critical common goals with a percentage of their efforts," Marnett says.

"There is no one solution and definitely, in my humble view, 'big science' is not THE answer," agrees Randy Blakely, Ph.D., director of the Vanderbilt Center for Molecular Neuroscience. "Big science … can become totalitarian, wasteful and misguided, just like any large enterprise when it is seen as the only way to go.

"Nothing in my view will beat the creativity of individuals empowered with sufficient resources to explore biology and medicine's problems."

In his 2007 book, "Happy Accidents: Serendipity in Modern Medical Breakthroughs," Morton Meyers, M.D., wrote that many advances in biomedical science come not from a "predetermined research path" or from a committee, "but from an individual, a maverick who views a problem with fresh eyes."

"Serendipity will strike and be seized upon by a well-trained scientist or clinician who also dares to rely upon intuition, imagination and creativity," Meyers asserted. "Unbounded by traditional theory, willing to suspend the usual set of beliefs, unconstrained by the requirement to obtain approval or funding for his or her pursuits, this outsider will persevere and lead the way to a dazzling breakthrough." – Bill Snyder much more effective in the workforce, because those people would be able to solve problems on the assembly line and in the workplace," Alberts maintains.

That's important, he adds, because in order for the United States to thrive amidst the challenges of the 21st century, its citizens "need to be problem-solvers. They need to be independent thinkers. They need to see how to fix things that are wrong, and then move forward."

Sell the story

Given the global financial crisis, it will not be easy to increase support of research and education.

One possible solution: health care reform.

According to Peter Buerhaus, Ph.D., RN, an expert on health care workforce issues in the Vanderbilt Institute for Medicine and Public Health, our nation's health care delivery system wastes 30 cents of every dollar – about $700 billion a year. "That's 20 times the NIH budget," he points out.

"Something we can all agree on is to get rid of the waste and inefficiency in the delivery system that results in nothing," Buerhaus continues. "It's not as if we have to create a lot of extra dollars (to support research). It's just that we need to put some discipline into this crazy system that is going to get way out of control as we move forward with these 80 million Baby Boomers" who are entering their retirement years.

William Lawson, M.D., assistant professor of Medicine at Vanderbilt who has advocated nationally for more federal funding for research, notes that the nation spends between $6,000 and $7,000 per year on health care for each of its 300 million citizens, but "less than $100 per person" each year for NIH-sponsored extramural medical research. "That's a huge gap," he says.

And while health care reform has been a political "third rail," electrocuting all who come near, it is equally true that scientists have failed to sell the story of biomedical research in a clear and consistent manner.

"Information is the most important thing in clarifying … misimpressions and/or wrong-headed thinking about things," says Harvard's Melton, who is studying how cells might be reprogrammed to cure type 1 diabetes. "If you look in the political arena, it's usually the way words are twisted or there's seeding purposefully of misinformation that leads people … to the wrong opinion."


DANA JOHNSON

Douglas Melton, Ph.D., co-director of the Harvard Stem Cell Institute

For example, to scientists the word "cloning" means making copies of DNA or cells. But "to my neighbor it means making copies of people, and I don't know any scientist who wants to do that," Melton says.

"Scientists make a grave mistake if they think people should just know (intuitively) about this," he continues. "We are an important part of society, and it's our obligation to talk to people about not only what we do but why we do it."

Scientists should avoid making extravagant claims, like promising a cure for cancer in a decade. But there is nothing wrong with spurring the public's imagination.

"There are two great problems that society faces now, at least as I see the world," says Melton. "One of them is renewable energy. If I were a young person, I would be fascinated to figure how why chloroplasts in green plants harness energy from the sun so much more efficiently than our best solar panels.

"The second one, it won't surprise you to hear, is renewable bodies. I think the concept of keeping my body healthy, healthy aging, is very interesting and fascinating … The public has a great appetite to increase their body's natural ability to replenish and repair itself."

More consistent research funding. Partnering with industry. Diversified support. Investing in education. Selling science's story to the public. Good ideas all.

But there is one more quality that is essential for keeping biomedical research high on the nation's agenda – leadership.

Hamm argues for "a 100-year national strategy for investment in scientific research leading to breakthroughs in our understanding of disease," while Magnuson calls for a presidential cabinet-level position to help guide the nation's science and technology enterprise.

For Melton, it's a matter of "setting the tone."

National politics and policy debates have "devalued" science in recent years, says Melton, despite the fact that "science as a way of knowing has proved to be the most powerful way of understanding the great questions of life and, fortunately also a great economic engine."

"It's not that I mean we should have experiments going on in the White House," he says. "I'm talking about setting the tone … That's why we have a central government – to ask what's important for our society, how do we solve problems and set a tone that engages society to help others.

"That's what I mean by leadership."

"What made America great?" asks Vanderbilt's Caprioli. "In the early 1900s, we launched into the world. Why? What was in our spirit, our culture that allowed that meteoric rise? Is there something in our history that can give us a glimpse of what our solution should be?

"This goes very deep into the fabric of who we've become," he says. "Who we've become is not all good. We have to understand the parts that are limiting us and get past them." **LENS**

Lisa A. DuBois contributed to this story

ANNE RAYNER

Pictured at left: Q-vaughnia Hornbeck (right) goes over her research with Virginia Shepherd, Ph.D., director of the Vanderbilt Center for Science Outreach. Jennifer Ufnar, Ph.D., (not pictured) mentored Hornbeck's senior project.

One student's story

By Nicole Garbarini

Every Tuesday afternoon, Q-vaughnia Hornbeck leaves her public high school early, bound for a laboratory on the Vanderbilt University campus where she is investigating a new way to identify sewage contamination in lakes, rivers and other recreational waters.

"Everyone wants to know why I leave early," says Hornbeck, a senior at Whites Creek Comprehensive High School in Nashville. "They say, 'You're so smart!'"

Undoubtedly, but Hornbeck says the best part of her experience in the School for Science and Math at Vanderbilt is the friendships she's made with her teachers and fellow students.

It's also changed her career choice – from dentistry to neuroscience.

"It's changed everything," she says confidently. "I like the fact that you have a question and then you can develop ways to answer the question. I also like that you don't have someone telling you what to do next. You can decide that on your own."

Hornbeck is one of 10 seniors and 49 underclassmen from Nashville public schools currently enrolled in the innovative Vanderbilt program. It is the latest effort by Virginia Shepherd, Ph.D., and her colleagues to enhance K-12 science education.

In 1994, Shepherd got her first science education grant to fund summer workshops for teachers. That led to a variety of programs, including the Girls and Science summer camp, the involvement of graduate students in K-12 classrooms and, in 2002, establishment of the Center for Science Outreach (www.scienceoutreach.org), which Shepherd directs.

Then, in 2007, Vanderbilt University Medical Center, in partnership with Metropolitan Nashville Public Schools, launched the School for Science and Math ((http://theschool.vanderbilt.edu/).

Directed by Glenn McCombs, Ph.D., the school has four full-time, Ph.D.-level instructors. Most of the students spend one day a week at Vanderbilt receiving accelerated classroom instruction and laboratory experience, while still keeping up with their studies in their public schools. The seniors also conduct summer research projects.

In the past two years, three of the seniors have achieved semifinalist recognition in the prestigious Siemens (formerly Westinghouse) national science competition.

Too often in regular science classes, "students … find themselves doing a cookbook kind of lab, and there's not the open-ended question and hypothesis-driven kind of project," says Shepherd, a professor of Pathology and Medicine and associate professor of Biochemistry.

"We're trying to do that here … To me, that's the way to build critical thinkers and problem solvers, and that's what I'd love to see in schools" throughout the country.

Shepherd recognizes that high schools and universities have very different cultures. But "with a good relationship between a university or institute of higher education and the K-12 system," she insists, "there can be some wonderful partnerships built up that can be mutually beneficial."

The goal is nothing short of revolutionary.

"What's the Sputnik of your generation?" Shepherd challenges the students. Cures for cancers? A vaccine that prevents AIDS? A solution to the energy crisis?

"You want to give something to these students that they can grab a hold of, so they can say, 'Yeah, I want to be that kind of scientist,'" she says.

"The challenge is what will excite students and keep the spark going." LENS

By the numbers

Vanderbilt University Medical Center's Research Enterprise

FACULTY

Total number of faculty	1,929
Faculty engaged in sponsored research*	1,032

RESEARCH FUNDING

NIH funding (2007)	$ 282.2 million
NIH funding (1999)	$ 94.4 million
Funding from all external sources (2007)	more than $ 389.0 million

FACILITIES

Research space (2007)	678,000 square feet
Research space (1999)	315,000 square feet
Research centers and institutes	nearly 40

STUDENTS

Medical students	442
Residents and clinical fellows	about 850
Nursing (includes doctorate and master's degree programs)	750
Bioscience Ph.D. students	about 520
Post-doctoral fellows	474
Hearing & speech sciences (Ph.D. and M.S.)	88
M.D./Ph.D. students	83
Other master's degree programs	115

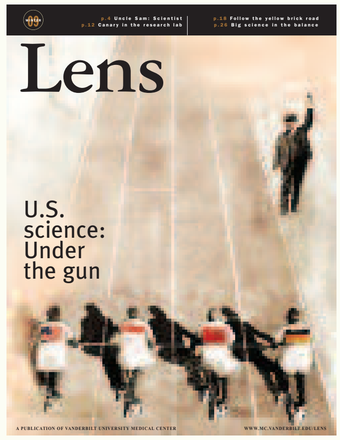
NOBEL LAUREATES

Earl Sutherland Jr., M.D. (1971) – for his discovery of cyclic AMP

Stanley Cohen, Ph.D. (1986) – for his discovery of epidermal growth factor

** Faculty members who received research dollars from either grants or contracts*

Figures as of December 2008, except where noted



Tell us what you think of this issue

Your opinions are important to us. To continue the discussion, we will post your comments and letters on the *Lens* Web site – www.mc.vanderbilt.edu/lens – and publish some of them in the next issue of the magazine.

Comments, questions and letters can be e-mailed to the editor at lens@vanderbilt.edu; faxed to (615) 343-3890; or mailed to:

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IN THE NEXT ISSUE:

Tsunami of childhood obesity
Findings in genetics and molecular biology are yielding new ideas for stemming the tide.

It's not a zero sum game
Development is guided by a synergy of genetic and environmental factors, including nutrition.

The fragile brain
Learning how the brain grows may help solve the riddles of autism and learning disorders.

A 2-month-old baby is soothed by his mother at the Monroe Carell Jr. Children's Hospital at Vanderbilt.

Photo by Dana Johnson

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