

1 BRAIN, HEAL THYSELF
Weill Cornell researchers marvel at the brain's ability to rewire itself after major trauma.

2 LUNG CANCER "GENDER GAP"
Why are women twice as likely to get this cancer but only half as likely to die from it?

4 JOB STRESS & HYPERTENSION
Study finds that chronic work-related stress is not a primary cause of hypertension.

6 ROBOTS SAVING FERTILITY
Robotic surgery system removes uterine fibroids without harming a woman's fertility.

8 TEACHING EXCELLENCE
Physician-teachers are recognized for commitment to training the future leaders in health care.

the **S**cope

Weill Cornell

News of the Joan and Sanford I. Weill Medical College and Graduate School of Medical Sciences of Cornell University

September • October 2006

A Real-Life Rip Van Winkle

Weill Cornell researchers explore how the brain of a patient in a minimally conscious state "rewired" itself

How does science explain a miracle? That was the tough task set for a Weill Cornell-led team probing the improbable: the unprecedented cognitive and physical recovery of 42-year-old Terry Wallis, who spent 20 years in a "minimally conscious state" after suffering a severe brain injury in a 1984 truck accident.

Unlike either coma or a persistent vegetative state, patients in a minimally conscious state may display rare, fleeting signs of awareness or simple communication, but typically undergo no sustained recovery. Every expert involved in Terry's case deemed it hopeless, since no one had ever come back from such a state after so many years.

Then, on a June day three years ago, Terry uttered one word: "Mom."

And he didn't stop there. Regaining the power of speech over a three-day period, he began making steady, impressive gains. Although he cannot yet walk, Terry has regained much of his physical strength. His personality has slowly returned, but like a modern-day Rip Van Winkle, he has no memory of his time spent in the minimally conscious state.

"He still thinks Ronald Reagan is president, and up until recently has insisted that he's still 20 years old," said Terry's father, Jerry, who now cares for his son in Mountain View, Ark., with the help of his wife, Angilee, and their daughter, Amber, who was born shortly before the accident. Jerry says that, in many ways, his son "seems almost exactly like his old self, and he very often tells us how glad he is to be alive."

Wallis' "miracle recovery" first made headlines in the summer of 2003, and Weill Cornell neuroscientist Dr. Nicholas Schiff describes it as a "one-in-300-million" event, since such a case has never been documented before in the United States.

But the recovery also puzzled Dr. Schiff, who is associate professor of neurology and neuroscience at Weill Cornell and director of the



Terry Wallis, 41, of Mountain View, Ark., center, speaks with his sister Tammy Baze (right) before a doctor's appointment as Terry's mom, Angilee Wallis (left), listens in. Three years ago, Terry emerged from a 19-year-long coma-like state resulting from a 1984 car accident that injured his brain.

AP PHOTO/MIKE WINTROATH

Laboratory of Cognitive Neuromodulation. "We were left with one obvious question," he said. "Why Terry?"

To find out, he joined forces with Dr. Henning Voss, assistant professor of physics in radiology at the Medical College's Citigroup Biomedical Imaging Center. Over an 18-month period, the two researchers used both PET scans and a cutting-edge technology called diffusion tensor imaging (DTI) to track changes in the neural circuitry of Terry Wallis' brain, beginning at about nine months after his initial recovery.

"DTI is basically a new way to extract information from MRI scans," Dr. Voss explained. "It tracks the diffusion of water molecules in and around brain cells to highlight brain tissue integrity and its changes." What they found astounded them.

>>> page 4

Using Philanthropy to Combat Third-World Disease

Abby and Howard P. Milstein gift to establish state-of-the-art Chemistry Core Facility and Program in Chemical Biology

Although no longer a significant public health threat in the U.S., malaria and tuberculosis continue to have a devastating impact on much of the world, particularly in the former Soviet Union and sub-Saharan Africa. A recent gift of \$7.25 million from Howard and Abby



EILEEN MILLER

Howard P. Milstein

Milstein will target these diseases and others that affect the developing world by establishing the Abby and Howard P. Milstein Chemistry Core Facility and the Abby and Howard P. Milstein Program in Chemical Biology at Weill Cornell Medical College. The gift is part of the recently completed \$750 million *Advancing the Clinical Mission* capital campaign.

Specifically, the gift will be used to create and staff a core facility that will design and purify compounds to support research within the Chemical Biology Program, as well as help scientists study many other diseases. The new, multidisciplinary Chemical

>>> page 7

Leading WCMC Biochemist Shows His MERIT

NIH award gives Dr. Frederick Maxfield's pioneering work a \$2.8 million boost

NO ONE KNOWS BETTER THAN DR. FREDERICK Maxfield that the living cell never stops moving.

The Weill Cornell researcher's breakthrough work on intracellular trafficking—the ceaseless to-and-fro of receptors, transporters, lipids and other key molecules essential to life—is the kind of basic science that could end up changing all our lives.

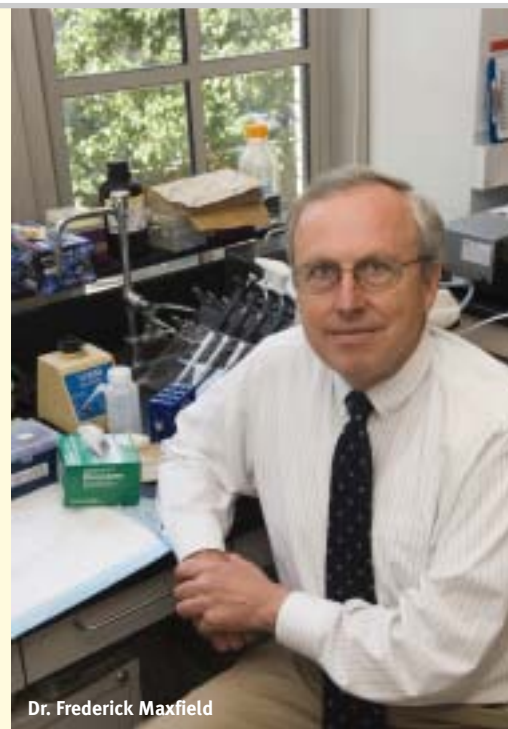
Luckily, that research is now guaranteed to keep moving forward, too: the U.S. National Institute of Diabetes and Digestive and Kidney Diseases recently named Dr. Maxfield the recip-

ient of a prestigious five-year, \$2.8 million NIH Method to Extend Research in Time (MERIT) Award.

Dr. Maxfield is the Israel Rogosin Professor of Biochemistry and chairman of the Medical College's Department of Biochemistry. His lab develops and uses cutting-edge optical and biophysical tracking techniques to examine relationships between molecules as they interact inside and outside the cell.

"Our focus on 'endocytic trafficking' helps us understand how nutrients

>>> page 5



Dr. Frederick Maxfield

Two Gifts Create New Centers for MS, IBD

Feil Unit and Roberts Center to build upon existing resources to better serve patients and advance research

How do you make something great even better? Thanks to the generosity of two benefactors, patients with multiple sclerosis or inflammatory bowel disease are about to find out. Weill Cornell Medical College Overseer Jeffrey J. Feil, president of the Feil Family Foundation, announced in June a gift of \$5 million to establish the Feil Family Multiple Sclerosis Clinical Unit as a much-needed addition to the Medical College's Multiple Sclerosis Clinical Care and Research Center. The new unit is slated to open its doors in January 2007, and will be located in the new Ambulatory Care and Medical Education Building at York Avenue and 70th Street.

Then another June announcement: Jill Roberts, a long-standing friend and patron of NewYork-Presbyterian Hospital and Weill Cornell Medical College, pledged \$4 million for the creation of the Jill Roberts Center for Inflammatory Bowel Disease. The Roberts Center has been up and running since July in its location in the Stich Building at 69th Street and York Avenue—right beside NewYork-Presbyterian/Weill Cornell's Jay Monahan Center for Gastrointestinal Health and the Center for Colon and Rectal Surgery.

"The foresight and generosity of benefac-

tors like the Feils and Jill Roberts will help advance research into these two illnesses, which together afflict millions of Americans. The new centers will build on the world-class resources already in place, providing patients with unparalleled treatment," said Dr. Antonio M. Gotto Jr., dean of the Medical College.

The new MS unit was inspired, in part, by the Feil family's personal experience. The Feil family has funded the Multiple Sclerosis Clinical Care and Research Center since

"The foresight and generosity of benefactors like the Feils and Jill Roberts will help advance research into these two illnesses, which together afflict millions of Americans.

— Dean Antonio M. Gotto Jr.

2000, when they established the Louis and Gertrude Feil Professorship of Clinical Neurology in honor of Dr. John Caronna. In addition, Jeffrey Feil has been a member of the Medical College's Board of Overseers since 2003.

"Weill Cornell's multiple-sclerosis program is well-known for its excellence in research," said Mr. Feil. "Our family is very grateful for the care given by the department to my late father, Louis, and our family."

The new unit is directed by Dr. Brian Apatoff, a nationally recognized authority

in MS treatment and research. "This gift secures urgently needed new space and we expect patient visits to more than double," he said. Already, the Feil unit offers patients state-of-the-art diagnosis and treatment for MS and related disorders, including cutting-edge investigational therapies. Many of those therapies are the product of the center's innovative research, including immune-modulatory approaches and gene therapy aimed at suppressing the rogue cells that help drive MS.

"The Feil gift—which also endows two Feil Family Clinical Scholar Awards in Multiple Sclerosis—will ensure that this research moves forward," Dr. Apatoff said.

Over at 69th Street, patients are already reaping the benefits of Jill Roberts' generosity in the creation of the new Roberts Center for Inflammatory Bowel Disease. In fact, the addition of the new center—led by Dr. Ellen Scherl—means the entire Stich Building is now dedicated to the investigation and treatment of digestive disease.

"The Roberts Center will allow us, more

than ever, to uniquely offer IBD patients the multidisciplinary treatment and care they need—all in one building," said Dr. Scherl.

According to Dr. Herbert Pardes, president and CEO of NewYork-Presbyterian Hospital, "Working synergistically with its sister programs next door, the Roberts Center will be a model of patient-centered care, offering convenience and innovative treatment options to patients with IBD."

The center will offer comprehensive can-

cer screening for IBD patients, improved access to the latest in diagnosis and treatment, a patient library, nutritional and genetic counseling and other supportive services. It will also be a national locus for IBD research, housing the Tissue Bank—a source of endoscopic biopsy samples crucial to a better understanding of gut inflammation.

"More than one million Americans suffer from the painful symptoms of IBD," Dr. Gotto said. "The Jill Roberts Center will pursue promising clinical research to improve their lives." ■

the Scope

Published by the Office of Public Affairs, Joan and Sanford I. Weill Medical College and Graduate School of Medical Sciences of Cornell University

THE STEPHEN AND SUZANNE WEISS DEAN, WEILL MEDICAL COLLEGE
Dr. Antonio M. Gotto Jr.

DEAN, WEILL GRADUATE SCHOOL OF MEDICAL SCIENCES
Dr. David P. Hajjar

VICE PROVOST FOR PUBLIC AFFAIRS
Myrna Manners

DIRECTOR OF COMMUNICATIONS
Jonathan Weil

DIRECTOR OF PUBLICATIONS/EDITOR
Michael Sellers

SCIENCE WRITER
Ernie Mundell

FEATURE WRITER
Gabriel Miller

CONTRIBUTING WRITERS
Jarrett Kroll, Georgia Tucker

EDITORIAL ASSISTANT/COPY EDITOR
Andria Lam

DESIGN
Shostak Studios, NYC

PRINCIPAL PHOTOGRAPHY
Amelia Panico

Office of Public Affairs
1300 York Avenue, Box 144
New York, New York 10021
212-821-0560
publicaffairs@med.cornell.edu

For PDF copies of *The Scope* and other Weill Cornell publications, please visit our Web site at www.med.cornell.edu/publications.

The Lung Cancer "Gender Gap"

Study shows that women are twice as likely to get the disease, but half as likely to die from it

Lung cancer, the nation's No. 1 cancer killer, doesn't play favorites. Every year, a similar number of men and women will die from the disease, which claimed more than 160,000 lives in the United States last year.

But a major new Weill Cornell

study shows that patterns of lung cancer diagnosis and survival do vary between the sexes.

"We found that women smokers face more than double the risk of developing lung malignancies, but they are also twice as likely to survive the cancer, compared to men," said lead researcher Dr.

Claudia Henschke, chief of Chest Imaging in the Department of Radiology at NewYork-Presbyterian/Weill Cornell.

The study, which appeared July 12 in the *Journal of the American Medical Association*, "really clears up the confusion surrounding gender and lung cancer, and

suggests that women smokers may need to get screened earlier for the disease," said Dr. Henschke, who is also professor of radiology at the Medical College.

The findings stem from her role as principal investigator for the ongoing, international Early Lung Cancer Action Project (ELCAP), which involves researchers from 37 academic medical centers worldwide.

"We had already published results focused on about 2,500 ELCAP participants in the New York City area, but this newer study expands that data to include nearly 7,500 female and 9,500 male smokers, all of whom underwent CT lung cancer screening at centers across the U.S.," Dr. Henschke explained. All the participants were 40 years of age or older and showed no symptoms of lung tumors at the time of screening.

However, "screening picked up signs of malignancy in about 2 percent of female participants compared to just 1.2 percent of males," she said. "After adjusting for differences in age and smok-



Attacking Antibiotic Resistance

Bold new strategies are necessary to beat stubborn bugs, Weill Cornell expert advises

Like soldiers battling their way uphill, antibiotics have helped us beat back infectious disease for decades. In recent years, however, the emergence of “superbugs” resistant to nearly every available drug is raising the specter of microbial wars we just can’t win.

New, effective antibiotics are needed and needed soon, but “antibiotic development in the pharmaceutical industry is steeply declining,” warns Dr. Carl Nathan, chairman of the Department of Microbiology and Immunology at Weill Cornell Medical College.

As the author and co-author of two articles published over the last two years in *Nature* and *Nature Reviews Drug Discovery*, Dr. Nathan notes that the sectors of private industry, regulatory agencies and academia are responding as best they can while operating in the current system.

“Government agencies and professional societies have addressed antibiotic resistance, but little has changed,” according to Dr. Nathan. “All three sectors will be accountable if we let society down by not responding to the obstacles with a restructured approach.”

This new approach will require new ways of doing business. Because antibiotics are most desperately needed in cash-poor populations typically shunned by the private sector, Dr. Nathan supports the development of “another kind of player on the scene: a not-for-profit drug company.”

Focused primarily on identifying and patenting drugs overlooked by industry, these non-profits would license their intellectual property “gratis to any company or agency that commits to producing or distributing the resulting drugs” to those that need them, he said.

Then there’s the current regulatory system, which Dr. Nathan believes hinders the development of new antibiotics.

Patent life on new antimicrobials should be extended, he said, and drug-makers should be encouraged to test out “synergies” between combinations of drugs. Most importantly, “all new antibiotics should be banned from widespread administration to healthy animals,” since the use of antibiotics in agriculture remains a key source of resistance in humans today.

Finally, academics need to undergo a sea change in their approach to antibiotics research, Dr. Nathan contends. For too long, investigators have focused on the same group of microbial targets, “producing almost nothing but variants of older antibiotics,” he said. Now, “the well has gone dry.”

Exploiting recent insights in genetics and cell biology should help scientists identify whole new microbial “points of vulnerability” for developing new drugs, Dr. Nathan believes. And since wide-spectrum antimicrobials tend to encourage resistance, the next generation of antibiotics should focus on a more narrow range of pathogens.

“Is it hopelessly unrealistic to envision not-for-profit companies, a smart regulatory environment, and fresh scientific approaches to antibiotic development?” the Weill Cornell expert asks. Perhaps not: Not-for-profit groups like the Bill and Melinda Gates Foundation and the Medicines for Malaria Venture are already pushing drug discovery forward, he points out.

Dr. Nathan’s concern is echoed by others. One recent study found cases of *Staphylococcus aureus* infection resistant to first-line antibiotics rose 100-fold at one Texas hospital from 1990 to 2001. And both the American Academy of Family Physicians and the American Academy of Pediatrics have issued new guidelines urging doctors to avoid antibiotics for ear infections and other common ailments. Concerned officials at the CDC have also launched a nationwide “Get Smart” campaign, aimed at educating Americans about the problem.



Dr. Carl Nathan (seated) and Dean Antonio Gotto at the June 5 press conference announcing the Abby and Howard P. Milstein gift of \$7.25 million to support research into fighting antibiotic-resistant malaria and tuberculosis.

Ultimately though, industry, regulators and researchers remain the “advance guard” in this war against bacteria. Every player in drug development “has a major stake in the control of infectious diseases,” Dr. Nathan concludes, “not only for medical reasons, but also for global economic development and security.” ■

ing history, that meant that women smokers had nearly twice the odds of developing lung cancer compared to men.”

But the study uncovered another intriguing discovery: Women who developed lung cancer were also 52 percent less likely to die from the disease than men.

“We’re not sure why that might be,” Dr. Henschke said. “Is the women’s cancer just less aggressive? Or is it more curable? It’s definitely an area worthy of future research.”

Right now, though, the take-home message is clear.

“We’ve got to get the word out to women and teenage girls, especially, that their long-term risk of getting cancer is much higher than that of males, even if they smoke at the same rate and for the same period of time,” the researcher said.

And because women are at higher risk for smoking-linked tumors, they may need to be screened for lung cancer earlier than men. “We now believe that the screening threshold should be some 50 pack-years lower for women than for men,” Dr. Henschke said.

Every smoker stands to benefit from early detection. According to the Weill Cornell expert, “Lung cancer is a tough foe, but finding it early at least gives patients that fighting chance.” ■

sciencebriefs

When—and Where—Does Alzheimer’s Begin?

Weill Cornell study suggests that disease begins long before protein “plaques” have formed

For years, scientists believed that an abnormal clumping of beta amyloid protein “plaques” around the outside of brain cells marked the beginnings of Alzheimer’s disease.

But researchers at Weill Cornell Medical College are rewriting the textbooks when it comes to that theory, as they push the illness’ origins much further back in time.

“We’re realizing now that beta amyloid is collecting and ‘clogging up’ the machinery inside the neuron long before we see any external clumping, and long before any noticeable symptoms appear,” said Dr. Gunnar Gouras, director of the Laboratory of Alzheimer’s Disease Neurobiology and associate professor of neurology and neuroscience at Weill Cornell.

His team’s study, published in a recent issue of the *Journal of Neuroscience*, focused on brain cells from special “transgenic” mice engineered to develop an Alzheimer’s-like illness.

“We took care to extract the cells from these mice long before they developed any symptoms of disease,” said lead researcher Dr. Claudia Almeida, who was a graduate



Dr. Gunnar Gouras

student at the time the study took place.

Peering at the cells with an electron microscope, the researchers discovered a buildup of beta amyloid on the outer membrane of an intracellular trafficking structure called the “multivesicular body.” This struc-

ture is key to endocytosis—the intracellular transport of nutrients and other substances the cell needs to thrive.

“We had noted this buildup on the multivesicular body as far back as 2002, however,” Dr. Gouras said. “The question now was, how might it affect the brain cell?”

To find out, they used a special fluorescent “tag” to track various steps in the endocytic process. “Beta amyloid appears to ‘gum up the works’ in a late stage of endocytosis dedicated to the cell’s waste-disposal mechanisms,” according to Dr. Almeida.

“Increasingly, problems in waste disposal mechanisms—especially the ubiquitin-proteasome system—are being linked to synaptic processes that control cognitive activity.”

While prior research has suggested that breakdowns in this system help spur degenerative brain illnesses such as Parkinson’s disease, Alzheimer’s had always been “the odd man out” in terms of intracellular accumulation,” Dr. Gouras said.

“Based on this new evidence, that notion may now have to change,” he said. “It seems as if we’re getting closer to the very first steps in a long and devastating disease.” ■

Job Stress Is One Thing—Hypertension Is Another

Study finds that on-the-job aggravation is not the primary cause of hypertension

A demanding or rude boss or co-worker can have most of us seeing red in no time.

But, aggravating as work stress might be, it probably won't lead to chronic high blood pressure.

Just ask Dr. Samuel Mann, a Weill Cornell researcher who has authored the most exhaustive review of the data on the subject ever conducted, in which he looked at the relationship

To clarify the issue, Dr. Mann pored over data from 48 studies, published between 1982 and 2004, that focused on chronic stress and hypertension. Overall these studies included a total of more than 100,000 participants. Dr. Mann published his conclusions in a recent issue of *Current Hypertension Reviews*.

Most of these studies found either no link between job stress and hypertension, or a link that only showed up in a narrow subgroup.

studies have shown that stress-reduction techniques do not ease chronic high blood pressure.

"That suggests that job stress isn't the cause of hypertension in the first place," Dr. Mann reasoned. But he emphasized that while job stress does not cause hypertension, it is not harmless.

"Ongoing job stress does boost the risk for coronary artery disease, something that cannot be discounted," he said.

So, if most of the evidence

"Although it's long been a cherished notion that chronic stress—in this case, job stress—contributes to hypertension, it's time to set the record straight."

— Dr. Samuel Mann

between on-the-job stress and chronic high blood pressure.

His conclusion: No such relationship exists.

"Although it's long been a cherished notion that chronic stress—in this case, job stress—contributes to hypertension, it's time to set the record straight," said Dr. Mann, professor of clinical medicine at Weill Cornell Medical College and a hypertension specialist at NewYork-Presbyterian Hospital. "Doctors should not be advising patients to quit their jobs to help them avoid hypertension," he said.

"In that case, if any specific subpopulation was particularly susceptible, you'd expect that different studies would identify the same subgroups," Dr. Mann noted. "But it didn't happen."

Other studies found a weak link between hypertension and a single measure of job stress, but no link with all other job-stress measures that were assessed. And some studies found an effect only on diastolic pressure—the bottom number in a blood pressure reading—but no effect on systolic pressure.

Dr. Mann also noted that most

points to the contrary, why do so many people—including many researchers and clinicians—still believe the job-stress myth? One reason is that, without question, stress increases blood pressure in the moment. It is also true that many researchers have a vested interest in keeping the notion of job stress and hypertension alive.

"As in many other fields, articles are published that strain to support a particular point of view," Dr. Mann said. "But it's our job as scientists to weed out the faulty data and show that, in this case, 'the emperor has no clothes.'" ■

<<< from page 1

Rip Van Winkle

"It's something that we can't wholly prove yet, but it seems as if the unaffected areas of Terry's brain have, for years, been quietly growing novel connections that are making up for functional loss in heavily damaged sites," Dr. Schiff said. "It's a process called 'axonal regrowth.'"

Reporting their findings in the July 1 *Journal of Clinical Investigation*, the researchers—with the help of collaborators at Weill Cornell and elsewhere—stress that they haven't got all the answers they are seeking.

"Axonal regrowth cannot fully account for Terry's very late recovery," Dr. Schiff said. "Other changes were no doubt at play and pushed him past a threshold for further recovery. His ongoing rehabilitative therapy is, without question, speeding up the process, too."

Other mysteries remain, not least of which is the fact that Terry's speech improved despite

little evidence of axonal regrowth in his brain's language centers. "We're still learning the rules here, and there's so much we don't yet understand," Dr. Voss said. "But this research has already opened a whole new window onto the minimally conscious state."

The Wallis recovery could have implications for the management of minimally conscious patients, the researchers say.

"What if other patients' brains have this ability to 'reconnect'?" Dr. Voss said. "It argues for better monitoring of their brain structure and function—especially within the first year or two after injury, to track the potential for recovery."

In the meantime, Terry Wallis continues to improve with daily physical and speech therapy sessions.

"We were just so surprised and amazed," his father said. "But we knew he would recover. He's got such a great spirit." ■

science at a glance

Lending Stroke Patients a Hand

BLURRING THE LINE BETWEEN man and machine, a new device called the NESS H200 helps hand-impaired stroke patients literally "get a grip." Worn on the forearm, it delivers small electrical impulses that instruct the weakened hand to open, close and perform other simple movements. According to Dr. Michael O'Dell, associate chief of rehabilitation medicine at NewYork-Presbyterian/Weill Cornell, "We have found that our stroke patients have experi-



Dr. Michael O'Dell and the NESS H200

enced very positive results through the use of the NESS H200." Occupational-therapy manager Kerri Morris said that "our occupational therapists here at Weill Cornell are currently the only ones in the city offering this technology. In less than two months, patients can resume simple but important functions—things like feeding themselves or holding a book." ■

Synaptic Sleight of Hand

UNRAVELING THE BACK-AND-FORTH OF CELLULAR ENDOCYTOSIS—the transport of nutrients and other substances within cells—is crucial to understanding how the synapse works as it transmits information between brain cells. In his team's latest work, published in July in *Neuron*, Weill Cornell biochemist Dr. Tim Ryan used fluorescently tagged proteins to track the process. "We discovered that the synapse's transport vessel, the vesicle, exchanges its own cache of proteins with those pooled on the surface of the cell's axonal membrane," he said. "It's an exciting discovery in terms of basic science and could also shed light on the origins and treatment of neurological disease." ■

NYP Is #6 in the Nation—and Climbing

U.S. News & World Report ranking moves Hospital up another step

NEWYORK-PRESBYTERIAN HOSPITAL, WEILL Cornell Medical College's primary health-care partner, ranks first in New York City and sixth in the nation, according to the 2006 U.S. News & World Report "America's Best Hospitals" survey. It is the sixth consecutive year that NewYork-Presbyterian is the only New York metropolitan-area hospital on the list.

It is also the sixth consecutive year that the NewYork-Presbyterian's "Honor Roll" ranking has advanced, having ranked seventh in 2005. (The Honor Roll lists the top 14 hospitals nationally based on reputation, mortality rates and other care-related factors.)

For the second year, NewYork-Presbyterian is the

only New York metropolitan-area hospital—and one of only five Honor Roll hospitals—to rank in all 16 medical specialties included by U.S. News.



NewYork-Presbyterian ranks among the top five in five specialties: Gynecology (#4); Kidney Disease (#5); Neurology & Neurosurgery (#4); Psychiatry (#3); and Urology (#5). The Hospital ranks among the top 10 in an additional three specialties: Heart & Heart Surgery (#8); Hormonal/Endocrinology (#8); and Pediatrics (#6).

U.S. News has issued the annual rankings of medical centers for the last 17 years. The full rankings can be viewed at www.usnews.com/besthospitals. ■

Research Reveals Renin's Role in Arrhythmia

Research shows that in cardiac crisis, mast cells secrete the enzyme locally, boosting the risk of arrhythmia

Building on their previous breakthrough research, a pair of Weill Cornell investigators say they've found a cause—and possible treatment target—for potentially deadly cardiac arrhythmias.

Last year, a team led by Drs. Roberto Levi and Randi Silver discovered that renin, an enzyme previously thought to originate in the kidneys, is also produced locally by mast cells in cardiac tissue.

Reporting in April in the *Journal of Clinical Investigation*, they expanded further on renin's role, finding that it sets off a biochemical cascade that may explain why heart attack patients are at such high risk for arrhythmias.

"Obviously, drugs that inhibit local renin release could help prevent this potentially deadly complication," said Dr. Levi, who is a professor of pharmacology at Weill Cornell.

The new findings arose from experiments with guinea pigs that underwent cardiac ischemia and then reperfusion—the sometimes traumatic rush of blood back to the heart.

"We noticed a release of renin into the coronary effluent that we just didn't see under normal conditions," remarked Dr. Silver, associate professor of physiology and biophysics.

This surge in local concentrations of renin coincided with an increase in activity of angiotensin 2, a downstream product of renin that's long been linked to cardiovascular disease. In fact, millions of Americans take angiotensin-converting enzyme (ACE) inhibitor drugs to reduce their blood level of the compound.

"High levels of angiotensin 2 also appeared to trigger the release of norepinephrine from nerves in and around the heart," Dr. Silver added. "We already know that in

such high amounts, norepinephrine can disrupt normal cardiac rhythms. In other experiments, we found that the most common result was a type of arrhythmia called ventricular fibrillation."

Drs. Silver and Levi are basic scientists, but also understand the finding's pharmaceutical implications. "It looks promising. Agents that prevent local renin release could prevent this whole cascade—and, potentially, heart-attack-linked arrhythmias," Dr. Levi said.

The finding might have broader implica-



tions, Dr. Silver added. "We speculate that patients with chronic conditions such as angina may be releasing small but significant amounts of renin—and therefore angiotensin—all the time," she said. "Over time, that might encourage enlarged heart muscle and even heart failure. So, lowering angiotensin via local renin inhibition might help curb those conditions, too." ■

FDA OKs Revlimid for Multiple Myeloma

PATIENTS BATTLING DEADLY MULTIPLE MYELOMA HAVE A NEW WEAPON at their disposal—a powerful drug called Revlimid—thanks, in large part, to a Weill Cornell trial. "When the FDA granted this pill final approval in June, we of all the centers participating in the Phase III trial had enrolled the largest number of patients," noted researcher Dr. Ruben Niesvizky, director the NewYork-Presbyterian/Weill Cornell Multiple Myeloma Program. Multiple myeloma is an incurable cancer of the white blood cells that affects some 50,000 Americans. In the trial, patients receiving a combo of Revlimid (lenalidomide) plus dexamethasone survived an average of almost 30 months, compared to 20 months for those on standard therapy. ■



Dr. Ruben Niesvizky

Illuminating the Cell's Anti-Cancer Cascade

EVERY DAY, INSULTS AS COMMON AS SUNLIGHT TRIGGER SERIOUS DNA DAMAGE IN HUMAN CELLS— damage that could lead to cancer. But cells almost always repair that damage, and new work by Weill Cornell researcher Dr. Pengbo Zhou is sorting out how that happens. Reporting in a recent issue of *Molecular Cell*, his team brought fresh insight into the complex relationship between DNA-repair "tagging" molecules called DDBs, and a well-known cellular enzyme called c-Abl. "c-Abl is one of the most intensely studied molecules in cancer research," noted Dr. Zhou, an associate professor of pathology and laboratory medicine. "Among our other findings, we discovered that it works in a completely unexpected way as it interacts with DDBs to help 'fix' damaged DNA. It's a finding that could have broad implications for cancer treatment," he said. ■

Dr. Jonathan Weinsaft Receives \$400K Grant

FOR HIS IMPORTANT RESEARCH INTO THE EARLY DETECTION OF LIFE- threatening embolisms, Dr. Jonathan Weinsaft has received a \$400,000 grant from the Doris Duke Charitable Foundation—one of only 11 such grants bestowed each year. "I'm honored by this award, which will fund the first major clinical study on the use of cardiac MRI to assess the clinical risk associated with blood clots in heart attack patients," said Dr. Weinsaft, who directs the cardiac MRI program at NewYork-Presbyterian/Weill Cornell and is the Michael Wolk Heart Foundation Clinical Scholar, assistant professor of radiology and assistant professor of medicine at Weill Cornell Medical College. The study—a collaboration between the MRI center and a number of the Hospital's cardiovascular programs—will compare MRI to traditional echocardiographic techniques. ■



Dr. Jonathan Weinsaft

WEILL CORNELL ART & PHOTO

<<< from page 1

MERIT Award

and other compounds get into cells, first of all, and then how they move around once they are there," Dr. Maxfield explained. "It's really a microscopic 'mass transit system' that's constantly ferrying a variety of cargoes to different destinations, all guided by complex signals."

His efforts to study this intracellular "traffic grid" have already yielded important insights into the activity of LDL ("bad cholesterol") lipoprotein receptors, as well as transferrin receptors lying on the cell surface. The Maxfield lab also uses natural fluorescent sterols to track the movement of cholesterol and other important molecules within cells.

"This grant—a five-year renewal of a previous NIH award, with a streamlined review for an additional five years—will greatly help to further these types of research," Dr. Maxfield said. "Obviously, a better understanding of cholesterol uptake and transport has tremendous implications for cardiovascular disease research. And scientists are beginning to realize that cholesterol levels may be key to a wide range of illnesses, including Alzheimer's and diabetes."

Others lauded Dr. Maxfield's MERIT award as well-deserved.

"I congratulate Dr. Maxfield, whose important work has already yielded key insights into intracellular trafficking and its role in maintaining the health of cells and—when things go wrong—in fostering illness," said Dr. Antonio M. Gotto Jr., dean of Weill Cornell Medical College.

Dr. David P. Hajjar, Rhodes Professor and dean of the Weill Cornell Graduate School of Medical Sciences, said the NIH grant is bound to foster new scientific breakthroughs.

"It's hard to overestimate the importance of Dr. Maxfield's research and it's promise—both in terms of medical science and innovations at the bedside. He's simply a superb scientist," Dr. Hajjar said.

Dr. Maxfield, who received his Ph.D. in chemistry at Cornell, spent time on the faculties of New York University School of Medicine and Columbia University's College of Physicians and Surgeons before moving to Weill Cornell in 1995. The recipient of numerous awards and appointments, he regularly serves as a member or chair for NIH ad hoc panel reviews, is a past president of both the New York Society of Experimental Microscopists and The Harvey Society, and served as editor of the *Journal of Cellular Physiology* from 1989 to 2002.

But for Dr. Maxfield, it's still all about the science—and what new discoveries might mean for patients down the line.

"Our work focuses on a fundamental piece of cell biology—how proteins that carry essential nutrients get into cells and move around while they're there," he said. "I have no doubt that MERIT funding will open up new windows onto those processes. And that has huge implications for better understanding—and treating—a wide range of illnesses." ■

Robots May Be a Baby's Best Friend

High-tech surgery removes uterine fibroids without harming future chances of pregnancy

For the estimated one in four women with painful uterine fibroids, robotic surgery pioneered at Weill Cornell can help ease the condition without putting their fertility in danger.

"This minimally invasive approach is a real advance, especially for the removal of large fibroids," explained Dr. Glenn Schattman, an associate attending physician of obstetrics and gynecology at the Center for Reproductive Medicine at NewYork-Presbyterian Hospital/Weill Cornell Medical Center.

Benign uterine fibroids are the most common pelvic tumor seen by gynecologists. While some cause abnormal bleeding, pain, miscarriage and infertility, others progress without symptoms.

"Typically, doctors use open surgery to remove these tumors, but many women undergo hysterectomy," explained Dr. Schattman, who is also associate professor of clinical obstetrics and gynecology at Weill Cornell Medical College. "Our new robotic surgery gets around that, especially for tough-to-remove, large or embedded fibroid tumors."

At the start of the procedure, tiny



Dr. Glenn Schattman at the console of the da Vinci Surgical System.

cameras are inserted into the patient's body via small incisions. The surgeon, seated at a nearby console, uses these cameras to view a 3-D image of the procedure and direct the precise movements of tiny surgical instruments at the site of surgery. Dr. Schattman's team relies on the da Vinci Surgical System, made by Intuitive Surgical

of Sunnyvale, Calif.

"Due to its precise movements, the robot can repair the uterine muscle with very little damage to the surrounding tissue. That's so important for women who choose this surgery because they hope to retain their fertility and bear children in the future," Dr. Schattman said. "Especially with larger tumors,

doctors have traditionally resorted to open surgery, which carries added risk and a longer recovery time. In the case of robotic surgery, patients can normally return home the day after the procedure, which is a tremendous advantage."

Robots can help boost fertility in other ways, too. Dr. Schattman was the first surgeon on the East

Coast to use robotic tools to reverse tubal ligation, thereby restoring fertility. In fact, the first patient to undergo this procedure has already given birth.

"Use of robotic devices to excise fibroids is just the latest innovation in robotics here at NewYork-Presbyterian/Weill Cornell," Dr. Schattman pointed out. The Hospital pioneered robotic techniques such as the first robot-assisted atrial septal heart defect repair (in 2001) and the first robotic lung lobectomy (in 2002).

And just this May, Dr. Kevin Holcomb performed the first robotic radical hysterectomy and pelvic lymph node dissection in New York City. "I'd already used the system to perform the city's first-ever robotic pelvic and paraaortic lymph node biopsy," said Dr. Holcomb, who is an assistant attending ob/gyn at the Hospital and an assistant professor of obstetrics and gynecology at Weill Cornell Medical College.

"It's a real advance, because it allows a surgeon to operate with a dramatic reduction in patient blood loss. The robot's 3-D optics help me see and avoid even the smallest blood vessels," he said. ■

academic affairs and appointments

New Division Chiefs

DR. ROBERT GRANT

DIVISION OF PLASTIC AND RECONSTRUCTIVE SURGERY



Dr. Robert Grant has been named chief of the combined Division of Plastic and Reconstructive Surgery at NewYork-Presbyterian Hospital/Weill Cornell Medical Center and NewYork-Presbyterian Hospital/Columbia University Medical Center. He holds academic appointments

at Weill Cornell as adjunct associate professor of clinical surgery (plastic surgery) and at Columbia College of Physicians and Surgeons as associate clinical professor of surgery.

DR. NITSANA SPIGLAND

DIVISION OF PEDIATRIC SURGERY



Associate Professor of Clinical Surgery Dr. Nitsana Spigland has been appointed chief of the Division of Pediatric Surgery in the Department of Surgery. Dr. Spigland served as the Division's acting chief from 1997 to 2000. Actively involved in student education, her numerous roles include associate director

of medical student education in the Department of Surgery, faculty adviser and member of the Postgraduate Education Advisory Committee, mentor for medical students and residents, and member of several committees.

DR. BRUCE SCHACKMAN

DIVISION OF HEALTH POLICY



An expert in the study of cost-effectiveness in health care and health-care policy, Assistant Professor of Public Health Dr. Bruce Schackman has been named chief of the Division of Health Policy in the Department of Public Health. The division, previously called the division of Health Services and Policy

Research, focuses on issues such as allocation of scarce resources, financing and reimbursement, health-care technology assessment, program evaluation and organization of the health-care delivery system.

New Associate Dean of Student Affairs



Following the retirement of Dr. Bruce Ballard, Weill Cornell Medical College has named alumnus and Clinical Instructor in Medicine **DR. CARLYLE HARVEY MILLER** to associate dean of student affairs and equal opportunity programs in the Department of Academic Affairs. Dr. Miller is the recipient of numerous honors for teaching and

for his commitment to volunteerism and community outreach. He has served as a mentor to high-school-age and college students, and has provided guidance to minority youth with an interest in biomedical research.

New Clinical Scholar Announced



Nanette Laitman Clinical Scholar in Public Health/Clinical Evaluation

DR. LISA KERN, assistant professor of public health and public health in medicine, has been named the Nanette Laitman Clinical Scholar in Public Health/Clinical Evaluation. Dr. Kern received her M.D. from Harvard

Medical School and completed her residency in internal medicine at Mt. Sinai Hospital. She then received her M.P.H. from Johns Hopkins University, where she was also a Robert Wood Johnson Clinical Scholar. Since joining the

Medical College faculty in 2002, her research has focused on evaluating screening and diagnostic tests for diseases such as osteoporosis, diabetes, high cholesterol and cardiovascular disease. She also studies the impact of health information technology on health-care quality and other outcomes. This scholarship will enable Dr. Kern to continue her work in both of these areas.

Clinical scholar awards, granted for an initial period of three years, are created with a gift of \$1 million and are granted to junior faculty members who have demonstrated outstanding research or clinical care and are in the early stages of their careers. Awards are made for an initial period of three years, and may be renewed for an additional consecutive three-year period. Clinical Scholar Awards may not be held for more than six years.

Finding the Angiogenesis “Missing Link”

Growth factor could hold clues to treating vascular disease and cancer

Millions of patients suffer from disability, even amputation, caused by deteriorating circulation in the legs and elsewhere. The obvious medical solution would be drugs that spurred angiogenesis—the growth of new blood vessels—to help replace that worn-out vasculature.

Now, researchers at Weill Cornell Medical College believe they’ve moved a big step closer to that goal with the identification of a key player in the angiogenic cascade.

“Up until now, we’ve been looking for a ‘missing link’ in the process, whereby blood-forming cells in the bone marrow head to the site of injury to rebuild and sustain new blood vessels. We believe that a secreted protein called stromal-derived factor 1 (SDF-1) could be that missing link,” explained Dr. Shahin Rafii, the Arthur B. Belfer Professor of Genetic Medicine and director of the Ansary Center for Stem Cell Therapeutics at Weill Cornell.

According to Dr. Rafii, researchers bent on jump-starting angiogenesis have long focused on another protein, called vascular endothelial growth factor-A (VEGF-A). “Prior studies showed that VEGF-A-focused therapies do

work to rebuild vessels—but only over the short-term,” he said. “Something was missing.”

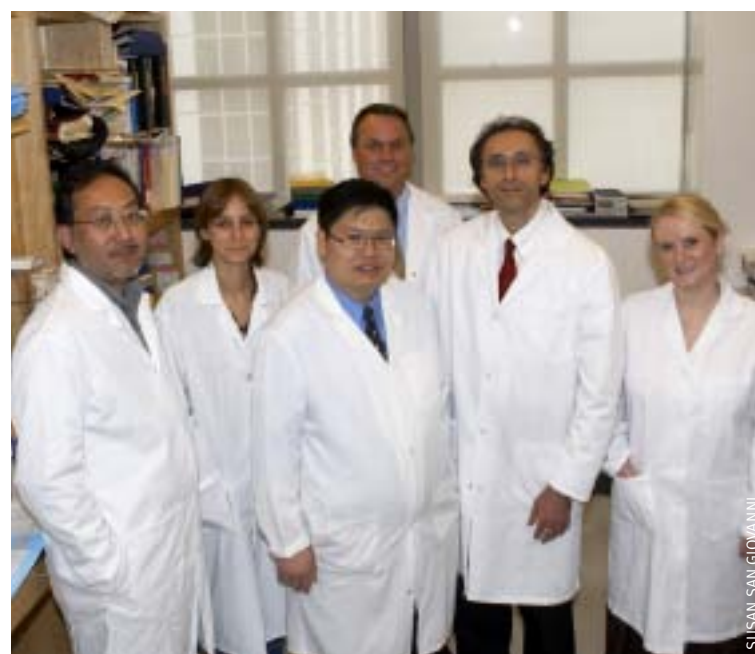
So, in a study published recently in *Nature Medicine*, the Weill Cornell team sought to figure out what was going wrong. They focused on SDF-1, which is released by blood platelets under the direction of a number of cytokine signaling chemicals.

In a mouse model of human vascular damage, the researchers discovered that mice unable to produce these SDF-1-targeted signals failed to regenerate new blood vessels.

In contrast, stimulating the activity of SDF-1 quickly led to the mobilization of pro-angiogenic, blood-building cells the team christened “hemangiocytes.”

“It’s important to note that SDF-1 jumps into the process much later than VEGF-A,” Dr. Rafii added. “So, if your treatment is only focused on VEGF-A and not SDF-1, you’re just not going to get the long-lasting effect you’re hoping for.”

According to Dr. David Jin, lead author of the paper,



(From left) Dr. Koji Shido, Dr. Isabelle Petit, Dr. David Jin (front), Dr. David Lyden, Dr. Shahin Rafii and Andrea Hooper.

“Based on the phenotypic characterization of hemangiocytes, these bone-marrow-derived cells are not just essential for new blood vessel formation and stabilization, but they also participate in other processes such as inflammation and wound healing.”

This finding could be key to new treatments for vascular disease, and it might even have implications for future cancer research. ■

<<< from page 1

Combating Third-World Disease

Biology Program will combine genetics, biochemistry, molecular biology and immunology with chemical biology to create novel chemical compounds with which

to validate drug targets. Ultimately, compounds of significant interest will be donated to public-private partnerships that are oriented toward not-for-profit drug develop-

ment, fostering collaboration between the medical research and business communities.

“This is a very important step that will enable us to make significant progress toward developing new therapies,” said Dr. Antonio Gotto Jr., dean of Weill Cornell Medical College. “It also represents a new type of partnership between philanthropy, academia and industry.”

The Milstein family has a long history of generosity in support of Weill Cornell. Over the years, Howard P. Milstein has been a strong supporter of the Medical College’s neuroscience initiatives and benefit events.

The idea originated with a presentation by Dr. Carl Nathan, the

R.A. Rees Pritchett Professor of Microbiology and chair of the Medical College’s Department of Microbiology and Immunology, during a meeting of the Medical College’s Board of Overseers.

“We have a part to play in the business community by supporting selfless doctors and researchers,” said Mr. Milstein, who has been an overseer of the Medical College since 1989. He is chairman of New York Private Bank & Trust as well as chairman, president and CEO of Emigrant Savings Bank.

“It was the logic of Dr. Nathan’s presentation and the need that rang the bell—this is a vital area,” he said.

Dr. Nathan, who will direct the Program in Chemical Biology and serve on an advisory committee to the Core Facility director, is specifically interested in combat-

ing antibiotic-resistant strains of tuberculosis and malaria that have evolved over the last half-century, an area largely neglected by the pharmaceutical industry because of its poor market value. According to the Global Forum for Health Research, currently less than 10 percent of global spending on medical research goes to conditions that account for greater than 90 percent of the global disease burden, a problem that has come to be known as the 10/90 gap.

“The question is, do we want to go back to a time when life-threatening infections are considered routine?” asked Dr. Nathan.

“This is not a past we want as our future,” he said. “University-based scientists can step in and help find solutions to these diseases.” ■

Organizational Changes in Administration and Finance

RISK MANAGEMENT

George Meeker, the Medical College’s senior director of risk management, is retiring and will be replaced by Tom Lawrence, who held a similar position at NYU for almost 20 years. Mr. Lawrence will be engaged in all facets of risk management and insurance procurement.

FINANCE

Scott Puccino has been promoted to the position of senior director for budgeting and financial planning, reporting directly to Stephen Cohen, associate provost and executive vice dean for administration and finance.

FACILITIES MANAGEMENT

Barry Duignan, Weill Cornell’s senior director of facilities management, has expressed his desire to work part-time. He will stay on as full-time senior director of facilities management until the fall, when his successor is named. He will then move to an advisory role, working with Stephen Cohen on a number of facilities-related issues.

CAPITAL PLANNING

The success of Weill Cornell’s strategic plan is critically dependent on our ability to integrate programmatic priorities, infrastructure constraints, and economic considerations into executable facility plans. Richard Thomas will move into a new position, senior director of capital planning, where he will have responsibility for communicating with users, and effecting the integration described above.

INFORMATION TECHNOLOGY

After many years of leading the Office of Academic Computing (OAC), Steve Erde will be taking a sabbatical, and the Medical College will initiate a national search for a new chief information officer. In the interim, Vinay Varughese will have the lead responsibility for managing the Medical College’s information technologies. Additionally, OAC has been renamed to Department of Information Technologies and Services. ■



COURTESY OF MITCHELL/GIURGOLA ARCHITECTS

Up, Up and Away!

The long-awaited construction of three new floors atop E Building and the renovation of the existing sixth floor got under way this summer.

The additional three floors, the first of the Medical College’s “Major Upgrade Projects,” will bring the building’s total number of floors to nine.

Located on the corner of East 68th Street and York Avenue, E Building houses Weill Cornell Medical College offices and labs. The sixth floor, which is currently empty, is designated for neurology offices; the seventh floor will be occupied by RARC; the eighth floor will be shared by pharmacology, neurology and pediatrics; and the ninth floor will be home to dermatology.

The design and preparation for the new floors began several years ago as part of the Medical College’s master plan. Building “up,” rather than “out” is an example of the Medical College’s commitment to utilizing every possible resource as the institutions grows.

Designed by Mitchell/Giurgola Architects, the renovation is expected to be completed by fall of 2007. ■

Celebrating the Teacher at Weill Cornell

Creativity and dedication of Medical College faculty recognized as vital to the overall student experience

Weill Cornell Medical College held its Seventh Annual Celebration of Teaching at the Cornell Club on June 12 to honor outstanding teachers and their contribution to the educational mission of the Medical College through Excellence in Teaching Awards.

"I salute all of the individuals who have helped craft the excellent educational experience at Weill Cornell Medical College," said Dr. Carol Storey-Johnson, senior associate dean of education. "In my position, I marvel at the level of creativity and problem-solving exhibited by the faculty in these endeavors."

The Excellence in Teaching Awards were inaugurated at the end of the 1999-2000 academic year, after the first class had completed the Medical College's redesigned curriculum, which challenged conventional teaching models by focusing on self-directed inquiry and small groups. Specifically, the new curriculum highlighted the sophisticated managerial and leadership position of course director—those



Weill Cornell faculty, administrators and student representatives honor the 26 recipients of the 2006 Excellence in Teaching Award.



A toast to teaching: (from left) Deirdre Mole, Dr. Veronica LoFaso and Dr. Carol Capello.

charged with developing a particular course and overseeing its implementation by the multiple instructors who teach sections of the course. In addition, many more faculty teach in multiple modalities in the new, now current, curriculum.

The award-selection process includes both the input of students through course evaluation forms, as well as course director comments, which recognize substantial contributions by instructors "behind the scenes" that may not be visible to students. Instructors from Weill Cornell and NewYork-Presbyterian Hospital Healthcare System af-

filiates are eligible for the awards.

While the awards specifically honor teaching, they also subtly recognize the myriad responsibilities of a physician-teacher.

"As physicians and teachers, we are committed to meeting our obligations to provide care to all who need it in an ethical and humanistic way," said Dr. Antonio Gotto Jr., dean of the Medical College.

The celebration also recognized the contributions of the Medical College's Board of Overseers and the outgoing student representative on the board, Joe Habboushe.

"We could not have done as much as we have done with this curriculum and these awards without the support of our overseers," Dr. Storey-Johnson said.

Twenty-six Weill Cornell instructors were recognized, many of whom not only teach and provide clinical care, but also run laboratories or play a role in the Medical College administration.

"Sometimes our educational tasks are frustrating and it takes every ounce of our energy to see our way through and run the lab and treat the patient," said Dr. Storey-Johnson. "But we wouldn't be in this work if it didn't give us enormous satisfaction to ultimately graduate the next group of trainees into our profession." ■

the **Scope** at a glance

September • October 2006

Non-Profit Org.
U.S. Postage
PAID
New York, NY
Permit No. 5503



1 COVER STORY:
A Real-Life Rip Van Winkle

Weill Cornell researchers explore how Terry Wallis' brain "rewired" itself after nearly 20 years in a minimally conscious state, to a point where he can now speak to members of his family.

2 SCIENCE STORIES:
NEW CENTERS FOR MS, IBD

Gifts to establish the Feil Unit and the Roberts Center will build on existing resources and expand research to benefit patients.

COVER STORY:
Abby and Howard P. Milstein Gift to Combat Third-World Disease

1 Chemistry Core Facility and Program in Chemical Biology to target diseases such as malaria and tuberculosis, both prevalent around the world.

3 SCIENCE STORIES:
ATTACKING ANTIBIOTIC RESISTANCE

Dr. Carl Nathan warns of "superbugs" that are growing resistant to standard antibiotics and urges pharmaceuticals to devote more resources to the development of new antibiotics to fight world-wide infection.

3 SCIENCE BRIEFS:
WHEN—AND WHERE— DOES ALZHEIMER'S BEGIN?

Accepted theory of beta-amyloid "clogs" in the brain challenged in a Weill Cornell study.

4 STRESS AND ITS ROLE IN HYPERTENSION

On-the-job aggravation is not the primary cause of hypertension, according to Dr. Samuel Mann.

5 RENIN & ARRHYTHMIA

In cardiac crisis, production of the enzyme renin may boost the risk of deadly arrhythmia.

4 SCIENCE AT A GLANCE:
UPDATES AND BREAKTHROUGHS

From a new drug for multiple myeloma to a device that helps stroke patients regain their grip and mobility, Weill Cornell researchers have had a busy summer.

8 FOCUS ON:
CELEBRATING THE TEACHER

The Medical College recognizes faculty who go above and beyond in the classroom and lab.

COVER STORY:
Leading WCMC Biochemist Shows His MERIT

Dr. Frederick Maxfield has been awarded a \$2.8 million NIH "Method to Extend Research in Time" (MERIT) grant to continue his groundbreaking work in intracellular trafficking.



Weill Medical College and Graduate School
of Medical Sciences of Cornell University
Office of Public Affairs, Box 144
1300 York Avenue
New York, NY 10021

ADDRESS CORRECTION REQUESTED