Medicine@Yale

Advancing Biomedical Science, Education and Health Care

Volume 1 Issue 1
June/July 2005

Yale physiologist elected to National Academy of Sciences


Steven Hebert

Steven C. Hebert, M.D., spent the early part of his career exploring the kidney's basic processes using the tools of traditional physiology—radioactive tracers to track ions as they cross cell membranes and light microscopy to measure the volume of cells in the nephron, the complex and convoluted structure that forms the kidney's basic unit.

Then in the late 1980s, he faced a choice: continue with the tried-and-true laboratory methods at his disposal or risk a leap headlong into the world of molecular genetics. Using a technique called expression cloning, in which genes are isolated according to their function, Hebert and his colleagues saw the chance to identify the molecules that transport salts across membranes and regulate calcium levels in the blood. Maintaining these functions is critical to a healthy heart, strong bones and normal blood pressure.

"My feeling at that time was the gamble was worth it, because I didn't see that we could advance in our understanding without doing these things," Hebert said on May 3, the day he was elected to the National Academy of Sciences (NAS). Hebert is the chair and C.N.H. Long Professor of Molecular and Cellular Physiology and professor of medicine. "It was do or die."

Apparently, the risk paid off. In the early 1990s, Hebert's laboratory made three fundamental discoveries about how the kidney handles potassium, sodium and calcium. His group identified a channel that regulates potassium excretion and is involved in Bartter's syndrome type II, an inherited disorder that causes sodium and potassium to be lost in the urine. He and his colleagues also identified two sodium chloride transporters that

Hebert, *page 6*

New Kavli center for neuroscience research will untangle mysteries of the human brain

A mere 2 millimeters may separate us from other members of the animal kingdom. That's the approximate thickness of the cerebral cortex, a sinuously folded sheet of tissue on the outermost surface of the brain where the neural machinery resides for many capabilities, such as language and reasoning, that we think of as distinctively human.

Pasko Rakic, M.D., PH.D., the chair and Dorys McConnell Duberg Professor of Neurobiology, has spent a lifetime deciphering how the nervous system cells present at birth manage to arrange themselves into the highly ordered, densely interconnected and immensely complex circuitry of the adult cortex.

Now, thanks to the unique philanthropic vision of the Kavli Foundation, formed by California industrialist Fred Kavli, Rakic and other Yale neuroscientists with a special interest in the cortex have the tools to dig even more deeply into the mysteries of the human brain. Last year, the foundation announced the establishment of the Kavli Institute for Neuroscience at Yale, one of only three such centers in the world devoted to brain research.


Norwegian-born engineer and philanthropist Fred Kavli at his home in Goleta, Calif.

David Auston, PH.D., president of the foundation, says that he and Kavli believe that Yale's "outstanding group of neuroscientists will make important advances in understanding the basic functioning of the brain."

Most organizations that fund biomedical research, whether public or private, have a quite specific mission, often focused on finding treatments for particular diseases. But the Kavli Foundation bears the distinctive stamp of its Norwegian-born founder, a man with a sweeping

Kavli, *page 6*

Magazine innovator celebrates 101 years with gifts for his medical school "family"


Gus Berkes

You don't have to meet Gus Berkes to learn about his accomplishments. They're right in front of you whenever you pick up a magazine.

Berkes, who turned 101 in March, spent his working life as a production director at *Esquire, Better Homes & Gardens* and *McCall's*, where he pioneered the use of innovations we now take for granted—bound-in subscription cards and advertising supplements, foldout pages and the legendary (and wonderfully self-explanatory) ad gimmick known as "Scratch-n-Sniff."

"See all these cards?" Berkes asks as he riffles through a copy of *Better Homes* at East Hill Woods, the retirement community in Southbury, Conn., where he has made his home since 1993. "That's me."

Thirty years ago, just after being treated at Yale by Clarence T. Sasaki, M.D., the Charles W. Ohse Professor of Surgery, Berkes and his wife, Josephine, who were childless, created trust funds and placed instructions in their wills to support their favored charities. Because of his gratitude to Sasaki and the warm rapport the two men enjoyed, the School of Medicine was at the top of Berkes' list in his bequest.

But four years ago, with his 100th birthday on the horizon, Berkes happened upon a magazine story detailing Sasaki's recent research in head and neck surgery, and he

Berkes, *page 3*

Welcome to *Medicine@Yale*


Dean Robert Alpern

This is the inaugural issue of a new publication created to keep you up-to-date with the many exciting things happening at Yale School of Medicine. Every other month, we will report on the accomplishments that make the school one of the world's great biomedical institutions.

The school's mission is to provide outstanding education to our students; to advance the frontiers of science; and to serve the medical, public health and educational needs of the residents of Connecticut, the Northeast and the world over. We are excited to have the opportunity to share our achievements in these many areas with you.

I hope you will enjoy reading this premiere issue. Please drop us a line at the address on page 2 and tell us how you like it.

Robert J. Alpern, M.D., *Dean*

Inside this issue

Want to find out more about medicine at Yale?
E-mail us at medicine@yale.edu or phone (203) 785-5824.

Medicine @Yale
P.O. Box 7612
New Haven, CT 06519-0612
www.medicineatyale.org

Non-Profit Org.
U. S. Postage
PAID
New Haven, CT
Permit No. 526

Present at the creation

Expert on gene swapping joined molecular biology at its very beginnings

Lifelines
Charles M. Radding

DNA researcher Charles Radding has done some of his best thinking on buses.

Charles M. Radding, M.D., professor emeritus of genetics, did sculpture as a hobby in medical school, and his portraits demonstrated a natural aptitude for plastic surgery, according to an influential mentor who also happened to be his older brother, Philip. The elder Radding, an orthopaedic surgeon, hoped the two would someday practice in side-by-side offices. Although the scheme had some appeal, Charles already knew his passion was biochemistry, not medicine.

It was 1953, and Watson and Crick's double-helix model of DNA had opened a new door to understanding for biologists, a door the fledgling biochemist Radding eagerly entered. Radding, who recently retired after 37 years at Yale, went on to become a leader in illuminating the theoretical and biochemical underpinnings of genetic recombination. Also known as gene swapping, recombination orchestrates the orderly transmission of genes from generation to generation in all organisms, and it is now recognized as an important anticancer defense that human cells use to repair tumor-causing mistakes in the genome.

In the mid-1970s, while traveling on a bus filled with fellow scientists through the Scottish Highlands, Radding and Matthew Meselson of Harvard University hatched a new theoretical model of recombination. The 1975 paper they co-authored describing the model formed the basis for much of the experimental work in recombination in the years that followed.

Radding's experimental approach combined his expertise in enzymes with the latest techniques in DNA research. In 1979, he scored an experimental coup by enticing a bacterial enzyme to swap genes between two strands of DNA in a test tube. For decades thereafter, his lab in the Sterling Hall of Medicine was the source of progressively more detailed biochemical investigations of this swapping reaction. "Radding's meticulous studies contributed greatly to understanding the individual steps involved in the recombination of DNA molecules," says Meselson.

Franklin Stahl, Meselson's partner in the landmark "Meselson-Stahl experiment" on DNA replication, also praised Radding as lecturer and teacher. "Charlie showed a lifelong dedication to understanding the enzymology of recombination and communicating that understanding to his colleagues and students," says Stahl, now professor emeritus of biology at the University of Oregon.

A symposium to honor Radding drew Meselson, Stahl and other colleagues and former students from around the world to Yale last fall. "Charlie has trained so many successful people," says Patrick Sung, D.PHIL., professor of molecular biophysics and biochemistry, an expert on DNA repair. Sung joined other speakers at the vibrant daylong conference, which was followed by a celebration that lasted late into the evening.

In retirement, Radding looks forward to reading and writing poetry—and perhaps trying his hand at art once again.

Lifelines profiles those who make Yale School of Medicine one of the world's premier institutions for biomedical science, education and health care.

For new deputy dean, focus is on top-notch care, service to patients

David Leffell

As the new deputy dean for clinical affairs, David J. Leffell, M.D., continues a task he began 10 years ago, when he added a new portfolio to his work as a dermatologist: improving the business side of medicine.

As head of the Yale Medical Group (YMG), the medical school's 750-member faculty practice, Leffell has encouraged physicians and other caregivers to move outside traditional departmental boundaries into interdisciplinary, disease-based teams.

"Because our knowledge of disease is so much more refined, we understand that solutions to illness are not limited to a particular organ in which the disease is expressed," says Leffell, who will oversee the growth and development of the practice in his new role.

In addition to helping move scientific knowledge from the bench to bedside, Leffell is focused on making sure the day-to-day operations of the practice run flawlessly for the sake of patients and referring physicians. Ensuring that the world-class medical care at Yale reaches patients quickly and efficiently all boils down to good communication and good coordination, Leffell says.

"To teach medical students to be doctors of the 21st century," he adds, "and to take care of patients with new technology and medications of the 21st century, you have to have a clinical practice of the 21st century."

Kidney researchers celebrate a banner year

Stefan Somlo

Walter Boron

First Stefan Somlo, M.D., Yale's chief of nephrology, learned that he would be heading off to Singapore in late June to accept the field's top award for research in polycystic kidney disease, a life-threatening condition that affects more than 12.5 million people worldwide.

Next Steven C. Hebert, M.D., the chair of physiology, was tapped to receive the A.N. Richards Award at the same June meeting, the World Congress of Nephrology.

Then another Yale kidney researcher, Walter Boron, M.D., PH.D., was selected for the Homer W. Smith Award from the American Society of Nephrology (ASN).

Finally, Hebert was elected to the National Academy of Sciences (see related story, Page 1) for his discoveries leading to new drugs that benefit more than 1 million kidney patients worldwide.

Is there something in the water?

"It's just that Yale has great strength and great depth in this area of science," says Dean Robert J. Alpern, M.D., a nephrologist himself, who was attracted to Yale in part by its long tradition in the field dating to the work of John Peters, M.D., during the 1930s.

Somlo, the C.N.H. Long Professor of Medicine, and a colleague will share the Lillian Jean Kaplan International Prize for Advancement in the Understanding of Polycystic Kidney Disease for their work in discovering genes that cause polycystic kidney and liver diseases. Somlo and frequent collaborator Gregory G. Germino, M.D., of the Johns Hopkins School of Medicine will receive $50,000 each from the PKD Foundation and the International Society of Nephrology.

National Academy honoree Hebert will receive the A.N. Richards Award from the International Society of Nephrology (ISN) for his fundamental discoveries about how the kidney regulates salt balance. The Richards Award, which carries a $10,000 cash prize, is the ISN's highest award for basic research. It is presented every two years at the World Congress and is named for Alfred Newton Richards (1876–1966), a member of the Yale College Class of 1897.

Boron is the eighth Yale professor to receive the Homer W. Smith Award, the ASN's top honor for basic research. The award, which carries a $10,000 cash prize, will be presented at the ASN's annual meeting in November in Philadelphia.

Boron, a professor of cellular and molecular physiology, has performed pioneering work on the processes regulating intracellular pH, which must be maintained in the neutral range for normal cell function. His contributions include the development of methods to measure and manipulate intracellular pH, the use of these methods to discover several transport processes for acids and bases across cell membranes and the cloning of cDNAs that encode several of these transporters.

Medicine@Yale

Peter Farley, *Managing Editor*

Contributors: Douglas Barnes, John Curtis, Michael Fitzsousa, Maureen Grieco, Jane Hadjimichael, Rhea Hirshman, Justine Levin-Allerhand, Joel Maupin, Pat McCaffrey, Crystal Neuhauser, Christopher Pates, Patricia Pedersen, Eric Schonewald, Cathy Shufro, Marc Wortman
Photographs and Illustrations: Brett Anderson, Toby Appel/Cushing-Whitney Medical Historical Library, Isabel Chenoweth, John Curtis, Terry Dagradi, Jerry Domian, Bob Elliott, Edwin Ewing, Jr./CDC, Ann Freeman, Jorge Galán, Given Imaging, Michael Marsland, David M. Phillips/Photo Researchers, Sheila Westman, Keck Laboratory/ Affymetrix GeneChip Core
Design: Tom Strong, Amanda Damour/Strong Cohen

Medicine@Yale is published six times each year by Yale Medicine Publications, P.O. Box 7612, New Haven, CT 06519-0612. Editorial offices are located at 100 Church Street South, Suite 212, New Haven.
Telephone: 203.785.5824 Fax: 203.785.4327
E-mail: medicine@yale.edu
Website: medicineatyale.org

If you have a change of address or do not wish to receive future issues of *Medicine@Yale*, please write to us at P.O. Box 7612, New Haven, CT 06519-0612 or via e-mail at medicine@yale.edu.

Postal permit held by Yale University, 155 Whitney Avenue, New Haven, CT 06520

Yale School of Medicine
Robert J. Alpern, M.D., *Dean*

Martha E. Schall, *Associate Vice President for Development and Director of Medical Development*
Mary Hu, *Director of Planning and Communications*

Michael Fitzsousa, *Director of Publications*

Pfizer and Yale join forces for research and education

Like many enterprises with international reach, Pfizer Inc. makes its corporate home in New York. But the company has deep roots in southeastern Connecticut, having built what was then the world's largest manufacturing plant for antibiotics in Groton in 1946.

Today, more than 6,000 Pfizer scientists and R&D personnel continue to do much of the company's work in drug discovery and testing in laboratories in Groton and at its Global Research and Development headquarters in nearby New London.

With the April opening of the $35 million New Haven Clinical Research Unit (CRU), a 52-bed dedicated facility for Phase I drug trials, Pfizer further strengthened its ties to Connecticut and added new luster to a multifaceted Pfizer-Yale research alliance that began three years ago.

At the CRU, one of only four such Pfizer facilities in the world (the others are in Ann Arbor, Mich.; Brussels, Belgium; and Singapore), volunteers will take part in studies in which they will receive potential medicines that have cleared several years of safety studies in the laboratory. Although the CRU is wholly owned and operated by Pfizer, some studies there will be collaborations between Pfizer and bioimaging experts at the School of Medicine, who will use positron emission tomography (PET) and other technologies to track where and how drugs under study are acting in the body.

Yale scientists will collaborate on drug studies at the New Haven Clinical Research Unit.

Diane K. Jorkasky, M.D., Pfizer's vice president of clinical pharmacology, says that the ability to draw on the expertise of Yale scientists in a mutually beneficial partnership figured heavily in the company's decision to locate the CRU in New Haven, citing "a world-class medical imaging center with a strategic interest in PET scanning and research on the central nervous system and a university that understood the value of academic-industrial relationships."

But the planned collaborative studies at the New Haven CRU are just one example of Pfizer's research and education partnerships with Yale.

In 2003, the company established a fellowship in memory of the late Patricia S. Goldman-Rakic, a renowned Yale neurobiologist, which provides tuition, health insurance and a stipend every year to a promising graduate student in neuroscience in Yale's Combined Program in the Biological and Biomedical Sciences (see related story on Page 5). Through Pfizer Faculty Development grants, five assistant and associate professors in the School of Medicine have been granted up to $50,000 worth of research time at the medical school's Magnetic Resonance Research Center.

And in a new joint effort of Pfizer's Women Leaders Network and the medical school's Office for Women in Medicine, a visiting professorship has been created that allows a woman on the medical school faculty to spend 12 weeks working alongside Pfizer researchers in Groton and New London each year.

In the most ambitious Yale-Pfizer partnership to date, construction is under way on a PET research center, where high-resolution scanners will allow Yale scientists to pinpoint drug action in the human body, especially in the brain. In addition to an initial start-up investment of $5 million, Pfizer has pledged $20 million over 10 years for the new center, which is slated to open this fall.

"The relationship is one of win-win for Yale and Pfizer," Jorkasky says, "and the biggest winners will be the patients who will benefit from the science that the partnership explores."

Class of 1954 makes a lasting impact with scholarship gift

The School of Medicine's Class of 1954, the last of the "small classes" of 65 students, is a tight-knit group. Through the years, class members have kept in touch via birthday cards and holiday greetings. Until his death in 1998, Class Agent John K. Rose, M.D., compiled frequent newsletters that nurtured the class's unusual closeness over the past five decades.

But to mark their 50th reunion last June, its members looked squarely to the future by establishing the Class of 1954 Memorial Scholarship.

In creating the fund, which will provide a permanent source of support to students with financial need, the class joined a select group of medical school alumni who have established class-based scholarships.

When the class was considering a 50th reunion gift, Frank L. Gruskay, M.D., of Woodbridge, Conn., suggested establishing a scholarship fund honoring all members of the class, alive and deceased. The class agreed, and contributions rolled in steadily for five years.

The medical school's Class of 1954, the last of the "small classes" of only 65 students.

Last year, when 33 of the 42 surviving members of their class converged on New Haven for the 50th reunion, they learned over dinner that the fund had surpassed its $100,000 goal, and that their generosity would be helping to support a first-year student the following fall.

"The class was euphoric," recalls Arthur C. Crovatto, M.D., of York, Pa., who served as alumni affairs director at the School of Medicine from 1990 to 1996.

"For some years, we had wanted to do something," says Donald D. Davis, M.D., who in retirement divides his time between Cranberry Township, Pa., and Naples, Fla. "At the point of our 50th anniversary, we decided to do something major. We felt that a scholarship like this would be something that would live longer than some other tributes."

The fundraising effort for the scholarship—the fund is now valued at $138,000—was spearheaded by Harry C. Miller, M.D., of Great Falls, Va., who says that the memorial scholarship was a class act in the truest sense. "Everybody in the class with whom we have contact contributed to the scholarship fund," Miller says.

"Everybody in this class can stand up straighter and smile a little more broadly and walk a little more proudly knowing what they have accomplished."

Berkes *continued from page 1*

decided to give half of his trust immediately to support Sasaki's work. Berkes called Sasaki on the phone, and in the no-nonsense manner well-known to his East Hill Woods neighbors, he said, "Do you remember me? You treated me 30 years ago, and I want to give you some money."

He did just that, in the form of a $400,000 endowment for Sasaki's Section of Otolaryngology. Berkes' beloved wife, Jo, had since died from heart disease, so he soon followed up his first gift with a $200,000 endowment for Yale's Section of Cardiothoracic Surgery, headed by John A. Elefteriades, M.D.

Berkes went on to set up two charitable annuities for the Department of Surgery, but because he had little need for the income they generated, he deposited the money in yet another trust earmarked for the School of Medicine. This newest trust has appreciated to the point where he may be able to leave Yale an additional gift that matches his original donation, Berkes says with a laugh, adding, "I feel like I've discovered perpetual motion."

In sum, Berkes' gifts to the medical school will total as much as $1.4 million, and he says it was the right decision to donate sooner rather than later, because his gifts are a "two-way street": he takes great joy from seeing the fruits of his generosity. Berkes says it was "the greatest thrill" to pay a recent visit to the medical school and discuss current research with Elefteriades and a group of medical students.

Berkes stresses that the germ of his proud association with Yale physicians and fundraisers—he calls them "family"—lies in the solid doctor-patient bond he formed with Sasaki all those years ago, and he fondly hopes that doctors-in-training will learn to engage deeply with their patients.

Among Berkes' inventions at *Esquire* was a small symbol placed at the end of articles that alerted readers when a piece had come to an end. In his honor, we've placed one below. But at a vigorous 101, Berkes' story is far from over. Instead, he seems irrepressibly eager to see whatever may lie on the next page. M@Y

Advances

Health and science news from Yale

The base of the *Salmonella* needle complex is 300 angstroms long; this sheet of paper is about 1 million angstroms thick.

Salmonella "syringe" ready for its close-up

Salmonella bacteria are tiny, but they wreak mighty havoc on human health, causing serious, sometimes fatal, food poisoning. In 1998, Jorge Galán, PH.D., D.V.M., the Lucille P. Markey Professor of Microbial Pathogenesis, threw new light on *Salmonella*'s virulence when his research team revealed that the bacteria infects cells by forming "needle complexes," syringe-like tubes through which *Salmonella* exchanges proteins with its host.

Now Galán and his colleagues have joined forces with the laboratory of Vinzenz M. Unger, PH.D., associate professor of molecular biophysics and biochemistry, to paint a vivid three-dimensional portrait of the *Salmonella* syringe using a state-of-the-art technique known as cryoelectron microscopy.

In this method, an electron microscope scans samples that contain many copies of the object of interest suspended in an ice-like solid at every possible angle (background in image above). Researchers then feed scores of images of the object seen from these myriad perspectives to powerful computers, which combine the information in the two-dimensional views to calculate the object's three-dimensional structure.

Possible cancer inhibitor found in worm study

Yale scientists studying the microscopic worm *C. elegans* have discovered a cellular brake on a gene implicated in about 20 percent of human cancers, especially lung cancer. The finding opens up new possibilities for cancer diagnosis and treatment, says Frank J. Slack, PH.D., assistant professor of molecular, cellular and developmental biology.

Slack and his colleagues found that a snippet of genetic material in the worms called *let-7* shuts down the activity of *Ras*, an "oncogene" that can cause cell proliferation to spiral out of control, as happens in cancer. In Slack's experiment, in developing worms that lacked *let-7*, cells continued to divide instead of differentiating.

Scientists use *C. elegans* in the laboratory because the worm shares many genes with more complicated animals. According to Slack, *let-7* and *Ras* are almost identical in humans and *C. elegans*, and Ras protein, the product of the oncogene, is abundant in human lung cancers.

Lung cancer has a poor prognosis, but the lungs may be an ideal target for inhalable gene therapy agents. This may not cure the cancer, Slack said, but "gene therapy with *let-7* may be a way to alleviate it or slow it down."

Vaccinating wildlife suggests a new strategy in continuing battle against Lyme disease

In the summer of 1975, children from the rural towns near Lyme, Conn., began developing an odd type of arthritis. Yale rheumatologists Allen Steere, M.D., and Stephen Malawista, M.D., were called in to investigate, and they quickly determined that the strange seasonal flare-up had all the markings of an infectious disease. Eventually, Steere and other Yale investigators discovered that a corkscrew-shaped bacterium known as a spirochete was responsible for the condition they dubbed Lyme disease.

Malawista, Steere and colleagues went on to show that humans contracted Lyme disease after being bitten by deer ticks, which pick up the bacterium themselves from wild mice. Yale scientists went on to develop successful antibiotic treatments for the disease that prevent the painful arthritis and debilitating neurological problems that occur in some people.

But these stunning early successes of Yale scientists in the diagnosis and treatment of Lyme disease have not been matched by equal gains in prevention. Residential development in rural areas has placed more people in contact with ticks. A Lyme disease vaccine proved unpopular with consumers and was taken off the market. The disease now ranks as the most common tick-borne illness in the United States, with the number of new infections rising 35-fold since 1982. In 2002, over 23,000 cases were reported to the Centers for Disease Control and Prevention (CDC).

Entomologist Durland Fish, PH.D., of Yale's Department of Epidemiology and Public Health, decided to revisit the vaccine strategy, but instead of humans he targeted the white-footed mouse, a key player in the spread of Lyme disease.

A scanning electron micrograph of a deer tick, a carrier of the Lyme disease bacterium.

Working in the woods outside New Haven, Fish and his colleagues captured nearly 1,000 wild mice and injected them with the Lyme vaccine. As reported in the *Proceedings of the National Academy of Sciences*, the next year the researchers found lower rates of Lyme infection in both mice and ticks in the study areas.

"This is the first field study to show that we can decrease natural infection rates for a tick-borne disease by immunizing wildlife," says Fish. "Obviously it's not feasible to catch all the mice in a large area and inject them, but an edible vaccine, something you could incorporate into bait, should work as well."

Lyme disease prevention expert Joseph Piesman of the CDC hopes that Fish's results will stimulate more studies of wildlife vaccination. "We need more options for controlling and preventing Lyme disease, and these ecological, host-targeted approaches are very important," Piesman says.

Newborn deer ticks are infected with the Lyme disease bacterium during a single, summertime feeding on a mouse, and the bacterium spends the winter inside the tick's gut. In spring, when the ticks feed on humans, the bacterium can be released into the bloodstream, causing Lyme disease.

According to professor of medicine Erol Fikrig, how the bacterium sets up residence in the tick during winter has been a mystery, but late last year, Fikrig's group wrote in the journal *Cell* that they had discovered a receptor that serves as a docking station in the tick gut for the Lyme disease bacterium.

"If you manipulate the ticks so that they no longer have this receptor, you reduce the spirochete," says Fikrig, who envisions the creation of a receptor-blocking vaccine that would prevent ticks from carrying the Lyme disease bacterium.

A heart is repaired, the patient grows up

Program helps growing number of adult survivors of congenital disease

Congenital heart disease (CHD), the most common of birth defects, affects more than 32,000 children born in the United States each year. Three decades ago, many of these children would have died shortly after birth, but thanks to great advances in surgical and medical techniques most children with CHD can now expect to live well into adulthood.

To meet the special medical needs of this group, the Yale Medical Group recently launched the Adult Congenital Heart Program, the first program of its kind in Connecticut and one of only two dozen in the country. "We are looking at a population of patients that hardly existed 20 or 30 years ago," says James C. Perry, M.D., who staffs the program's outpatient clinic with coordinator Nicole K. Boramanand, A.P.R.N.

The multidisciplinary program provides treatment for common medical problems experienced by survivors of CHD, especially arrhythmias caused by irregularities in the heart's electrical system and heart failure, which can occur when structural or electrical abnormalities impede the heart's ability to pump blood.

James Perry and Nicole Boramanand specialize in a new group of patients.

"Pediatric heart patients were often discharged based on age, but adult cardiologists are not usually trained to manage congenital heart disease. Those patients had nowhere to go," Perry says. "Our program offers access to pediatric and adult cardiologists and other medical staff with essential expertise."

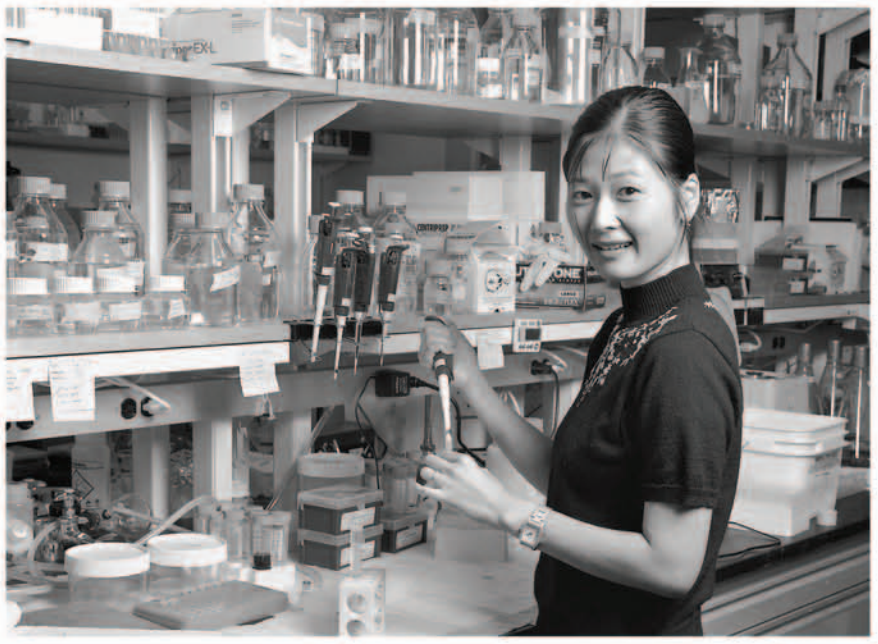
The program also offers specialized patient education. "Our focus is on preventive maintenance," Boramanand says. "What treatments and lifestyle adjustments can increase the length and quality of life? For instance, we emphasize that the old notion that all people with adult CHD should avoid exercise is no longer accepted."

Those who survive congenital heart disease into adulthood also experience a full range of other health concerns, of course, from catching the flu to developing arthritis to managing pregnancy. Perry notes that the new program will help clinicians learn more about how common health problems affect this population.

Perry and Boramanand predict that vanguard programs like Yale's will inspire future clinicians to specialize in treating adult survivors of congenital heart disease. "This is a group of patients we are just beginning to learn about," Perry says. "But to see people with complex congenital heart defects going strong into middle age is remarkable."

A long, fruitful collaboration: Bristol-Myers Squibb and Yale

Thirty-year partnership fosters innovations in education and research



BBS student Tomomi Tsubouchi has advanced our understanding of cell division.

Continuing a partnership with the School of Medicine that was forged more than 30 years ago, the Bristol-Myers Squibb Co. has renewed its fellowship support for graduate students in the Combined Program in the Biological and Biomedical Sciences at Yale.

The Combined Program, commonly known as the BBS Program, has transformed the university's graduate education in the life sciences since its inception in 1996. At that time, Bristol-Myers Squibb (BMS) made a substantial, multiyear gift that contributed decisively to both the initial success of the BBS Program and its long-term effectiveness.

Directed by Lynn Cooley, PH.D., professor of genetics and cell biology, the program spans faculty and laboratories in both the School of Medicine and on Science Hill, where the life sciences departments of Yale's Graduate School of Arts and Sciences are located. Underpinning the program is the conviction that educational structures should reflect the increasingly fluid, interdisciplinary nature of biological science. Students select an area of study—such as immunology or neuroscience—but they choose courses and lab work in numerous departments which together comprise more than 285 faculty.

For Tomomi Tsubouchi, a member of the BBS Class of 2005, the final year of the program has been a heady experience. Tsubouchi uses yeast to study the basic mechanism of cell division known as meiosis, and she recently observed a chromosomal process that had never been seen since meiosis was discovered in the 1880s. This May, Tsubouchi and her mentor, G. Shirleen Roeder, PH.D., Eugene Higgins Professor of Molecular, Cellular and Developmental Biology, published the findings in the journal *Science*.

Tsubouchi says that the BBS program has broadened her scientific horizons. "I hope that what I do will affect medicine in some way," she says, "so I'm glad that BBS has combined biology and medicine in one big program."

Bristol-Myers Squibb's support for the BBS Program is part of a broader collaboration with Yale to advance shared educational objectives. For example, the Yale/Bristol-Myers Squibb Educational Alliance—also set up in 1996—has enabled Yale graduate students to gain exposure to private-sector biomedical research through summer rotations at BMS' research and development campus in nearby Wallingford, Conn.

For more than three decades, BMS—or Bristol-Myers, as the company was known prior to its 1990 merger with Squibb—has encouraged Yale education and research in genetics, therapeutics for cancer and HIV and perinatal medicine. Most recently, the School of Nursing's Program for the Advancement of Chronic Wound Care, an effort to devise clinical "best practices" for wound treatment, got under way in 2002 with support from the BMS Foundation and BMS's ConvaTec unit. And with the guidance of Michael H. Merson, M.D., the Anna M.R. Lauder Professor of Public Health, the foundation has recruited Yale experts to evaluate the effectiveness of its Secure the Future initiative, which supports community-based initiatives in Southern and West Africa aimed at stemming the AIDS pandemic.

Last September, Dean Robert J. Alpern, M.D., and Yale University President Richard C. Levin hosted BMS Chairman and CEO Peter R. Dolan, M.B.A., and other senior executives at a celebration of the alliance and other collaborations between BMS and Yale. Alpern and Dolan joined John Damonti, president of the BMS Foundation, and Francis Cuss, M.D., BMS senior vice president for drug discovery, for an unveiling ceremony in Sterling Hall of Medicine, where a permanent plaque now honors the company's extraordinary contributions to medical research and education at Yale.

"When you think about the history of this collaboration, it is truly impressive," says Levin. "It helped shape the direction and range of intellectual activity at the School of Medicine." For his part, BMS' Dolan offers a succinct assessment of the company's long relationship with Yale: "We are all better off."

More integrated care for cancer patients, collaboration of scientists and clinicians are goals of proposed new YNHH building

According to Yale-New Haven Hospital President and CEO Joseph A. Zaccagnino, M.P.H., the hospital's planned new pavilion for cancer care is one of the biggest projects ever proposed in New Haven. The facility's impact can be measured in cost ($430 million), size (14 stories, 497,000 square feet), new patient beds (112) or the number of permanent jobs the center is expected to bring to New Haven (400).

These figures are undeniably impressive, but the plans for a new clinical center also represent something that numbers alone can't capture, say Yale Cancer Center Director Richard L. Edelson, M.D.; Edward Chu, M.D., the center's director of clinical research; and Ira Mellman, PH.D., its scientific director: a rare opportunity to provide state-of-the-art patient care while advancing the science of cancer therapy.

The proposal derives from "an intense focus on cancer that is truly uniting the medical school, Yale-New Haven Hospital and the university as a single effective team," says Edelson, a cancer immunologist who developed a widely used immunotherapy for T-cell lymphoma. "The people whom we're recruiting are leaving outstanding positions at other university medical centers to come to Yale because they recognize that this new facility is not just another building at another cancer center. Something quite special is happening in the field of cancer at Yale."

From the patient's perspective, too, the proposed 14-story clinical center will be far more than bricks and mortar, Chu says, because it will consolidate services now scattered around the medical complex, including diagnostic imaging, surgery, radiation treatment, social services and palliative care. "For the first time, we'll actually have a dedicated facility for the clinical care of our cancer patients," says Chu. "We're really making the patient the focus."

To achieve a marriage between basic and clinical research, Chu says, the School of Medicine has hired nine clinical investigators, most of whom will arrive this summer. The heart of the new effort, says Mellman, will be an unusually close collaboration between these investigators and the teams of basic scientists who will develop new therapies and test and refine them in clinical trials.

An architect's rendering of the proposed new pavilion for cancer care at Yale-New Haven Hospital.

Mellman says that the construction of the new center comes at an auspicious time, when basic research on the molecular biology of cancer is ripe for translation to human treatments.

"Increasingly, Yale faculty on the basic science side are becoming deeply committed to applying what we have learned in the laboratory to problems of human biology in general and human cancer in particular," says Mellman, the Sterling Professor of Cell Biology and a prominent figure in cancer research, "because the problems are so great from a human point of view, and the challenges are so great from a scientific point of view."

And although researchers can learn a great deal studying fruit flies and mice, Mellman says, clinical trials are vital to advancing cancer care: "The only true model for human cancer is human cancer."

The proposed new Clinical Center is part of a larger Yale Cancer Center endeavor, which will have as a central goal the combination of scientific advances with creative and seamless delivery of the best available clinical care.

According to Mellman and Chu, because understanding cancer requires a multidisciplinary approach, the Yale Cancer Center's research focus will not be on particular tumor types but on disciplines: cancer immunology, cancer genetics, imaging, stem cell biology and drug development. The new clinical facility is, therefore, a central part of the broader Yale cancer effort.

Once the construction cranes are gone and the hard hats are hung up, Mellman says he looks forward to seeing clinicians, students, laboratory staff and basic scientists brainstorming over coffee in the new building. "The first step in any new scientific collaboration," he says, "is communication."

Advances

Health and science news from Yale

New test easier for patients to swallow

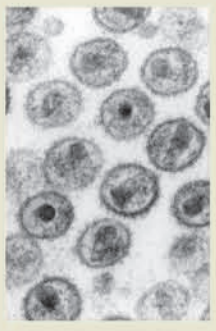
Physicians at the Yale Medical Group (YMG) are using a remarkable new procedure to diagnose digestive disorders. Instead of undergoing standard endoscopy, in which a long tube is threaded through the mouth into the esophagus, stomach and small intestine, some YMG patients can now swallow a pill about the size of a large vitamin capsule that contains a tiny video camera.

As the PillCam—manufactured by Given Imaging of Israel—makes an eight-hour journey through the upper digestive tract, the camera transmits full-color image data at a rate of two frames per second to an array of sensors in a belt worn by the patient. Doctors then upload the data from the belt to a workstation, where they can view the collected information either as still images or as a movie.

"The procedure is totally noninvasive, no radiation is involved, there is no discomfort and no need for sedation," says Deborah D. Proctor, M.D., associate professor of medicine (digestive diseases). "Once the camera and belt are in place, patients can go about their normal day."

Study finds payoff in wider HIV testing

One of the deadliest features of the human immunodeficiency virus (HIV; micrograph below) is its insidiousness. Those infected often live for years without obvious symptoms, unwittingly passing the virus on to others while their own immune systems steadily weaken. Public health experts estimate that nearly a third of the 900,000 Americans infected with HIV are unaware that they carry the virus.



The Centers for Disease Control and Prevention recommends regular HIV testing for high-risk groups with infection rates of 1 percent or more, but A. David Paltiel, PH.D., of the Department of Epidemiology and Public Health wondered whether the United States could cost-effectively expand testing to include groups at lower risk.

To find out, Paltiel and Boston-based colleagues devised a mathematical model, and as reported in *The New England Journal of Medicine*, they found that expanding HIV testing to all but the lowest-risk groups would be well worth the additional cost, and would have a greater survival benefit for every dollar spent than other currently routine screenings, such as those for breast cancer, high blood pressure and diabetes.

According to Paltiel, the findings present "a golden opportunity to jumpstart the expansion of HIV testing services in the United States."

Drive to cure blindness hits $5 million

The Medical School's Anlyan Center was graced with white linen and fresh flowers at a March celebration to mark the successful completion of a five-year, $5 million campaign to build a new center for macular degeneration research at Yale.

The campaign was given a jumpstart at the outset, thanks to a $500,000 donation from the Connecticut Lions Club Eye Research Foundation in 2000. On its heels came a $1 million challenge grant from Foresight Inc., a Connecticut-based eye-research charity founded by former patients of Yale ophthalmologists.

Kenneth and Christine Lo, who traveled from Taiwan to attend the March event, contributed $500,000 to the effort, and two Yale Vision Galas organized by Cecilia Teitell of Stamford, Conn., raised another $385,000.

Rocky Cingari, a longtime Connecticut Lions member from Darien, crisscrossed the state during the campaign seeking additional contributions from local Lions Clubs, friends and business contacts.

Cingari coordinated a separate appeal to employees and customers of ShopRite supermarkets, including the seven he owns in southwestern Connecticut with his brothers Sam and Dominic, and he planned charity golf tournaments held in conjunction with ShopRite and the Darien Lions.

With donations from the Darien-based E. Matilda Ziegler Foundation for the Blind and from William Ziegler, the campaign reached its $5 million goal in January.

Offering thanks to all who made contributions toward building the center, which will be known as the Connecticut Lions Macular Degeneration Research Center, Bruce Shields, M.D., the chair and Marvin Sears Professor of Ophthalmology and Visual Science, said, "We have been very blessed with an incredible number of dedicated and talented people, to whom we are grateful beyond words."

Bruce Shields with Christine and Kenneth Lo at the new center. More photos at our website.

As donors mingled with Yale doctors and scientists during a cocktail reception, the vast Starr Atrium echoed with strains of the Beatles' "Blackbird" played on classical guitar. Lennon and McCartney's lyrics—*Take these sunken eyes and learn to see*—were never more apt.

Hebert *continued from page 1*

are the target sites for important diuretic drugs and explain their mechanism of action. His subsequent discovery of a calcium-sensing receptor known as CaSR led to the development of a new drug, Amgen's Sensipar, which is used to treat hyperparathyroidism, a hormonal disorder that affects most of the more than 1 million patients worldwide with end-stage kidney disease.

"What's really amazing," says fellow nephrologist Peter S. Aronson, M.D., "is that Steve has made breakthroughs in three quite different areas. What he's done is really remarkable."

Hebert is a past recipient of the Homer Smith Award, the top prize given by the American Society of Nephrology, and he is traveling in June to Singapore to accept the A.N. Richards Award from the International Society of Nephrology (see related story, Page 2).

According to Richard P. Lifton, M.D., PH.D., chair and Sterling Professor of Genetics, Hebert's election to the NAS was no surprise, given the major contributions he has made to his field.

"One of the major thrusts of Steve's work has been to put a molecular face on the abstract principles that have been defined by Gerhard [Giebisch] and other members of the physiology department here at Yale," Lifton said at a ceremony honoring Hebert. "By identifying these molecules, he has really allowed us to begin to see how this very intricate and complex machine works in all its integrated glory."

At the ceremony, Dean Robert J. Alpern, M.D., called election to the NAS "the greatest honor you can have as a scientist in the United States and certainly one that is reserved for a select few." For his part, Hebert was clearly elated, and in his remarks he returned to the development of Sensipar as one of the most meaningful events in his career. "Being involved with the translation of your science into medicine," he said, "is the greatest joy you can have as a scientist at a medical school."

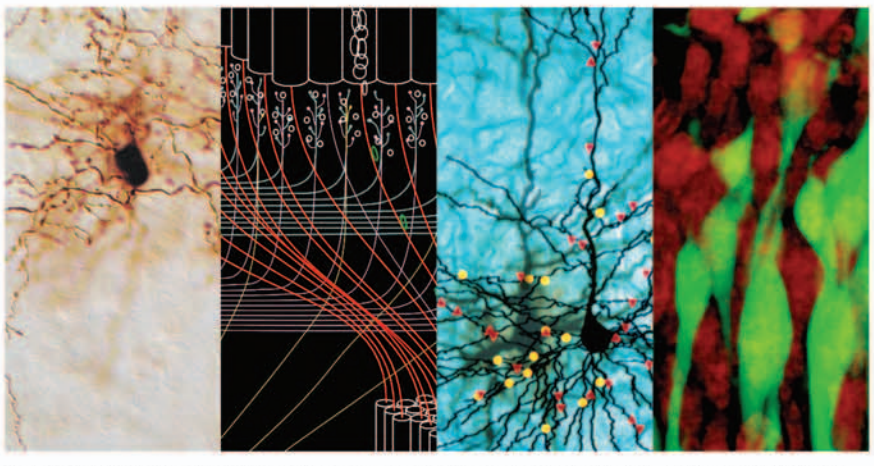
Kavli *continued from page 1*

intellectual interest in the fundamental scientific questions of our age.

The foundation has distributed more than $100 million in grants to create 10 Kavli Institutes that embrace science writ both enormously large and exceedingly small. Four institutes dedicated to astrophysics foster study of the origin and structure of the universe, while three others concentrate on nanoscience, a cutting-edge field devoted to the manipulation of matter at the molecular and atomic levels.

For Rakic, who serves as director of Yale's Kavli Institute, it is no accident that the foundation has chosen neuroscience to bridge these extremes. "Fred Kavli understands that only the human brain is capable of grasping both the whole universe and the tiniest particle," Rakic says, "so it has great intellectual appeal for him to learn how the human brain works."

Kavli also firmly believes that unfettered inquiry is the best route to cracking these great puzzles, and the foundation has won great respect among scientists for its nonintrusive style. "For a typical grant, we must provide a timetable, even specifying what we will do in three years," Rakic says. "Kavli realizes that in three years you might have changed your mind and decided that you need to do something else."



Left to right: Images from research on the cortex by Yale scientists David McCormick, Pasko Rakic, the late Patricia Goldman-Rakic and Nenad Sestan.

Often a scientist has an intriguing idea, but not enough data for a full-blown grant proposal. The Kavli Institute for Neuroscience at Yale has provided seed money for exploratory projects, Rakic says, helping scientists do the preliminary work that may lead to new lines of research. The institute has also sponsored lectures and informal brainstorming sessions with leading neuroscientists from around the world. Finally, the institute is planning annual symposia where acclaimed researchers will present the latest thinking in neuroscience.

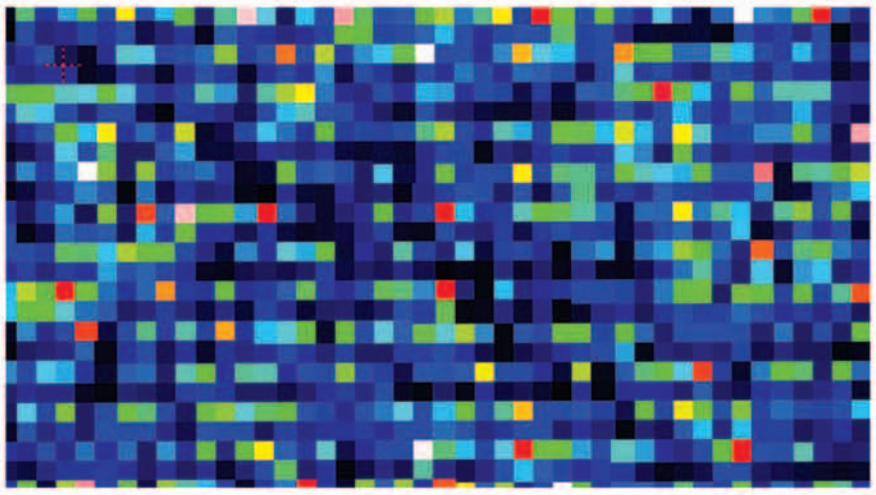
"We are confident," says Fred Kavli, "that the expert scientific team at Yale will make important progress in gaining understanding of some of the most complex and baffling secrets in nature hidden in the brain and mind."

Analysis of genome reveals clues to macular degeneration

Biomedical research into the genetic basis of disease has progressed at a rapid clip since the sequence of the human genome was announced in 2000, but March 10 saw the scientific equivalent of a triple play.

Three research teams, including one led by Josephine J. Hoh, PH.D., of Yale's Department of Epidemiology and Public Health, simultaneously announced that they had identified a gene variant associated with a greatly increased risk of age-related macular degeneration (AMD), a progressive disease leading to blindness that affects more than 10 million elderly Americans (see related story, Page 6).

The human genome can be thought of as a vast string of 3 billion letters in which each letter represents one of the four nucleotides that provide instructions to the body's protein-building machinery. The genome is 99.9 percent identical among humans, but after every 100- to 300-letter stretch on average are single nucleotide polymorphisms, or SNPs (pronounced "snips"), sites where one letter is substituted for another. Scientists believe that these single-letter variations may help explain why some people are predisposed to certain diseases or respond differently to drug therapies.



In this detail of the genome map of a person with macular degeneration, red and white squares mark strong matches with probes that find gene variants.

Remarkably, all three of the teams who published their findings in March independently zeroed in on precisely the same SNP, a spot on chromosome 1 that is home to a gene that codes for an immune system protein known as complement factor H (CFH).

In its usual form, CFH acts as a brake on the complement system, a component of the body's immune response. According to Hoh, whose group scanned the full genomes of 96 individuals with AMD and those of 50 controls, those who carry two copies of the newly identified variant in the CFH gene are nearly 7.5 times more likely than the rest of the population to develop AMD. "This is only an association," Hoh emphasizes. "It doesn't really tell you that this is the cause of the disease."

But a faulty version of CFH may indeed be a culprit in AMD, which has many features of an autoimmune disease. For example, yellowish deposits at the back of the eye known as drusen, the clinical hallmark of AMD, contain complement proteins.

Hoh, an assistant professor, credits the Raymond and Beverly Sackler Fund for the Arts and Sciences for making the study possible. "This particular kind of study is expensive, not the normal thing a junior faculty member can perform," she says. "I am extremely grateful for the support from the Sackler family."

Michael B. Bracken, PH.D., M.P.H., the Susan Dwight Bliss Professor of Epidemiology and Hoh's collaborator, adds that the work represents a wholly new way of doing epidemiology. "For the past 100 years, we've used a hypothesis-testing approach, where hypotheses were generated from animal studies or small human studies and then we did large epidemiology studies."

By contrast, whole-genome searches for SNPs are "hypothesis-free": "The association between a gene and disease is established first, and the biology is done after," Bracken says. "This takes all that we've thought about doing science and turns it on its head, and it's likely to have major payoffs in the future."

Grants and contracts awarded to Yale School of Medicine

January/February 2005

Federal

Karen Anderson, NIH, A Novel Approach for Studying Transient Enzyme Intermediates, 4 years, $1,219,062 • **Susan Baserga**, NIH, Assembly, Localization and Function of the U3 snRNP, 4 years, $1,433,671 • **Kevin Behar**, NIH, NMR Studies of Brain Energetics and Hypoglycemia In Vivo, 4 years, $1,438,800 **Walter Boron**, Office of Naval Research, Gas Transport Through Channels, 3 years, $189,683

Peter Bowers, NIH, Identification of a Gene Causing Aortic Stenosis, 2 years, $449,625 • **Lawrence Brass**, NIH, Stroke Hospitalization in the Elderly with Medicare FFS (SHEF) Study, 4 years, $1,244,091 **Cecilia Canessa**, NIH, Regulation of ENaC by SGK1, 5 years, $1,798,500 • **Michael Cappello**, NIH, The Role of MIF in Hookworm Infection and Disease, 5 years, $2,027,875 **James Duncan**, NIH, Integrated Function/Structure Image Analysis in Autism, 5 years, $1,835,724 • **Cynthia Epperson**, NIH, Neuroactive Steroids, GABA and Glutamate, in PMDD, 5 years, $614,117

Mark Hochstrasser, NIH, Degradation of Short-Lived Regulatory Proteins in Yeast, 4 years, $1,422,452 • **Stuart Katz**, NIH, Studies on Genetics in Heart Failure, 5 years, $803,994 **Kenneth Kidd**, NIH, ADH and ALDH2 Genes in Tanzanian Population, 3 years, $102,500 • **Walther Mothes**, NIH, Retroviral Egress via Multivesicular Bodies, 2 years, $489,788 • **Chirag Parikh**, NIH, Renal Failure in Non-Myeloablative Stem Cell Transplant, 3.5 years, $142,830 • **Archibald Perkins**, NIH, Leukemic Transformation by the AML1/MDS1/EVI1 Protein, 5 years, $1,507,211 **Robert Schultz**, NIH, The Fusiform Gyrus and Amygdala in the Pathobiology of Autism, 5 years, $1,635,000 • **Frederick Sigworth**, NIH, Fluctuations in Ionic Current through Membrane Channels, 4 years, $2,424,419 **Elisabetta Ullu**, NIH, RNA Metabolism in Trypanosomes, 5 years, $3,559,787 • **Anthony Van den Pol**, NIH, Response Properties of Hypothalamic MCH Neurons, 5 years, $1,701,420 • **Shu-Ming Wang**, NIH, Acupuncture and Low Back Pain During Pregnancy, 3 years, $654,000

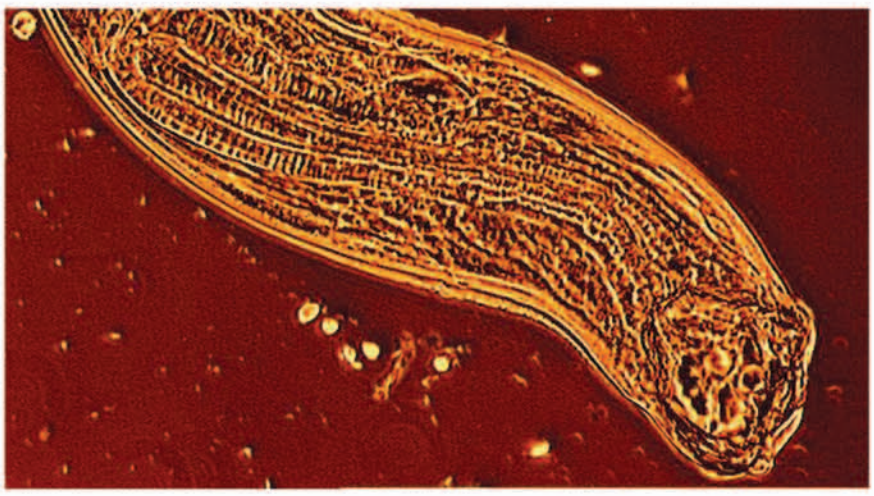
Non-Federal

Thomas Biederer, March of Dimes, Analysis of a Molecular Link Between Synapse Formation and Neurodevelopmental Disorders, 1 year, $150,000 • **Daniel Biemesderfer**, American Society of Nephrology, Megalin Function in Normal and Diseased Kidney, 1 year, $100,000 **Jonathan Bogan**, American Diabetes Association, Regulation of Glucose Transporter Trafficking, 1 year, $100,000 • **Mary Bogucki**, Sekos Inc., SCBA Oximetry for Fire-Fighter Physiological Monitoring—Phase II, 1 year, 8 months, $231,909 • **Yiqiang Cai**, The PKD Foundation, Study of Polycystin-1 Ciliary Localization/Trafficking and the Underlying Molecular Determinants, 1 year, $65,000 **Michael Caplan**, Cystic Fibrosis Foundation, The Effects of Curcumin Treatment on the Function of Gamma F508 CFTR, 1 year, $108,000 • **Thomas Carpenter**, The Gerber Foundation, Biomarkers of Dietary Calcium Insufficiency in Inner-City Infants, 3 years, $844,432 • **Joseph Craft**, The Arthritis Foundation, CNS Lupus: Mechanistic Dissection, 2 years, $200,000 • **Richard Edelson**, American Cancer Society, American Cancer Society Institutional Research Grant, 3 years, $420,000 • **Ramsay Fuleihan**, Bayer Healthcare, Molecular Pathogenesis of Antibody Deficiency Syndrome, 1 year, $74,760

Satish Ghatpande, American Heart Association, Elucidation of Retinoid Signaling Pathway for Cardiac Morphogenesis, 4 years, $65,000 • **Thomas Gill**, University of Florida, Exercise to Prevent Disability—Pilot Study, 7 months, $29,853 • **Walter Gilliam**, The William Caspar Graustein Memorial Fund, Preschool in Connecticut: Linking Community Data to a National Pre-K Context, 1 year, $38,220 • **Robert Kerns**, The Patrick and Catherine Weldon Donaghue Medical Research Foundation, CBT for Painful Diabetic Neuropathy, 3 years, $223,795 • **Dori Laub**, The International Psychoanalytical Association, Video Testimony Study of Chronically Hospitalized Holocaust Survivors in Israel, 1 year, $8,000 • **Chun Geun Lee**, American Thoracic Society, Genetic Factors Controlling TGF-beta 1 in the Pathogenesis of COPD, 2 years, $50,000 • **Graeme Mason**, Pfizer, Development of Non-Occipital, Multi-Volume GABA MRS at 4 Tesla—An Investigator-Initiated Proposal, 2 years, $472,095 • **Daniel Mathalon**, Alcoholic Beverage Medical Research Foundation, Automatic Processing of Alcohol Cues in Chronic Alcoholism: ERP and fMRI Data, 2 years, $100,000

Sherry McKee, Alcoholic Beverage Medical Research Foundation, Effect of Alcohol on Reactivity to Tobacco in Experimental Smokers, 2 years, $100,000 • **Linda Niccolai**, The Patrick and Catherine Weldon Donaghue Medical Research Foundation, Risk in Partnerships for Repeat Sexually Transmitted Infection, 3 years, $240,000 • **Timothy Quan**, Scleroderma Foundation, The Role of Fibrocytes in Nephrogenic Fibrosing Dermopathy, 3 years, $100,000 • **Joseph Schlessinger**, Ludwig Institute for Cancer Research, Intracellular Signaling Pathway for Cell Signaling in Cancer and Other Diseases, 1 year, $375,000 • **Nenad Sestan**, Whitehall Foundation, Molecular Control of Pyramidal Cell Identity and Connectivity, 3 years, $225,000 • **Hosanna Soler**, American Cancer Society, Psychosocial Factors, Race and Cancer Survival, 5 years, $129,400 • **Julie Ann Sosa**, Association for Academic Surgery, Effects of Parathyroidectomy on Neurocognitive Function in Primary Hyperparathyroidism, 1 year, $35,000 • **Stephen Strittmatter**, Christopher Reeve Paralysis Foundation, Axonal Regeneration Pharmaceuticals for Recovery from Spinal Cord Injury, 3 years, $805,477

Mary Tinetti, The John A. Hartford Foundation, Yale University Center of Excellence in Aging, 3 years, $300,000 **Li Wen**, The Seaver Institute, Dendritic Cell Therapy for Autoimmune Disease, 1 year, $120,000 • **James Yue**, Abbott Spine, ISD in a Caprine Model, 1 year, $240,242 • **Hongyu Zhao**, Bioinformatics Support for the Analysis of Panomic Data in Order to Identify Potential Biomarkers and Mechanisms of Drug-Induced Vascular Injury, 1 year, $270,000



Michael Cappello and colleagues are investigating the molecular pathogenesis of hookworm infection, which retards physical and mental development in as many as 1 billion people around the world. This photomicrograph shows the worm's mouth at lower right.

Unconventional physician-filmmaker receives "genius" grant

When Gretchen K. Berland, M.D., embarked on a research project in 2001 aimed at improving health care for the disabled, she took an unusual approach: she gave video cameras to three people in wheelchairs and asked them to record their lives.

Berland, an assistant professor of medicine who had worked as a producer for public television before medical school, hoped to make an intimate, first-person film that would give physicians and policymakers a fresh perspective on the day-in, day-out realities of coping with life in a wheelchair. The film that resulted, titled *Rolling*, won the Grand Jury Prize for best documentary at the Lake Placid Film Festival.


Gretchen Berland

Still, one of Berland's mentors, Harlan M. Krumholz, M.D., director of the Robert Wood Johnson Clinical Scholars Program at Yale, wondered whether Berland's maverick style might deny her work the academic recognition he thought it deserved.

He needn't have worried. Berland's work was validated in a big way last fall, when she won one of the John D. and Catherine T. MacArthur Foundation's famed "genius" grants.

"It's very empowering to know an organization like MacArthur believes in your work," says Berland, an assistant professor of medicine who serves on the core faculty of the Clinical Scholars Program.

Berland says that her film adds new perspective to the doctor-patient relationship, which she believes is undermined by the typical 15-minute office visit. The subjects of *Rolling* are "real and dimensional," she says, and we see their disability in the context of their whole lives.

Berland says she receives 100 inquiries about *Rolling* every week, and she has answered more than 7,000 requests for videotapes from throughout the world.

She used to charge $15 for tapes to cover her costs, but since winning the $500,000, no-strings-attached MacArthur, she has been distributing copies for free.

Berland is grateful for the open-minded encouragement she has received at Yale. "My work is very nontraditional," she says, "and they knew that when I came here. Not many other universities would have supported that."

New HHMI investigator says appointment liberates his science


Ronald Breaker

Ronald R. Breaker, PH.D., has never shied away from less-charted scientific waters, but he says the best thing about his selection in March as a Howard Hughes Medical Institute (HHMI) investigator is that the institute's largely unrestricted support will "allow me to become much more aggressive in taking bigger risks."

Breaker's penchant for unconventional science has served him well. In his pathbreaking work on "riboswitches," Breaker has shown that cells can regulate their function in ways that biologists would only recently have considered possible.

In the laboratory, RNA strands can fold into intricate three-dimensional structures known as aptamers, which precisely recognize targets, much like antibodies do. For example, Breaker has engineered aptamers to detect minute quantities of potential bioterrorism agents. But most biologists thought of aptamers as just a handy tool, and few imagined that they played any role in living things.

However, because aptamers work so well in the lab, Breaker was convinced that they must exist in nature. Three years ago, he stunned the scientific world by showing not only that aptamers exist in bacteria, but also that they switch genes on and off, a function previously thought to be the sole province of proteins acting on DNA. These natural aptamers, which Breaker calls riboswitches, may be important new drug targets in humans, and Breaker has co-founded a company to search for aptamer-based gene therapies.

Breaker, the Henry Ford II Professor of Molecular, Cellular and Developmental Biology, is one of 43 newly appointed HHMI investigators. He joins 15 other Yale HHMI investigators among the 341 designees at biomedical research centers across the United States.

Awards & honors

Hal Blumenfeld, M.D., PH.D., assistant professor of neurology, neurobiology and neurosurgery, has received the Dreifuss-Penry Epilepsy Award for his research on epilepsy and impaired consciousness. The award is made by the American Academy of Neurology to recognize physicians in the early stages of their careers who have made an independent contribution to epilepsy research.

Linda Degutis, DR.PH., M.S.N., associate professor of surgery (emergency medicine) and of epidemiology and public health, was elected chair of the executive board of the American Public Health Association (APHA). The APHA, with 35,000 members from a variety of disciplines, is the primary association for public health professionals and practitioners.

Roberto J. Groszmann, M.D., professor of medicine and director of the Section of Digestive Diseases at the VA Connecticut Healthcare System in West Haven, received the 2004 Ismar Boas Medal from the German Society of Digestive and Metabolic Diseases in Leipzig, Germany, for his scientific contributions to gastroenterology, hepatology and metabolic diseases.

Albert C. Lo, M.D., PH.D., assistant professor of neurology, received a Presidential Early Career Award for Scientists and Engineers from the White House Office of Science and Technology Policy at a reception at the White House last September. Lo was honored for his contributions to new therapeutic strategies to restore function in people with multiple sclerosis.

John D. MacMicking, PH.D., assistant professor in the Section of Microbial Pathogenesis, has been selected as a Searle Scholar by the Illinois-based Kinship Foundation. The award is one of the most prestigious given to junior scientists. MacMicking also received the Mallinckrodt Foundation Program Scholar Award in 2004, given annually to scientists starting their careers.

Susan T. Mayne, PH.D., professor of epidemiology, was appointed to the nutrition subcommittee of the Food Advisory Committee of the Food and Drug Administration's Center for Food Safety and Applied Nutrition, which provides advice to the center's director and the commissioner of food and drugs regarding emerging food safety, food science, nutrition and other food-related issues.

David McCormick, PH.D., professor of neurobiology, has received the Jacob Javits Award in the Neurosciences to study the basic operational mechanisms of the cerebral cortex. The award is made by Congress in honor of the late U.S. Senator Jacob Javits of New York with advice from the National Advisory Neurological Disorders and Stroke Council.

John A. Persing, M.D., professor of surgery (plastic) and neurosurgery, will begin his term as chair of the American Board of Plastic Surgery in May. Persing, who is just finishing his term as president of the American Association of Academic Chairmen in Plastic Surgery, has been chief of the Section of Plastic Surgery at Yale since 1992.

Raymond R. Russell, M.D., assistant professor of medicine (cardiology), has been named the 2004 Bayer Fellow. The award, endowed by the Bayer Pharmaceuticals Corp., provides a fellowship each year to a faculty member making significant advances in medicine or health care management.

Robert S. Sherwin, M.D., the C.N.H. Long Professor of Medicine, has received the Long-Standing Achievement Award from the Novartis Pharmaceutical Corp. for his role in developing insulin pump therapy, a crucial advance in diabetes care, in which insulin is infused continuously via a small pump. He also helped develop the most widely accepted method for measuring cells' sensitivity to insulin.

Robert Udelsman, M.D., M.B.A., the Lampman Memorial Professor of Surgery and Oncology and chair of the Department of Surgery, has been elected president of the American Association of Endocrine Surgeons (AAES), a society of board-certified surgeons who have a major interest in and devote significant portions of their practice or research to endocrine surgery.

Stephen G. Waxman, PH.D., M.D., professor of neurology, pharmacology and neurobiology and chair of the Department of Neurology, has been named the first recipient of the National Multiple Sclerosis Society's Stephen C. Reingold Award. The award recognizes the contributions of Stephen C. Reingold, PH.D., who, until his recent retirement, was responsible for the society's national research and training programs.