# NYU PHYSICIAN

THE MAGAZINE OF NEW YORK UNIVERSITY SCHOOL OF MEDICINE

FALL 2012
VOLUME 64 • NO. 1

## THERE'S NO BACKING AWAY FROM THE PAIN

The challenge of treating chronic back pain

PLUS DEAN GROSSMAN REFLECTS ON HIS FIVE YEARS AS DEAN & CEO
A CHILD SAVES HIS FAMILY • THE FACES OF HIV

# Help Us Make Dreams Come True

**EVERY ASPIRING PHYSICIAN DREAMS OF THE DAY SOMEONE WILL CALL HIM OR HER "DOCTOR" FOR THE FIRST TIME.** But getting there takes a lot more than hard work and dedication—it takes resources. By contributing to the NYU School of Medicine Alumni Campaign, you help ensure that our next generation of physicians will have access to the best teaching and research, along with a competitive financial assistance package.

When you make a gift, you help us guarantee that all of our students will have the means to complete our rigorous education. One day, you may even have the privilege of addressing them yourself as "Doctor."

**MAKE A GIFT ONLINE**
Please visit **www.nyu.edu/alumni**.

To discuss special giving opportunities, **call Anthony J. Grieco, MD, Associate Dean for Alumni Relations, at 212.263.5390.**

NYU Langone MEDICAL CENTER

**Thank you for your generosity.**

THE MAGAZINE OF NEW YORK UNIVERSITY SCHOOL OF MEDICINE

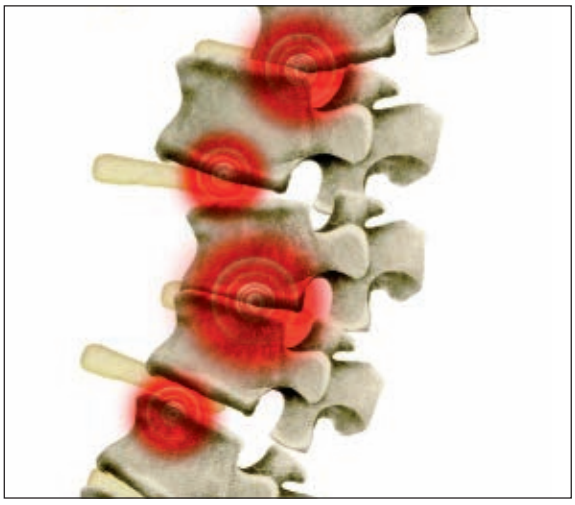
FALL 2012 VOLUME 64 NO. 1

# NYU PHYSICIAN



## COVER STORIES





## SPECIAL FEATURE



## DEPARTMENTS



ILLUSTRATION BY BRIAN STAUFFER

NYU School of Medicine
NYU LANGONE MEDICAL CENTER

# Our Expertise in Musculoskeletal Diseases

*FROM THE DAY A CHILD LEARNS TO WALK,* each step exerts a jolting 100 pounds of pressure upon the spine, a marvel of complexity and flexibility. Thereafter, a lifetime of sitting, standing, walking, running, bending, and twisting guarantees a steady increase in the strain. It is no wonder that some 80 percent of adults suffer from back pain at least once in their lives.

In this issue of *NYU Physician* magazine you will read about the rehabilitation specialists, orthopaedic surgeons, and rheumatologists who treat back pain and other common and agonizing conditions that affect the joints and muscles. Throughout these stories, the extraordinary health care professionals at our Hospital for Joint Diseases and Rusk Rehabilitation stand out. Most important, integrated care is often the key to successful treatment. • We are enormously proud of their dedication and expertise, recognized once again in this year's *U.S. News & World Report*'s Best Hospitals Survey: NYU Langone Medical Center was the only hospital in New York to receive top-10 rankings for orthopaedics, rheumatology, and rehabilitation. • Our new Center for Musculoskeletal Care at 333 East 38th Street, just a few blocks north of our main campus, is the gateway to outpatient orthopaedic, rheumatology, and rehabilitation services, offering some 110,000 square feet on three floors. More than 100,000 outpatients are expected to visit this state-of-the-art facility yearly, testimony to the Medical Center's ongoing outstanding reputation in these fields of medicine and to our commitment to being world-class. • There is every reason to believe that our expertise in musculoskeletal diseases will continue to shine. •

**DEAN & CEO** ROBERT I. GROSSMAN, MD



PHOTOGRAPH BY
**JOHN ABBOTT**

# Recently Approved Drugs Offer New Hope for Patients with Hepatitis C

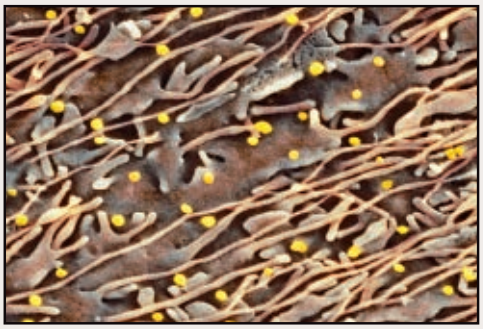
## Drugs may also be useful in liver transplant patients.


Hepatitis C is a silent killer that currently infects nearly 4 million people in the United States. The chronic viral disease, which causes cirrhosis and liver cancer, often goes undetected and undiagnosed. Symptoms may not appear for two decades or more. Until recently, first-line drug therapy consisted of grueling, protracted, and often ineffective treatment with the antivirals interferon and ribavirin, whose side effects include anemia, insomnia, anxiety, and depression, among many others.

That scenario has changed since the Food and Drug Administration last year approved Incivek (telaprevir) and Victrelis (boceprevir) to treat hepatitis C. Some 80 to 85 percent of patients can be cured with these medications—up from 50 percent under the old regimen, reports Hillel Tobias, MD, PhD, clinical professor of medicine and surgery and medical director of the Liver Transplant Service at NYU Langone Medical Center.

Dr. Tobias participated in the clinical trials for the drugs and considers them "a spectacular breakthrough." One of his patients, 60-year-old Rachel (not her real name), discovered her infection in 2006. She spent a year and a half taking ribavirin and injecting herself with interferon, and suffered from numerous side effects. She was happy when the regimen ended, but then her viral load resurged.

Rachel suspects that she was infected sexually, though this method of transmission accounts for only 10 percent of reported hepatitis C cases, according to the Centers for Disease Control and Prevention. The virus is nearly always transmitted via a blood-borne route such as shared needles. When Dr. Tobias offered Rachel a 12-week course of Incivek, she jumped at the chance. Both Incivek and Victrelis are protease inhibitors, which impede the action of enzymes that the virus needs to produce new virus particles. As a backup, patients also take ribavirin and interferon for 12 weeks, and then interferon and ribavirin alone for an additional 12 weeks. Patients must take each dose of Incivek—two pills, three times a day—with 20 grams of fat. A self-described chocoholic, Rachel assumed it would be easy, until she realized that the interferon was changing her sense of taste and smell, making fatty foods unappetizing. Nevertheless, she stayed the course and is now virus free.



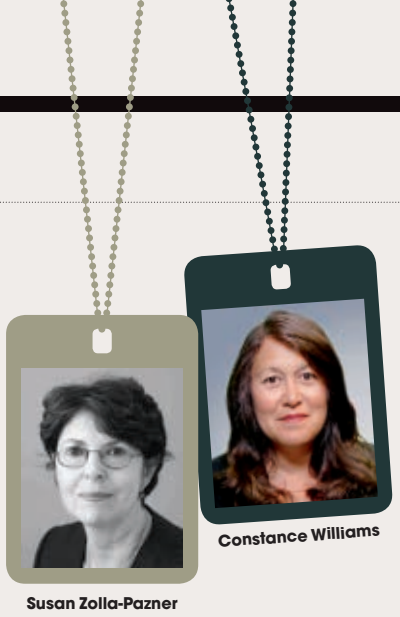
A colored transmission micrograph of hepatitis C virus particles (yellow) infecting cultured liver cells (brown).

These new treatments may also transform the outlook for liver transplant patients, according to Lewis Teperman, MD, chief of the Division of Transplant Surgery and director of the Mary Lea Johnson Richards Organ Transplant Center. With hepatitis C now the most common reason for liver transplantation in the United States, Dr. Teperman and his colleagues are piloting the use of Incivek and Victrelis following transplantation, with encouraging results. Hepatitis C recurs in every previously infected patient who receives a transplanted liver—most likely because the virus hides out elsewhere in the body—and about 40 percent of posttransplant patients develop fibrosis and/or cirrhosis of the liver within five years. Of the 10 patients Dr. Teperman has treated with the new protease inhibitors, the majority are now virus free.

Ultimately the goal is to prevent the need for transplantation by curing the disease before it can destroy the liver. "We can recapture the horse after the gate is open," Dr. Teperman says, "but I'd much rather make sure the horse never leaves the stable."

That goal may be within sight, as newer, better drugs now in the pipeline—polymerase inhibitors and nucleoside analogs, which further inhibit viral replication—become available and eventually make interferon obsolete. ● *—JOSIE GLAUSIUSZ*

THOMAS DEERINCK, NCMIR / PHOTO RESEARCHERS, INC




# HIV: A Virus with Many Faces and a Hidden Vulnerability

## A new study vindicates a longtime AIDS researcher.

Susan Zolla-Pazner, PhD, professor of pathology and director of the AIDS Research Center at the Manhattan VA Medical Center, describes HIV as a virus "with a million faces." The fact that HIV, which causes AIDS, "looks slightly different" in every person it infects has presented a huge obstacle to long-standing efforts to develop a global preventive vaccine, she says.

But Dr. Zolla-Pazner has long suspected that beneath the many faces that HIV uses to escape recognition by the human immune system lies a hidden structure common to all HIV viruses that might be vulnerable. This structure, found within the so-called variable regions, is part of the gp120 protein that projects from the virus's outer surface. The first three variable regions (V1, V2, and V3) help the virus infect cells, so Dr. Zolla-Pazner focused on them. The right antibody, she reasoned, might just see through the multitude of viral faces to that hidden structure and bind to it, thereby preventing infection. Her early research showed that monoclonal antibodies that recognize the variable regions could, in fact, identify many HIV viral types, indicating that something was conserved within those regions.

After the failure of early clinical trials testing vaccines designed to induce protective antibodies, many scientists turned away from this approach, but Dr. Zolla-Pazner persevered. Now her theory that antibodies to variable regions help block HIV infection has finally been validated by a study published April 5, 2012, in the *New England Journal of Medicine*.

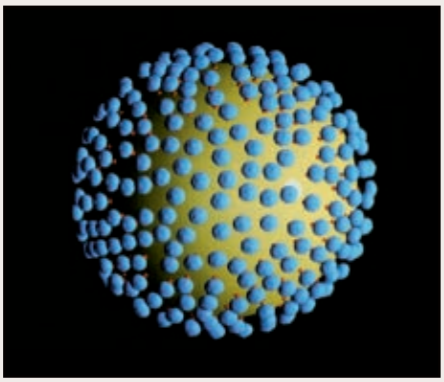
The study aimed to understand why, as reported in 2009, the RV144 HIV vaccine, designed and tested in Thailand by the United States Military HIV Research Program, demonstrated a 31 percent efficacy in reducing the risk of HIV infection. It was an important finding, even if the effect was modest, says Dr. Zolla-Pazner, who was not involved in the clinical trial. "The study provided the first evidence in humans that a safe and effective preventive HIV vaccine might be possible—but no one knew how it worked."

What followed was a massive effort to decode the immune response elicited by the RV144 vaccine. More than 75 investigators worldwide participated, including Dr. Zolla-Pazner and her longtime senior research technician, Constance Williams. Using blinded patient samples her group tested the hypothesis that antibodies recognizing gp120's variable regions played a role in reducing HIV infection in the vaccine recipients. The results came in a conference call in which Dr. Zolla-Pazner was asked to participate during the summer of 2011: Her assay testing for the presence of antibodies to the V1 and V2 regions of gp120 was the only one—out of more than 150 tested—to show a significant inverse correlation with risk of infection. RV144 participants who produced high levels of antibodies were less likely to become infected.

Dr. Zolla-Pazner admits to a sense of amazement about the outcome. "Never in my wildest dreams did I think antibodies to variable regions would be the only significant factor associated with protection. This was validation of 20 years of research."

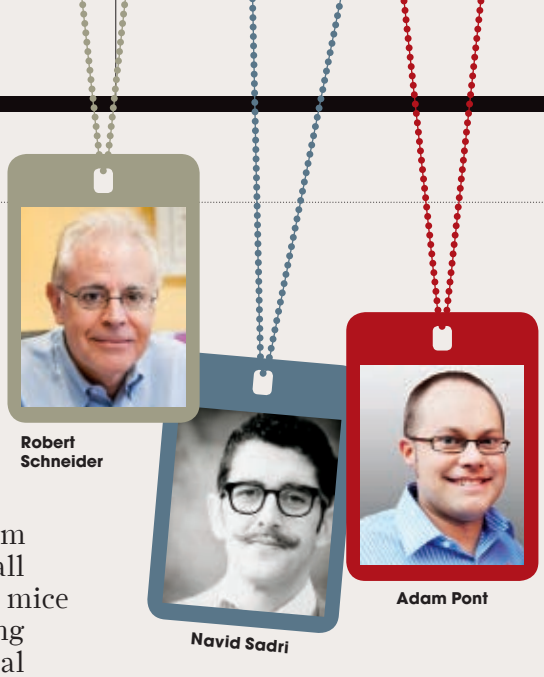
Now a human monoclonal antibody to V2 that Dr. Zolla-Pazner generated in 1994 will be part of new preclinical studies to directly test the protective activity of V2 antibodies. "We are still years away from having an HIV vaccine that can be used globally, but the work on RV144 is a huge step forward," she says. ●

*—RENEE TWOMBLY*



A computer-generated graphic shows the external coat of HIV, the virus causing AIDS. The spherical virus is covered by a membrane (yellow) that is studded with the gp120 protein (blue). Hidden in the protein is a structure that might be vulnerable to antibodies.

DIVISION OF COMPUTER RESEARCH & TECHNOLOGY, NIH / PHOTO RESEARCHERS, INC




# Too Old, Too Fast

## Scientists discover a direct link between inflammation and aging.

Seven years ago, Robert J. Schneider, PhD, and his laboratory team bred mice that lacked AUF1, a protein thought to play only a small role in moderating inflammation. To their surprise, however, the mice rapidly succumbed to a septic shock–like condition after receiving a nonlethal dose of endotoxin, an inflammation-inducing bacterial protein. "AUF1 clearly showed itself to be one of the major regulators of inflammation," says Dr. Schneider, the Albert B. Sabin Professor of Microbiology and Molecular Pathogenesis.

This initial finding was followed by another intriguing observation. The AUF1-knockout mice had abnormalities that became more pronounced with each new generation. "The mice were essentially aging more rapidly," Dr. Schneider says. "By the sixth and seventh generation we could no longer obtain adult animals—they died in the womb or shortly after birth."

This shortening of life span, a phenomenon called genetic anticipation, can signal a defect in telomerase, an enzyme that slows the rate at which our cells age. Without telomerase, the ends *(telomeres)* of chromosomes erode too quickly with each cell division, soon making them unstable; eventually cells are no longer able to divide. Mice usually have very long telomeres compared with those of humans, so a telomerase-deficiency trait takes a few generations to manifest.

Navid Sadri, a student in Dr. Schneider's lab who earned his PhD in 2008 and his MD in 2010, suspected that the absence of AUF1 was impairing telomerase activity, causing his lab mice to age rapidly. Over the next several years, Adam Pont, an MD/PhD student at the School of Medicine, continued to investigate and finally confirmed that AUF1 is a crucial activator of the enzyme, in addition to being a major dimmer switch for inflammation.

Their findings are published in the July 13, 2012, issue of *Molecular Cell*. "AUF1 turns out to maintain the integrity of our chromosomes and the speed with which our cells age," Dr. Schneider says.

The ends of chromosomes are capped with telomeres, regions of repetitive DNA sequences (red).

The finding is exciting, Dr. Schneider explains, because scientists have long noted that chronic inflammation seems to age cells more rapidly than normal and also makes them more prone to cancer. These effects are partly due to the stresses that inflammation puts on cells, but the new finding shows that there is also a more direct link—a single protein, AUF1, that keeps inflammation under control and keeps cells youthful, or at least prevents them from aging prematurely.

"Through linking telomerase activation to suppressing inflammatory response, AUF1 may hit two flies with one swat," wrote Liuh-Yow Chen and Joachim Lingner of the École Polytechnique Fédérale de Lausanne in a commentary accompanying Dr. Schneider's study in the same issue of *Molecular Cell*. Further studies, they note, may help scientists "to better understand the biological meaning of putting so many functions under the control of one genetic locus."

AUF1 may have evolved in part as an all-clear signal after a wound or infection, switching off inflammation and freeing up cell division to allow the replenishment of damaged tissue and the immune system. But the profound effects of its absence suggest that even subtle variations in the AUF1 gene could cause disease and accelerate aging. Genetic studies published by Dr. Schneider's group have already linked some variants of the AUF1 gene to the inflammatory condition psoriasis.

Dr. Schneider plans to study AUF1 gene variants and life span with investigators at the National Institute on Aging. "There are a surprising number of AUF1 gene variants in the human population, and it remains to be seen what effects these have on a variety of inflammatory and aging-related diseases," he says. ●

*—JIM SCHNABEL*

Edward Fisher

Kathryn Moore

# A New Finding Shows Why Immune Cells Are Stuck on Plaque

## Discovery points to a novel way to fight heart disease.

Imagine if immune cells that contribute to chronic and destructive inflammation could be forced to "just get up and leave," says Kathryn Moore, PhD, associate professor of medicine and cell biology. "Consider how this would help patients with rheumatoid arthritis or prevent some of the destruction of brain tissue in Alzheimer's disease."

Dr. Moore can speculate about such a future because her laboratory recently found a molecule, netrin-1, that keeps immune cells glued in plaque on the inside of heart arteries. There they fight an ongoing and losing battle to eliminate toxic fat.

Her experiments, published earlier this year in *Nature Immunology*, demonstrated that immune cells known as macrophages were secreting netrin-1 as a way to stay inside arteries.

By studying atherosclerotic plaques in mice and humans, Dr. Moore found that macrophages that entered the artery wall to clear out low-density lipoprotein (LDL), the bad cholesterol, began expressing netrin-1. "The immune cells were signaling, through netrin-1, that they were still needed due to chronic inflammation," Dr. Moore says. But what heart health really requires, she says, is to force these cells to migrate out of arteries, which would reduce both plaque buildup and the risk of heart attack.

Her path to this discovery took her from Harvard Medical School to NYU Langone Medical Center in 2010, to work with a scientist she had long admired—Edward Fisher, MD, PhD, the Leon H. Charney Professor of Cardiovascular Medicine, professor of pediatrics and cell biology, and director of the Marc and Ruti Bell Vascular Biology Program.

The journey began about a decade ago, when Dr. Moore saw a laboratory analysis of adult immune tissues showing high amounts of a protein called Unc5b. Up until then this protein had been described only as a molecule that netrin-1 binds to, and it had been associated with guiding neurons in the developing embryo.

The new analysis was immediately exciting to Dr. Moore, because it suggested netrin-1 could be regulating the movement of immune cells around the body. "There has been a lot of research done on how immune cells are first attracted to a tissue. But why, in chronic inflammation, do these cells continue to accumulate? What is holding them there?"

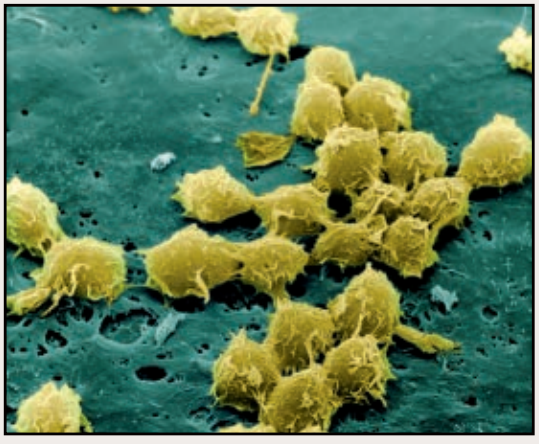
Dr. Moore's research dovetailed nicely with that of Dr. Fisher, who also understood that coronary artery disease was driven by chronic inflammation.

Dr. Fisher had discovered that macrophages are recruited to heart arteries to pick up and digest the fat deposited there by LDL, and he was also studying why the macrophages never leave.

Both scientists contributed to the answer. Dr. Fisher discovered late last year that a cell surface receptor known as CCR7 can signal macrophages to migrate out of plaque with their fatty cargo. Dr. Moore demonstrated that netrin-1 is blocking the ability of macrophages to respond to CCR7.

Netrin-1 may be just one of a family of proteins that force immune cells to stay at the site of chronic inflammation. If so, then "it may be possible to design therapies that tailor that response when it is destructive," Dr. Moore says. "It's a lovely idea." ●

*—RENEE TWOMBLY*



Macrophages cover the endothelium, or cellular lining, of blood vessels in this color-enhanced, scanning electron micrograph.

DAVID M. PHILLIPS / PHOTO RESEARCHERS, INC

Thomas Wisniewski

# Screen Identifies Potential Drugs to Treat Rare Prion Diseases

## Finding raises the possibility of treating mad cow disease.

The outlook for victims of prion diseases is particularly grim. The brain-destroying disorders progress unrelentingly, and death follows in about six months. There is no treatment for these rare diseases, which are caused by an unusual infectious agent called a prion, a misshapen version of a normal cellular protein.

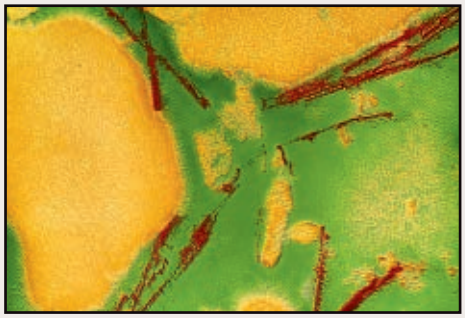
Now there is hope that potential treatments may be found by screening compounds for antiprion activity in cell cultures. NYU School of Medicine researchers recently reported having found several chemical compounds, including an antidepressant, that have powerful effects against prion infections in mice, opening the door to possible therapies for human prion diseases.

The researchers, led by Thomas Wisniewski, MD, professor of neurology, pathology, and psychiatry, reported their findings in a recent issue of the journal *PLoS One*.

They found that trimipramine, an antidepressant, and fluphenazine, an antipsychotic, have activity against prions. Since the drugs are already in clinical use, Dr. Wisniewski believes that doctors can test them in human patients with Creutzfeldt-Jakob disease, the most common human prion disease.

Dr. Wisniewski and his colleagues had previously found 68 chemical compounds, known as styryl-based compounds, bound tightly to amyloid-beta protein deposits in the brains of people who died of Alzheimer's disease.

Since the disease-causing aggregates of amyloid-beta and prion proteins are widely believed to have similar structures, his team screened these 68 styryl-based compounds for their ability to inhibit prion infection in a standard cell culture. They found two that seemed both effective and nontoxic, and confirmed their effectiveness by showing that on average they markedly delayed the onset of symptoms in prion-injected lab mice. The styryl-based compounds also reduced the signs of disease in the mouse brains.



This false-color transmission electron micrograph shows aggregations of protein, or fibrils (red), in the brain of a sheep infected with scrapie, a brain-destroying disorder caused by prions.

Dr. Wisniewski's team found similar results for the antidepressant trimipramine and the antischizophrenic drug fluphenazine. Both are chemically related to the antiprotozoal drug quinacrine, which is known to slow prion infection in cell cultures, although it fails to protect prion-infected mice or humans. Their chemical differences from quinacrine apparently enable the two drugs to bind more tightly to toxic prion aggregates, and—like the styryl-based compounds—prevent these aggregates from assembling new copies of themselves.

"One of the trimipramine-treated mice stayed healthy throughout the 400-day study," Dr. Wisniewski says.

The National Institutes of Health funds the work in Dr. Wisniewski's laboratory to develop potential prion-disease vaccines. Prion diseases in animals have been known to jump to the human population.

A prion disease known as bovine spongiform encephalopathy (BSE, also known as mad cow disease) swept through cattle in Britain in the 1980s and infected humans via beef products, killing more than 200 people worldwide.

Currently a prion disease known as chronic wasting disease (CWD) is spreading through the deer and elk population of North America. Humans are increasingly exposed to CWD—by eating venison, for example—and although CWD so far doesn't seem transmissible to humans, it has been shown to infect other primates.

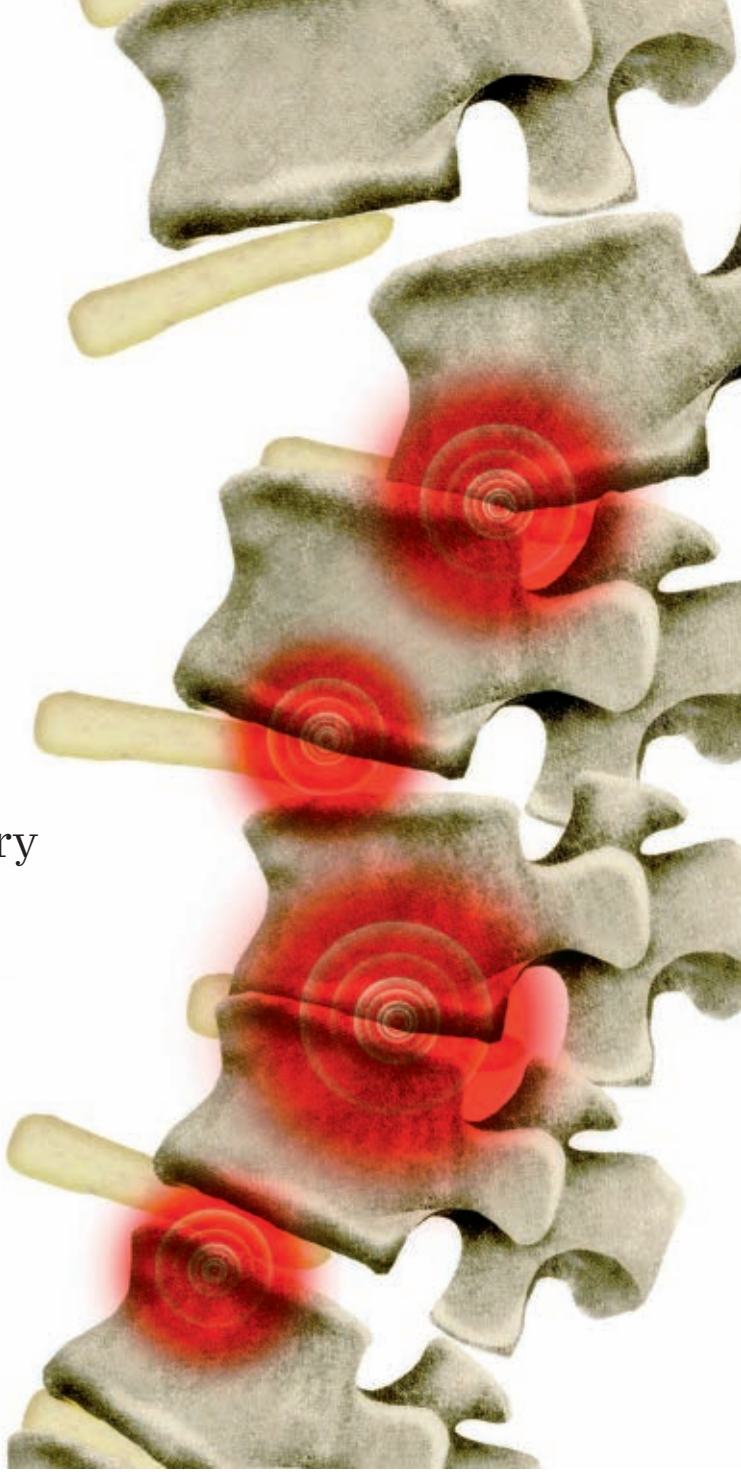
Dr. Wisniewski and colleagues are testing an oral vaccine for CWD in deer and elk in Colorado. ● *—JIM SCHNABEL*

EM UNIT, CVL WEYBRIDGE / PHOTO RESEARCHERS, INC

# Oh, My Aching Back!

## Many people seek relief through back surgery, but surgery should be the last resort.

**BY JANE BOSVELD**



IF YOUR BACK HURTS, you're in good company. About 8 out of 10 adults suffer from lower back pain at least once in their lives, according to the Academy of Orthopaedic Surgeons. Each year more than a million Americans undergo spinal surgery; many more take pain medication, get steroid injections, and endure hours of physical therapy to manage their back pain.

The spine is one of evolution's masterpieces of complexity. Comprising 33 vertebrae linked by a series of movable facet joints and supported by some 400 muscles and 1,000 ligaments, the spine is enormously flexible; it can bend and twist, support our weight, and withstand a lifetime of shocks. Along its length are three gentle curves, allowing us to negotiate movement backward and forward over the center of gravity. Thirty-one pairs of spinal nerves emerge from the spinal cord to nearly all areas of the body, and nearly all the bones in the body link in one way or another to the spine.

But all this flexibility and resilience comes at a price: The spine is vulnerable to injury. Falls and sports injuries, lifting a heavy object, sitting too long, or even just twisting your body suddenly can strain a back muscle or send it into spasms. Excruciating back pain can begin when disks in the spine break down or rupture; when the cushioning material between vertebrae bulges out (called a herniation) and presses on a nerve; when misalignments occur in the spine; or when the spaces between vertebrae narrow due to arthritis. "It's not like the knee, where there's one joint. The spine is much more complex," says Thomas Errico, MD, chief of the Spine Division at NYU Langone Medical Center's Hospital for Joint Diseases.

Back pain sufferers frequently seek surgery, but Dr. Errico says that should be the last resort. "What we as spine surgeons want to see," he explains, "is that people have used all the nonsurgical options available, including simple things like losing weight and getting in better condition."

Dr. Errico's office staff prescreens patients to make sure

ILLUSTRATION BY **BRIAN STAUFFER**

they have tried other treatments before considering surgery. Patients who have not exhausted nonsurgical options are referred to the NYU Langone Center for Musculoskeletal Care (CMC), where there are physiatrists, who specialize in functional disabilities, and pain management physicians, who evaluate whether less invasive treatments might help. "Most back pain is due to muscular or temporary problems in the spine that resolve on their own or with conservative treatment," Dr. Errico says, "but if the pain continues for more than three months, we start to worry that there's a chronic condition going on."

When pain persists despite conservative treatments, Dr. Errico will assess if it is being caused by a condition that surgery can fix. "The ideal candidate for a spine operation is someone whose pain is generated by only one set of vertebrae, maybe two," Dr. Errico explains. "To operate and decompress or stabilize only one or two levels [vertebral joints] is relatively easy, and if that's where the pain is coming from you have a good chance of stamping it out."

That was the case for 65-year-old Marie Davis, a retired New Jersey transit employee in Newark. About five years ago, she began being bothered by a stiff back. Eventually the stiffness turned to pain, and the pain became so severe that she sometimes walked bent over at the waist to relieve it. Davis sought all kinds of remedies from pain pills and cortisone shots to chiropractic adjustments. "I tried so many things to help the pain, but nothing really helped," she recalls.

Davis's doctor finally suggested surgery. She consulted three different surgeons, including Dr. Errico. The surgeons told her she was suffering from degenerative spondylolisthesis, a condition in which one of the vertebrae slips forward over the vertebra beneath it. She also had spinal stenosis, a narrowing or compression of a section of the spine. In Davis's case, the misaligned vertebra and the stenosis involved the same two vertebrae (L4 and L5) in the lower back, or lumbar region of the spine. She asked Dr. Errico to perform the surgery. "I was really scared of surgery," she recalls, "but the pain got so bad, I just wanted it to stop."

Under Dr. Errico's direction, a team of doctors removed the damaged disks in Davis's lower back using minimally invasive surgical techniques and replaced them with a small section of bone from her femur. They then secured the bone with specially designed screws inserted through two small incisions in her back. "They had me up and walking the next day," Davis says.

Davis was fortunate that the source of her pain was easily identified. Correctly diagnosing the source of back pain is one of the biggest challenges facing surgeons. "Sometimes it's just not clear what is actually causing the pain," explains Christopher G. Gharibo, MD, associate professor of orthopaedic surgery and anesthesiology and medical director of pain medicine at the CMC. "The patient may have a disk bulge or herniation and assume that that's the source of the pain, but it may not be. Sometimes the pain is coming from the muscles that are on the spine, not so much the spine itself."

**"Most back pain is due to muscular or temporary problems in the spine that resolve on their own or with conservative treatment."**

Some cases are especially hard to pin down and treat. To help with those, Dr. Errico and other NYU Langone spine physicians, including Dr. Gharibo, have a weekly Tuesday morning conference at the CMC. They present MRI scans of particularly tough cases and discuss treatment plans and options with other specialists. "It's critically important to arrive at the proper diagnosis," Dr. Errico says, "and getting perspectives from other specialists in physiatry, neurosurgery, neurology, or anesthesia pain management helps."

An innovative diagnostic scanning machine called EOS also aids the CMC spine specialists. The machine, which Dr. Errico compares to the full body scanners used in airports, images the entire back from the skull to the femur in two and three dimensions and in better detail than a traditional X-ray. It also exposes the patient to one-tenth the radiation. Because EOS images show the entire spine, not just a portion of it, surgeons can use it to see if the spine is aligned. "A prognosis for a spinal procedure often depends on a patient's overall global alignment," Dr. Errico explains. By using EOS and other technologies to help analyze a patient's alignment, surgeons can better decide what kind of surgery to perform.

More than a year after surgery, Marie Davis is walking upright without pain. But spine surgery isn't always so successful. "If you talk to most spine surgeons," Dr. Errico says, "they'd say the single thing that would improve our specialty would be better tools for diagnosing why a patient hurts and what corresponds to that pain in the spine. Knowing that is essential." ●

# Battling Chronic Pain

## Can the right therapy save your job?

**BY JANE BOSVELD**

THE STAFF OF THE NYU HOSPITAL for Joint Diseases' Occupational and Industrial Orthopaedic Center (OIOC) gathered around a conference table in their West Village offices and began updating each other on the condition of their patients, many with chronic back pain. Several patients had come there to join the Center's Return to Work program, a short-term intensive recovery plan designed to get patients in good enough condition to resume their jobs. The 21-year-old program boasts an impressive success rate: 95 percent of their patients are able to go back to work, though not always in the same job they had before.

More than 8.5 million U.S. workers are currently on disability, according to the Social Security Administration, many of them owing to chronic back pain. In fact, among people 45 and under, back pain is the leading cause of work-related disability. The cost to these workers is more than just financial: Studies have shown that long-term work loss is associated with a higher risk of heart disease, depression, low self-esteem, and a shortened life span. The longer someone is on disability, the less likely he or she is to rejoin the workforce. "Patients who are out of work for six months or more are at high risk of long-term disability," says Jeffrey Perry, DO, clinical instructor of rehabilitation medicine and orthopaedic surgery and a medical adviser to the OIOC. Those on disability for two years or more, researchers have found, almost never go back.

Treating back pain and getting patients back to work quickly, however, can be difficult. Although pain medication, physical therapy, and other treatments help patients heal, or at least manage their pain, numerous studies have shown that a focused, multidisciplinary approach is most effective.

At OIOC, each patient who enters the Return to Work program agrees to devote four hours a day, five days a week for up to a month for treatment that includes aerobic exercise, endurance and strength training, relaxation techniques, and other coping strategies. A physical therapist, physician, and psychologist assess each patient before the program begins. Explains psychologist Sherri Weiser, PhD, research associate professor of orthopaedic surgery and environmental medicine and director of Clinical Services and Research at OIOC: "It's usually not the pain that prevents people from going back to work. It's the fear that they could do more harm to themselves. They may think they are much worse off than they actually are, and they may be stressed out, depressed, or anxious."

Depression and anxiety are common among people with chronic back pain, and according to Dr. Weiser, studies have shown that they make recovering from back pain more difficult. In some cases, a patient's depression may exacerbate back pain; in others, unrelenting pain may trigger depression. Either way, Dr. Weiser explains, it needs to be treated.

Because some patients are reluctant to talk to a psychologist, the Center's physical therapists are trained to recognize the physical, emotional, and behavioral signs that keep a patient from getting better. Angela Lis, PhD, a physical therapist and associate clinical director at OIOC, points to research that details the warning signs that impede recovery, such as negative feelings about work and fear that being active will make their pain worse. "We spend a lot of time evaluating the patient at the beginning, so we can identify these predictors of delayed recovery," Dr. Lis says. Therapists also work with each patient to set recovery goals and modify them along the way if need be. "We don't want to set a patient up for failure, so it's important to be careful to set short- and long-term functional goals we can measure and meet," she says.

This design has worked well for patients such as Thomas Breland, a 41-year-old utility worker from Harlem, who recently finished the Return to Work program. He had been suffering from back pain on and off for more than 20 years. Earlier this year, his pain became so severe that his physicians referred him to the program.



ILLUSTRATION BY **BRIAN STAUFFER**

## Those on disability for two years or more, researchers have found, almost never go back.

After evaluating his spinal problems and fitness level, physical therapists designed a workout regimen for him that involved stretching to loosen the back muscles and increase his flexibility. They also tailored exercise for him. "I'd never exercised that much and it really helped," he says. He also found talking to Dr. Weiser about the stress in his life "helped me deal better with my back pain."

Breland has returned to work and, so far, there have been no new episodes of pain. "I'm good," he explains. "If the pain does come back, I'll know what to do for it."

Not everyone who starts the program succeeds in getting his or her old job back. Vincent Scimeca, a 41-year-old police officer who works at LaGuardia Airport, had to leave his job a year ago, after he hurt his back while carrying a sick passenger off an airplane. "I tried physical therapy, a chiropractor, had pain injections. Nothing helped," he says.

Scimeca's physician, Dr. Perry, suggested he try the Return to Work program. Scimeca started the program, but after three weeks he realized his back wasn't improving enough to go back to work. "They got me in good shape and taught me how to stretch out the back," Scimeca explains. But the specialized physical therapy that mimics the weight he has to be able to lift on the job caused him pain. He then realized that he might not be able to do his old job again. "I got a little depressed about it," he explains. As Dr. Weiser puts it, "He loves his old job, and he doesn't want any other job." As a last resort, Scimeca has decided to try surgery, even though he's been told he's not a good surgical candidate. Before discharging him from the program, Dr. Weiser discussed the risks he might be taking by having surgery and provided him with a list of questions to ask his surgeon.

Making sure patients have the information they need to understand their back pain and treat it effectively is at the heart of the program. "A talk with the physician about their condition is powerful, and even more powerful when it doesn't happen," says physical therapist Marco Campello, PhD, clinical associate professor of orthopaedic surgery and associate director of OIOC. Patients have come to the program worried because they've been told they have a herniated disk. "They think it's a diagnosis as bad as cancer," Dr. Campello explains. "Usually that's because no one has explained it to them."

Therapists at Return to Work also interact with companies, suggesting ways to improve workplace ergonomics and protect workers from injury. Such steps can save employers money in the long run by lowering workers' compensation and long-term disability payments. Improvements also send a message to employees. "When workers get injured on the job, they often blame the workplace," Dr. Lis explains. "They think their employer doesn't care about them. When those companies make changes to improve working conditions, it means a lot to the patient and is another helpful step toward recovery." ●

# RESTORING A BODY IN MOTION

BY AUBIN TYLER | PHOTOGRAPHS BY JOSHUA BRIGHT

Leonardo da Vinci's iconic drawing, *Vitruvian Man*, with its two superimposed figures of a man with outstretched arms and legs, suggests a human being in motion, one whose muscle, tendon, and bone function together in perfect symmetry. When a body is injured, restoring that symmetry in motion is the job of physical medicine and rehabilitation, a nonsurgical specialty also known as physiatry, from the Greek words *physics*, meaning "physical," and *iatreia*, "healer."

OUR SEDENTARY LIFESTYLES are a major reason why Americans spend at least $50 billion each year on low back pain. "Lumbar spine issues are starting to explode as people sit in a chair all day," says Wayne Stokes, MD, clinical associate professor and director of sports medicine at NYU Langone Medical Center's Rusk Institute of Rehabilitation Medicine. Before coming to NYU a year and a half ago, Dr. Stokes, himself an active skier, weight lifter, and runner, worked at a ski trauma clinic in Park City, Utah, and as a team physician for Pennsylvania State University. "We try to get across the idea that if the body doesn't move it's not going to work. You have to exercise if you are sitting all day, because sitting puts enormous pressure on the disks and joints."

After prolonged sitting, muscles become weak or tight from disuse and stop functioning properly. "That's why it's important to look at how the muscles function," Dr. Stokes says. "With the back, for example, the gluteal muscles can become weak and stop firing appropriately. That's where the role of exercise and stretching and proper movement comes in to return the body to its right movement patterns."

Chronic back pain frequently persists despite physical therapy if specific muscle imbalances and joint dysfunction aren't recognized and addressed. In the lower back, an MRI may show a herniated disk, but the pain often originates in the joints around the spine or the pelvis. Muscle and joint problems can also exist secondary to a disk injury or shoulder tendon problem. "As a physical medicine

Dr. Alex Moroz (left) and Dr. Wayne Stokes confer in the state-of-the-art exercise facility at the Center for Musculoskeletal Care at NYU Langone Medical Center.

Acupuncture is offered at Rusk Institute's integrative musculoskeletal medicine program. Pictured here is an acupuncture needle.

"We'll also usually start people early on with an exercise program or physical therapy, where they do stretching and strengthening of the low back and core (abdominal muscles), which can help treat and prevent low back problems."

rehabilitation doctor I want to hone in on that," Dr. Stokes says. "It's possible to do the wrong exercises and make things worse."

Along with establishing the correct diagnosis and treatment, lifestyle factors usually need to be addressed. For back pain, patients need to avoid prolonged sitting, says Dennis Cardone, DO, associate professor of orthopaedic surgery. "Setting an alarm clock to go off every 20 or 30 minutes is a good reminder to stand up. Even 15 seconds of standing helps break the seated cycle," he says. "We'll also usually start people early on with an exercise program or physical therapy, where they do stretching and strengthening of the low back and core (abdominal muscles), which can help treat and prevent low back problems."

Soft tissue injuries can occur in couch potatoes, weekend warriors, or superathletes—and everyone in between. "Even a gym rat might be slouching at the computer and develop a back problem," says physiatrist Jaclyn Bonder, MD, medical director of the Women's Health Rehabilitation Program at Rusk Institute of Rehabilitation Medicine. Dr. Bonder's own husband, a marathon runner, developed an overuse injury of the foot and ankle involving the plantar fascia, the connective tissue on the sole of the foot. "So you can be fit and still end up with pain if the muscles are imbalanced or used in the wrong way." Others have noted that even young athletes are susceptible to back pain. Gymnasts, weight lifters, and football players are prone to vertebral stress fractures as a result of repetitive lumbar extension, or backward bending.

"We're focused on the mechanics of the body and how the body acts as a whole as opposed to just one part," Dr. Bonder says. "For back pain, I look at everything from the feet to the neck. A lot of the time the answer is committing to lifelong exercise. If you have high blood pressure, you take a blood pressure pill for the rest of your life. Sometimes with arthritic knees, joints, and backs, regular exercise is necessary to manage the condition."

Dr. Stokes says he's seeing more people in their 40s and 50s with knee pain and arthritis who are not really candidates for knee replacements because of their younger age. (Most candidates are at least 65.) In those patients who are obese, losing weight is a priority. "Getting the weight off in someone carrying too much is mandatory," he says. Dr. Stokes is also seeing more patients who are developing knee arthritis earlier due to previous sports injuries—such as soccer players who have had ACL (anterior cruciate ligament) repairs. "They are a very driven group of people," he notes. "They're continuing to work out because it's part of their sanity and they want to maintain an active lifestyle."

Soon after a soft tissue injury, if a patient is too uncomfortable to exercise, there are a host of adjunctive therapies that can get them back in the game—anti-inflammatories, massage, injections, and acupuncture, among others, says Alex Moroz, MD, associate professor of rehabilitation medicine and director of the Rusk Institute's integrative musculoskeletal medicine program, who is both a physical medicine physician and a certified acupuncturist.

He often refers patients to integrative services, which offer meditation, tai chi, yoga, and other stress reduction techniques. "Part of my practice is talking to people a lot about the kind of exercise that's right for their particular condition, whether they're younger, older, fit, or not."

Joan Grant, 86, a retired advertising executive, first consulted Dr. Moroz for a pinched nerve in her neck. In her case, a few weeks of acupuncture worked wonders. "Joan had a combination of arthritis and muscle pain, two conditions for which acupuncture works nicely," he says. "It's a potent anti-inflammatory that releases muscle spasm and takes the pain away." Grant saw Dr. Moroz for acupuncture every week for three weeks and then a few more times after that. "I was so enchanted to find it worked without taking pills," she says.

Acupuncture also relieved Grant's pain and inflammation when she tore her right biceps muscle and later, her rotator cuff. "I was trying to open a window and it felt like a rubber band snapped," she says. Before returning to Dr. Moroz, she consulted an orthopaedic surgeon, who told her she was too old for anesthesia, and that he couldn't guarantee the results of surgery.

Dr. Moroz knew that Grant's type of injury would very likely heal on its own without surgery. "The people who get surgery are often high-level athletes," he says. "Many patients don't want to do surgery if they can avoid it." To further augment her comfort during the healing process, he injected Grant's shoulder, using a local anesthetic mixed with a small sample of her own blood, thought to concentrate factors that promote healing. "It relieved it tremendously," she says. "I made a deal with him—anything external—he takes care of me."

# THE ORIGINS OF PHYSICAL & REHABILITATION MEDICINE

The field of physiatry has grown since its beginnings during World War II, when a Missouri internist and Air Force major stationed in St. Louis saw that the boredom and inactivity of convalescence did wounded soldiers more harm than good. In response, he developed a program of aggressive physical and mental activity that reduced hospital readmission rates and sent more men back to active duty. It became a model for the nation, with an impact that persists to this day.

"Howard Rusk realized that bed rest was probably not the best thing, and that exercise is a medicine," says Steven Flanagan, MD, the Howard A. Rusk Professor of Rehabilitation Medicine and chair of the Department of Rehabilitation Medicine at NYU Langone. "In order to improve the outcome and get folks functioning—that's our specialty—you have to look at the whole person. That's his contribution."

Just as Dr. Rusk is recognized as the Father of Rehabilitation Medicine, Frank Krusen, MD, is considered the Father of Physical Medicine. As a young physician recovering from tuberculosis in a sanatorium in the 1920s, Dr. Krusen realized that physical conditioning could restore health to disabled and sick patients. He proposed the term physiatrist and lobbied the American Medical Association to grant it specialty status, which it did in 1947. That year, 80 physicians took the first board examination in Minneapolis.

During the late 1940s and early 1950s—until the Salk vaccine was invented in 1955—the U.S. polio epidemic dominated the work of physiatrists. Dr. Krusen, by then at the Mayo Clinic, advocated the controversial physical methods of an Australian nurse, Elizabeth Kenny, which included early movement of the affected limb. It turned out to be an important advance from the now discredited medical orthodoxy of the time, which supported immobilization of the affected limb in polio patients through splinting, casts, and braces. By that time, the twin disciplines of physical medicine and rehabilitation medicine were entwined, and have remained so ever since.

Today there are 8,000 members of the American Academy of Physical Medicine and Rehabilitation, a number that has doubled since the early 1990s. "In our field, we're trained to look for the specific cause—we're diagnosticians," Dr. Flanagan says. "The treatment may include physical therapy, heat, cold, electrical therapy, and lifestyle management. It's really quite comprehensive. So it's not just treating the elbow for tendonitis, but also teaching patients what else they can do to keep it from coming back. We really do try to look at the whole person." ●

Dr. Steven Flanagan

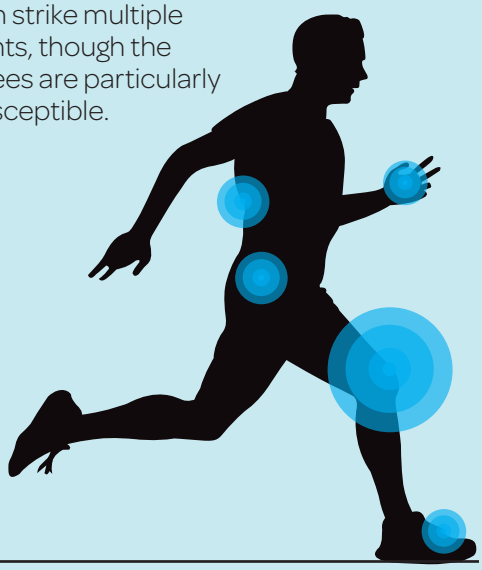
PHOTOGRAPH OF DR. FLANAGAN BY JOHN ABBOTT

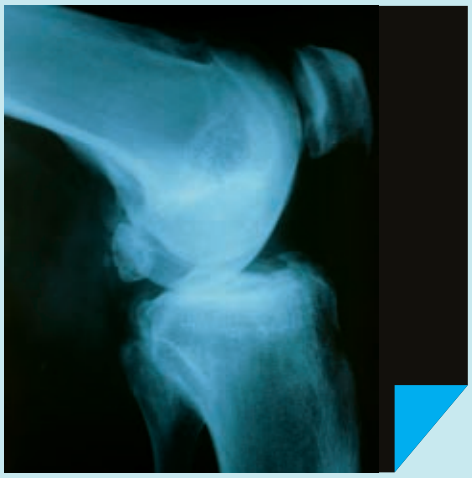
# THE WEAR + TEAR OF OSTEOARTHRITIS

ANY SPORTS INJURY (OR JOINT SURGERY) CAN LEAD TO THIS PAINFUL DISEASE. CAN ITS PROGRESSION BE HALTED? FIRST, RESEARCHERS HAVE TO IDENTIFY THOSE LIKELY TO DEVELOP IT.

**BY BRYN NELSON**

**OSTEOARTHRITIS** can strike multiple joints, though the knees are particularly susceptible.





# 70 MILLION

Number of people in the United States who will be at risk for osteoarthritis by 2030, some 20% of Americans

Source: National Institutes of Health

# 150,000

Number of **ACL** (anterior cruciate ligament) injuries in the United States every year

Source: American Orthopaedic Society for Sports Medicine

**NEARLY**

# $128 BILLION

**ESTIMATED ANNUAL DIRECT AND INDIRECT COSTS OF ARTHRITIS** and related conditions to the U.S. economy

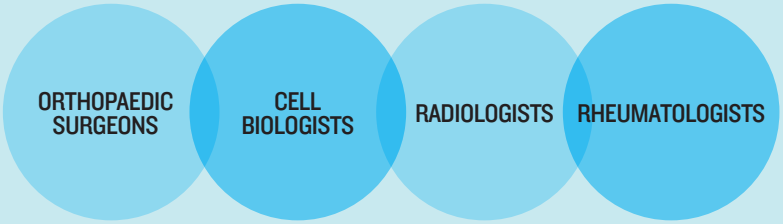
Source: Arthritis Foundation

# NO. 1

**RANKING** for arthritis and other rheumatic conditions as the nation's most common cause of disability among adults; the ranking has remained the same for the past 15 years

Source: Centers for Disease Control and Prevention

**AT NYU LANGONE**




**ARE COMBINING FORCES** in an effort to identify the early warning indicators of a disease that afflicts an estimated

# 27 MILLION

**NEARLY 1 IN 2** Lifetime risk for symptomatic osteoarthritis of the knee by age 85

Source: CDC

# 676,000

**TOTAL KNEE REPLACEMENTS** in 2009, the majority due to osteoarthritis

Source: National Center for Health Statistics FastStats

DR. P. MARAZZI / PHOTO RESEARCHERS, INC.

# LAST

April Jon Kline was driving for a layup in a pickup basketball game when something snapped. The 27-year-old trader at JP Morgan, a former high school and college athlete who also runs, works out, and plays golf, was just five minutes into the basketball game when his left knee gave out, and he crumpled to the gym floor in agony.

In the days that followed, Eric Strauss, MD, assistant professor of orthopaedic surgery, found that Kline had a torn anterior cruciate ligament and a partially torn medial collateral ligament, both of which provide critical stability to the knee joint. Kline underwent reconstructive surgery to repair his ACL; physical therapy is now preparing him for a return to the basketball court.

As clinicians have discovered, however, some sports injuries can lead to lasting damage long after the ligaments have healed. Trauma to the knee, studies suggest, is among the many potential triggers of osteoarthritis, a slow but inexorable erosion of the cartilage tissue that cushions the body's joints. By the time patients return to the doctor years or decades later with excruciating joint pain, the cartilage destruction is irreversible. Even worse, doctors have no way to halt the process or tell who may be most at risk.

"As orthopaedic surgeons, I think we've really improved our ability to reconstruct ligaments and treat meniscus and other cartilage injuries," Dr. Strauss says. "However, we still lack the ability to predict which patients are going to do well after treatment and who's going to develop arthritis after they twist or buckle their knee skiing or playing basketball."

At NYU Langone Medical Center, Dr. Strauss and other orthopaedic surgeons, cell biologists, radiologists, and rheumatologists have now combined forces in an effort to identify the early warning indicators of a disease that afflicts an estimated 27 million Americans. The recruitment of younger, active patients seeking treatment for knee injuries could help reveal cryptic signs of change within the cartilage cells well before the joint degeneration has run its course.

A long-term goal of the study, now funded by the Department of Orthopaedic Surgery, is to identify molecules that could be targeted by drugs or other interventions to slow or disrupt the progression of osteoarthritis. "We think the treatment is only successful if you start early, before the cartilage is fully destroyed," says Thorsten Kirsch, PhD, professor of orthopaedic surgery and cell biology and director of NYU Langone's Musculoskeletal Research Center. "It doesn't regenerate, so you have to start very early to stop the process."

Osteoarthritis can strike multiple joints, though the knees are particularly susceptible. Over time, the degenerative condition wears away the cartilage until only bone remains, leading to stiff joints and searing pain when the bones rub together. With little more than pain relievers as a temporary salve, many patients with advanced disease are eventually forced to have whole joint replacement surgeries to relieve their misery or immobility. Surgeons are already replacing more than 600,000 knees every year—the vast majority due to osteoarthritis—and that number is expected to climb precipitously over the next few decades.

Heading off the expected surge in disability will require a far better understanding of the disease pathway, something these collaborators hope to achieve through their focus on post-traumatic osteoarthritis, or joint degeneration triggered by an injury.

THE RECRUITMENT OF YOUNGER, ACTIVE PATIENTS SEEKING TREATMENT FOR KNEE INJURIES COULD HELP REVEAL CRYPTIC SIGNS OF CHANGE WITHIN THE CARTILAGE CELLS WELL BEFORE THE JOINT DEGENERATION HAS RUN ITS COURSE.

Dr. Strauss and Laith Jazrawi, MD, associate professor of orthopaedic surgery and chief of the division of sports medicine, are recruiting patients with sports-related injuries, like Kline. Kenneth Egol, MD, professor of orthopaedic surgery, is enrolling patients with more severe impact injuries known as tibial plateau, patella, and distal femur fractures. All of these breaks occur in or around the knee joint and can damage the cartilage surface, thereby heightening the risk of osteoarthritis. "In New York City, the most frequent cause of these injuries is being struck by a slow-moving car while in a crosswalk," Dr. Egol says. Other patients might sustain these bone fractures when landing awkwardly and forcefully, whether in basketball, soccer, or another high-impact sport.

"When there's trauma to the knee, a whole host of enzymes and proteins are released in response," Dr. Egol says. Many of these inflammation-linked molecules are part of the normal healing process, and the mix of inflammatory biomarkers within the joint often returns to normal levels relatively quickly after the injury. In other

patients, however, the markers remain elevated, heightening the risk of damage to cartilage cells, or chondrocytes, which secrete and maintain the cartilage tissue's scaffold-like matrix. Levels of more than 20 enzymes and molecules that might help predict disease progression are being measured in samples of urine, blood, and the viscous synovial fluid that bathes the knee joint.

Chuanju Liu, PhD, associate professor of orthopaedic surgery and cell biology, and colleagues are analyzing one of the most promising markers—fragments of a molecule called cartilage oligomeric matrix protein, or COMP. The researchers recently reported that levels of the fragments remain low in healthy volunteers with intact cartilage, but climb with disease progression, suggesting a role for the degradation protein as a biomarker of early risk.

Other proteins, such as annexins, a subject of Dr. Kirsch's studies, may modulate the disease. Eventually researchers may figure out how to minimize the negative effects of inflammation-linked molecules, thereby lessening the long-term cartilage damage. "Maybe you haven't cured it, but you've halted the progression," Dr. Jazrawi says. "And instead of these patients' being nonactive in their 50s and 60s, all of a sudden you can get them to their 80s or 90s or even their whole life without being nonactive because of this disease, and that's the exciting thing for me."

Kline knows the study may not directly benefit him. But after his ordeal, he wanted to help researchers reduce the long-term risk for other patients, even though his participation required him to get past his extreme fear of needles. "If someone's going to help me out, I might as well help them out a little bit with this research," he says. "This is a pretty awful thing to have happen, so if I can provide any kind of help for some research that eventually helps other people, then that's even better."

# AMONG

older patients with osteoarthritis of the knee, doctors have no way to tell who is most likely to get worse. Without a clear indication of which patients might benefit from a clinical drug trial, few companies are willing to risk the considerable time and expense needed to win approval for new therapies. "There's been a stalling of drug development in osteoarthritis, and in fact, many companies have left the field entirely because it's too hard a challenge," says Steven Abramson, MD, senior vice president and vice dean for education, faculty and academic affairs, and a professor of medicine and pathology.

Dr. Abramson, in collaboration with Mukundan Attur, PhD, assistant professor of medicine, has spearheaded a multidisciplinary effort to help prime the languishing anti-osteoarthritis drug pipeline. The top priority, Dr. Abramson says, is to identify biological markers that can reliably distinguish the 20 to 25 percent of osteoarthritis patients expected to decline over a three-year period—the typical length of a clinical trial.

The project, which recently won a 5-year, $2 million grant renewal from the National Institutes of Health, has already identified several promising biomarkers linked to inflammation. Researchers believe that joint tissue degeneration is mediated, at least in part, by the production of proinflammatory molecules.

With colleagues at Duke University, the NYU Langone Medical Center team discovered several potential genetic markers related to an infection-battling protein known as interleukin-1, considered an important contributor to cartilage degradation. The group's 2010 study in *Annals of the Rheumatic Diseases*, for example, reported that osteoarthritis patients with a natural variant of a protein that blocks interleukin-1 were significantly less likely to get worse than patients with different forms of the same protein.

The researchers also found in a study of 144 patients at NYU Langone's Hospital for Joint Diseases that white blood cells known as peripheral blood leukocytes are also activated in osteoarthritis, offering another way to track disease progression. Another finding was that patients with two overactive genes in these leukocytes—the inflammation-linked IL-2 and COX-1 genes—were three to five times more likely to get worse over a two-year period.

The researchers hope to validate their results in a national population of several thousand patients. The project will test whether the altered patterns of gene activity, specific variants of inflammation-linked genes, and other biochemical markers can distinguish among healthy volunteers and those with early or advanced osteoarthritis.

"In this phase of research, the most important reason to know who gets worse is so that osteoarthritis drugs can get back into the pipeline," Dr. Abramson says. With effective treatments in hand, he says, a reliable set of markers of progression could then help doctors and patients select the best options based on each individual's projected course of disease. ●

IN A STUDY OF

144 PATIENTS

researchers found that white blood cells known as peripheral blood leukocytes are also activated in osteoarthritis, offering another way to track disease progression.

# An Anniversary

AFTER FIVE YEARS AT THE HELM OF NYU LANGONE MEDICAL CENTER, ROBERT I. GROSSMAN, MD, REFLECTS ON HIS TENURE SO FAR.

***Did anything surprise you on becoming dean & CEO?***

I don't think I was surprised, exactly—I had a pretty clear idea of how much needed to be done if we were to take our destiny back into our own hands. I felt there were some serious issues with our finances, our infrastructure, and the pace of growth of our research. In that sense, I knew what I'd signed up for. But academic medical centers are incredibly complicated. It takes a while to get a thorough understanding of all the elements, all the niches, and to get the right people on the bus, so to speak. Setting up the proper processes and procedures takes longer than you'd like. Discovering the various roadblocks that can suddenly materialize—that was the part I hadn't fully anticipated.

***What are your most and least favorite parts of the job?***

I absolutely love watching our Medical Center move forward and upward. It's wonderful to see the vision of what we're capable of becoming take shape in the real world. I feel very proud of what we're creating together—I think you can feel the momentum in every aspect of our mission. The part I don't like is dealing with turf issues, where individuals or groups seem bent on trying to protect something that serves only them. In my view, that's a matter of failing to appreciate that there's a higher good that will ultimately benefit everyone who works here and—even more importantly—everyone we serve.

***What is the key to making this job manageable? Do you miss being a department chair?***

That's an easy one. The key is to have great people—people who not only excel at what they do, but who are incredibly dedicated and hard-working. One person doesn't do this job. Do I miss being a department chair? You know, I've always enjoyed what I was doing—being section chief, teaching, doing research, chairing Radiology. Whatever the size of your team, it's always great to feel the group has made progress on your watch. If I don't miss the chairmanship, it's because what I'm doing now feels so meaningful. I guess I thrive on challenge and am energized by seeing the pieces fall into place.

In a role like this, you do have to have confidence in yourself. That's very different from hubris, by the way. Humility is probably one of the most important attributes someone in charge of leading others should have. But you need to have an inner calm. You can't drive yourself crazy.

***You've said that one of your major goals is for us to become a 24/7 hospital. Why is that so important?***

As I'm sure you've noticed, we've implemented a lot of changes in that direction. For me, the issue is very clear: people fall sick at all hours, any day of the week. If we want to be responsive to that reality—in other words, to be really patient-centered—we have to be able to act accordingly. We have to be there, all systems go, every hour of the day, every day of the week.

***How would you characterize our research portfolio?***

We're privileged to have extraordinary scientists as part of our community. And the impressive increases we've achieved in National Institutes of Health [NIH] funding clearly reflect, I think, that our shift toward more team science is working. Historically, our Medical Center was focused almost exclusively on individually funded programs, often with remarkable results. But the way science is evolving, it's clear that no one person—however brilliant—can muster the requisite skill sets for the breakthroughs that need to happen. Nor even can a single lab. We were seriously lagging from that perspective.

That's why we're emphasizing collaboration and programmatically driven translational science—research that focuses on particular patient problems. The roots of disease are phenomenally complex—the genes you were born with, the way you live your life, the factors in the world around you that you can't control. We need to bring the widest possible range of perspectives and expertise to bear on

PHOTOGRAPH BY **JOHN ABBOTT**

unraveling the mysteries that underlie illness and finding new answers to the pain, fear, disruption, and loss of function it causes in someone's life.

***If you could start all over again in your role as dean & CEO, is there anything you would do differently?***

Well, I hope this doesn't sound cocky, but I don't think there's much I would change in how I've approached things. I had thought so long and hard about what I felt we needed to do, you know? In fact, just the other day, I came across the notes I put together for my job interview for this position, back in 2006. And I actually surprised myself, because the steps I emphasized back then as necessary to move the institution forward are pretty much exactly the ones we've taken.

Integrating the School and the Hospital sides of the house is just one example. When the dean & CEO search was under way, there was not only a complete lack of common purpose, but active competition between the two. I think most of us today would barely recognize the reality we had back then. Integration has made us palpably stronger across the board.

When I applied for this position, I clearly remember thinking that there was a form of collective resignation to settling for a future as a middle-of-the-road institution. And I felt very strongly that we didn't have to do that—in fact that we had a moral obligation not to do that for the sake of all that our mission stands for, as well as for our own sense of making a meaningful contribution to the world around us.

And maybe you remember the themes of my 2007 investiture speech: getting our financial house in order; vigorously pursuing philanthropy; creating a culture of mutual respect; attracting and keeping the best people; investing in IT; developing rigorous metrics across the board; augmenting our scientific portfolio by focusing on team science; creating strategic clinical programs in areas like musculoskeletal disease, neuroscience, and children's health; developing a new medical school curriculum; providing better student housing.

If you look back over the past five years, we've done all those things. So I feel I've kept my promises.

***What do you see as the most significant trends in patient care in the years to come? In medical education? In research?***

There's no question that there will be huge challenges, on all three fronts. In patient care, we'll see an intensifying emphasis on quality, with a proliferation of publicly available scorecards on outcomes. That's one reason excellence is so important and why I stress the importance of having high expectations of everyone who works here.

We want to own the quality space. You know, sometimes I hear people wondering whether all the hard work to become a world-class institution is worth it. It's worth it because our reputation will define our future. And even the skeptics—well, if they or someone they love got sick, what kind of care do you think they'd want?

The other big challenge, of course, is the cost of healthcare. It's a huge national issue that will be exacerbated by the aging population and the need to manage chronic diseases. That's why efficiency matters so much and why it's so vital to eliminate the waste of time and resources.

In medical education, I think we'll see a push toward studies of shorter duration. We want to lead in this regard, which is why we're working toward a three-year medical degree. One of the reasons is to help lower the amount of debt students incur. The other is that the role of doctors is changing. You can expect to see nurses and ancillary professionals take on more direct responsibility for primary care—especially in underserved areas. The solo MD practitioner will become a much rarer breed, which means that doctors will need skills beyond their medical expertise. They'll need to know how to work as part of a team, and many will apply their skills in arenas like global public health, bioethics, clinical investigation, administration, and so on.

"I've worked in some pretty prestigious places, but I truly believe there's a unique spirit here. The people who work here care very deeply about patients, and excellence, and what they do."

Our growing focus on dual degrees, in collaboration with other Schools of New York University, reflects this trend.

The challenge in research is the issue of funding. It's unclear what the trajectory of available grants from the NIH will be, so we have to be prepared to do more with less. The key will be creativity and innovation in designing research projects.

***What are you most excited about, looking forward?***

I think we are fabulously positioned. Thanks to everything we've implemented, we're poised to be true leaders in healthcare. Topping the charts is not important in and of itself, it's a matter of being a force for good in the lives of other people.

***What question would you like to answer that you haven't been asked?***

I guess I would have liked you to ask me why I love this place so much. In the course of my career, I've worked in some pretty prestigious places, but I truly believe there's a unique spirit here. The people who work here care very deeply about patients, and excellence, and what they do. That's the essence of a culture that's hard to replicate, and I think we all take pride in what we are creating together.

Sometimes, I get asked, "What's the secret sauce?" Well, the secret sauce is the incredible number of utterly amazing people who make us who we are. ●

Deborah Kelly, RN, monitors Marian Fay Levitt's transfusion at the Seligman Center.

# A Hub for Patient-Centered Rheumatology Research

Within the new three-story Center for Musculoskeletal Care on 38th Street and First Avenue, teams of clinicians and researchers are working side by side to advance the understanding of joint, bone, and connective tissue disorders and enhance patient care.

AT THE SELIGMAN CENTER FOR ADVANCED THERAPEUTICS, clinical studies of rheumatoid arthritis, osteoarthritis, vasculitis, lupus, and Behçet's disease are under way. There is a research office with 15 workstations, where trial coordinators and nurses review study data, an in-house pharmacy, a rehabilitation program in physical and occupational therapy, and a comprehensive imaging facility.

"Our center merges practicing rheumatologists—all our researchers have our own private practices—with an extensive clinical and basic science investigation program," says Yusuf Yazici, MD, assistant professor of medicine and director of the Seligman Center. "We see patients, and we also devote time to both investigator-initiated and industry-sponsored trials," Dr. Yazici says.

The Seligman Center's patient registry currently holds data on nearly 9,000 patients. Some 25 clinical trials are under way at any given time, about half of them randomized controlled trials. The large patient base allows physician researchers to propose their own randomized clinical trials for diseases like rheumatoid arthritis (RA), lupus, and Behçet's—a confounding inflammatory condition of the blood vessels that is rare in the United States but common in the Middle East and Asia. "We can get all the needed patients for a trial, because we have 17 rheumatologists and over 1,100 people with rheumatoid arthritis, 1,000 with Behçet's, and 500 with lupus in our registry," Dr. Yazici says.

The center's studies also include the nation's first minority registry for RA, jointly sponsored with Gail Kerr, MD, chief of the rheumatology division at the Veterans Affairs Medical Center in Washington, DC; an international collaboration on the natural history of vasculitis, in partnership with Oxford University; and clinical and research work on Behçet's syndrome with the NIH.

Chronic pain being a hallmark of so many rheumatologic conditions, the Seligman Center regularly monitors patients' pain levels, and patients complete a comprehensive self-assessment at every visit. "It helps patients focus on what's really going on with their condition right at their visit," says Ranit Shriky, the center's director. "Can they get dressed? Can they walk a block? Can they climb stairs? How is their fatigue? They can then walk in and hand the assessment to their physician, who can immediately address their concerns."

Dr. Yazici and Ms. Shriky also point out that patients have access to investigational therapies unavailable in a private practice. For example, they note that two drugs recently approved by the FDA for use in RA are available at the Seligman Center as part of research protocols for vasculitis.

Dr. Yazici believes the center offers an ideal vision for academic medicine. "Bringing all these people together in one place and providing infrastructure so they can pursue research goals and improve patient care—this is how universities should work." ● *—GINA SHAW*

PHOTOGRAPH: JOSHUA BRIGHT

# Steven L. Galetta, MD, Appointed Chair of Neurology

STEVEN L. GALETTA, MD, has been appointed the Philip K. Moskowitz, MD, Professor and Chair of the Department of Neurology. A nationally recognized leader in neurology and medical education, Dr. Galetta joins NYU Langone Medical Center from the University of Pennsylvania (Penn), where he was the Ruth Wagner Van Meter and J. Ray Van Meter Professor of Neurology, vice chair of the department, and director of the Division of Neuro-Ophthalmology.

At Penn, he also enjoyed the distinction of leading the Department of Neurology's residency and neuro-ophthalmology fellowship programs and serving as associate dean of admissions of the medical school. Laura Balcer, MD, MSCE, professor of neurology at Penn, and one of the first epidemiologists within the field of neuro-ophthalmology, will become vice chair of the department.

A native of Brooklyn, Dr. Galetta received his medical degree from Cornell University Medical College in 1983 and completed his neurology residency training at Penn and his neuro-ophthalmology fellowship at the Bascom Palmer Eye Institute in Florida. Dr. Galetta's areas of expertise include the treatment of double vision, multiple sclerosis, neuro-ophthalmology, and optic nerve disorders. He is a prolific researcher, having authored more than 200 original papers, as well as 113 editorials. He serves on the editorial boards of *Neurology* and the *Journal of Neuro-Ophthalmology*.

Dr. Galetta has received nearly 50 awards, including the Christian R. and Mary F. Lindback Distinguished Teaching Award, Penn's highest teaching honor; he was also recognized in 2004 for his role as an educator with the American Neurological Association's Distinguished Neurology Teacher Award, given each year to only one teacher in the United States.

Dr. Balcer and Dr. Galetta have been close collaborators for more than 20 years. She is an established clinical investigator whose team's work has focused on the development of visual outcome measures for multiple sclerosis. She has co-authored more than 150 publications. ●

# EDUCATIONAL INFORMATICS FACULTY FEATURED AT TEDMED 2012

**MARC TRIOLA, MD,** assistant professor of medicine and associate dean for educational informatics, and John Qualter, research assistant professor of educational informatics, spoke at TEDMED 2012 in Washington, DC, earlier this year. They discussed the importance of integrating technology into biomedical education and introduced the BioDigital Human, a new visual tool that allows students to virtually dissect and explore the human body in detail. The BioDigital Human can be viewed at *www.biodigitalhuman.com*. TEDMED is widely known for bringing together experts who are passionate about imagining the future of health and medicine. ●

## DR. VILCEK NAMED NEW TRUSTEE

**JAN T. VILCEK, MD, PHD,** professor of microbiology, has become a trustee of NYU Langone Medical Center. Dr. Vilcek is one of the medical center's most magnanimous donors, having pledged more than $100 million, an unprecedented level of giving by a faculty member of any institution. In addition to supporting research and other initiatives, his generosity extends to medical education in the form of full-tuition scholarships. Dr. Vilcek's extraordinary gifts flow from royalties earned from the anti-inflammatory drug Remicade, which was developed from antibodies he and his colleague at NYU Langone, Junming Le, PhD, discovered. Dr. Vilcek joined the medical center in 1965 after he and his wife defected from communist Czechoslovakia. ●

## Dr. Ogedegbe Receives More Than $2 Million From NIH

OLUGBENGA OGEDEGBE, MD, professor of population health and medicine and director of the Center for Healthful Behavior Change, received more than $2 million from the National Institutes of Health (NIH) to evaluate the impact of two strategies to reduce barriers to controlling hypertension in Ghana. The study was one of five projects funded by the NIH as part of its initiative to ease the impact of high blood pressure around the world.

Dr. Ogedegbe, a leading expert in health disparities research, focuses on implementing strategies identified through clinical trials. He has broad experience in community- and practice-based interventions targeted at reducing the risk of cardiovascular disease in African Americans. ●

## Dr. Ringstad Receives Award from President Obama

NIELS RINGSTAD, PHD, assistant professor of cell biology, received a Presidential Early Career Award, an honor bestowed by the United States government for scientists in the early stages of their research careers. Dr. Ringstad studies brain neurotransmitters associated with a host of neurological and psychiatric disorders, and he aims to identify new therapeutic targets for treatment of diseases associated with neurotransmitter dysfunction. He joined The Helen L. and Martin S. Kimmel Center for Biology & Medicine at the Skirball Institute for Biomolecular Medicine in September 2009. ●

## Dr. Robert Froemke Awarded a 2012 Pew Scholarship

ROBERT C. FROEMKE, PHD, assistant professor of otolaryngology, physiology and neuroscience, and a member of the Skirball Institute of Biomolecular Medicine, was named a 2012 Pew Biomedical Scholar. Recipients receive $240,000 over four years to pursue their research without restriction. Recently Dr. Froemke also received an Alfred P. Sloan Fellowship and a Klingenstein Fellowship. Dr. Froemke's research focuses on neuroplasticity, how the brain changes in response to learning and novel experiences. ●

# Dr. Link Wins NYU's Distinguished Teaching Medal

ROBERT "NATE" LINK, MD, associate professor of medicine and the new medical director of Bellevue Hospital, received New York University's 2012 Distinguished Teaching Award. The University awards the medal annually to faculty members who have demonstrated their excellence as educators over a sustained period of time and who have contributed significantly to the intellectual life of the University through their teaching.

During his 26-year career at NYU, Dr. Link's love of teaching and medicine and his exceptional kindness and concern for patients has inspired countless undergraduate medical students, residents, chief residents, fellows, and his own peers.

A native of Dayton, Ohio, Dr. Link graduated summa cum laude from Butler University, in Indianapolis, and from Washington University School of Medicine in St. Louis, where he received the prestigious Lange Memorial Award for Outstanding Academic Achievement. He arrived at Bellevue as a first-year resident in 1983, at the dawn of the AIDS epidemic. Except for a year spent with his wife and young daughter helping build a health center outside Nairobi, Kenya, Dr. Link remained at Bellevue.

In 1986 Dr. Link encountered the new field of evidence-based medicine at a conference led by Canadian physician David Sackett, MD. The discipline, which relies on the best available information from the literature to guide medical decisions, became a lifelong interest and eventually led him to develop to a curriculum in the subject for house staff.

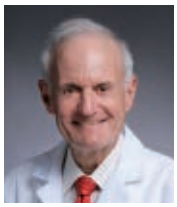
Dr. Link became medical director of Bellevue's primary care clinic in 1990, and nine years later gathered a group of physician-educators to create the Hospitalist Program at Bellevue. He subsequently recruited 30 Bellevue physician contributors, including co-editor Michael Tanner, MD, to compile the award winning primary care text, *The Bellevue Guide to Outpatient Medicine*, published in 2001. In the same year, he became chief of Bellevue's medical service, heading up the hospital's largest department. On August 1, 2012, Dr. Link became the new medical director of Bellevue, succeeding Eric Manheimer, MD, who stepped down earlier this year.

Dr. Link is the ninth member of the School of Medicine faculty to win the University's Distinguished Teaching Medal. ●

# CLASS OF 2012 HONORS THREE TEACHERS

**THE CLASS OF 2012** honored three teachers for their outstanding mentoring: Melanie Maslow, MD ('77), associate professor of medicine, Martin Kahn, MD ('63), professor of cardiology, and Michael Brabeck, MD, clinical associate professor of medicine.

Students honored Dr. Maslow for outstanding teaching in the basic sciences. "Both inside and outside the classroom, she made the intricacies and frustrations of pharmacology, bacteriology, and virology relevant, exciting, and enduring in our practice of medicine," a former student recalls.



Dr. Kahn's untiring dedication to furthering excellence in patient care, education, and research impressed his students. "After performing countless cardiac exams while standing next to him, I became convinced that he had a specialized, off-label stethoscope that would whisper 'mitral stenosis' or 'aortic regurge' whenever it detected that specific murmur," writes a former student.

Dr. Brabeck received the Leonard Tow Humanism in Medicine Faculty Award. One student describes him as a truly holistic health care provider, as he aspires to meet all of his patients' physical, psychological, and spiritual needs. "His exemplary communication skills make him an equally valuable mentor to students, for whom he is always accessible and whom he is always eager to advise." ●

PHOTOGRAPH OF DR. LINK BY JOHN ABBOTT

# Berson Award Winners Alumni Achievement Awards for 2012

The Solomon A. Berson awards are named in honor of the brilliant researcher and 1945 graduate of NYU School of Medicine whose work contributed to the development of the radioimmunoassay. The awards recognize distinguished alumni each year on Medical Alumni Day. On April 28, 2012, two physician alumni received this honor for extraordinary achievement in their fields. A third alumnus received the Julia Zelmanovich Young Alumni Award.

## ★ AWARD IN BASIC SCIENCE

**NINA BHARDWAJ, MD, PHD ('81),** professor of dermatology, medicine, and pathology, is a leading researcher in the field of immunotherapy, a form of therapy that recruits the body's own immune cells to fight disease. She is especially well known for her work on dendritic cells, sentrylike immune cells involved in the early detection of invading bacteria and viruses. These specialized cells direct the body's defenses to mount an appropriate response to check the spread of infection. Dr. Bhardwaj aims to understand the biology of human dendritic cells in cancer and viral infections and exploit their potential as therapeutic vaccines. She credits the School of Medicine for nurturing her interest in immunology.

A valued mentor, Dr. Bhardwaj has held leadership positions in numerous national professional organizations and has more than 150 peer-reviewed scientific publications. Among the many honors and awards recognizing her outstanding accomplishments are the School of Medicine's Alpha Omega Alpha Alumna Award, the 2002 Doris Duke Distinguished Clinical Scientist Award, the NIH Merit Award, and the Henry Silverman Melanoma Research Alliance Team Science Award.

Dr. Bhardwaj completed her residency in internal medicine at Brigham and Women's Hospital and a fellowship in rheumatology at Cornell. After finishing her postdoctoral work at Rockefeller University, she joined the faculty there and became an associate professor of clinical investigation. In 2002 Dr. Bhardwaj returned to NYU School of Medicine, where she is director of the Tumor Vaccine Program and scientific director of the Vaccine and Cell Therapy Core Facility.

## ★ AWARD IN CLINICAL SCIENCE

**HENRY J. BINDER, MD ('61),** is professor emeritus of medicine at Yale University. His studies of how electrolytes are transported in the colon have improved the treatment of diarrheal disorders, especially in resource-poor countries. In his investigations, he discovered that starch that is relatively resistant to breakdown by pancreatic enzymes could improve current therapy with oral rehydration solution in treating diarrhea. This type of starch enhances the production of short-chain fatty acids in the intestine, resulting in increased fluid and sodium absorption. Recent clinical trials of patients with cholera in India, he reports, have shown that treatment with these starches was successful, thereby establishing this improved formulation of oral rehydration solution. Additional clinical trials are beginning in Bangladesh.

Dr. Binder is the author of more than 160 peer-reviewed publications. The NIH has supported his research for 37 years, and The Bill and Melinda Gates Foundation currently supports his work. His many honors include the Distinguished Achievement Award and the Distinguished Mentor Award from the American Gastroenterological Association.

## ★ JULIA ZELMANOVICH YOUNG ALUMNI AWARD

**HERSH CHANDARANA, MD ('02),** assistant professor of radiology, has already received a number of honors and awards in his short career. Dr. Chandarana completed his residency in diagnostic radiology and a fellowship in body and cardiovascular magnetic resonance imaging (MRI) at NYU School of Medicine. His major research interest is the development and application of computed tomography and MRI techniques in oncologic imaging and renal functional imaging. Dr. Chandarana's research has been supported by grants from the Radiologic Society of North America, and he has published nearly 30 articles in peer-reviewed scientific journals, in addition to numerous reviews and abstracts. He co-leads the PET-MR working group at the School of Medicine, which is exploring potential applications of simultaneous MR and PET imaging.

Dr. Chandarana served on the Society of Uroradiology Research Award Committee (2011–12) and participated as a research fellow in MR research and development at Siemens Healthcare in Germany. He has received awards from the American Chemical Society and the Rho Chi Society. ●

# On Morality and Mortality

## Bioethics matures, and one of its master practitioners joins the faculty of NYU Langone.

BY CLAUDIA KAPLAN

AS MEDICINE GROWS increasingly high-tech and scientific advances proliferate, ethical quandaries multiply too. Should a healthy person at risk for Huntington's undergo a DNA test if nothing can be done to prevent or forestall the disease? Should a very sick patient receive aggressive therapy or be encouraged to consider palliative care? The role of bioethicists, who analyze moral and social challenges in medicine, has never been more critical. Arthur L. Caplan, PhD, recently appointed founding director of the Division of Medical Ethics in the new Department of Population Health at NYU Langone Medical Center, is eager to expand the field's reach. Bioethics has come a long way, Dr. Caplan explains, but more education and outreach is vital as patients, families, and physicians confront increasingly complex and vexing medical dilemmas.

***What lured you to NYU Langone?***
It's an exciting time to be here. I have a personal relationship with Dean Grossman dating back to our days as colleagues at the University of Pennsylvania, and I'm a big fan. I like the fact that New York University is gaining an international footprint, both through its satellite campuses and in global health. I think bioethics can play an expanding role in our far-reaching presence.

***Which areas of global health concern you the most, and what kind of impact do you hope to have?***
I'm really interested in vaccines—from cholera and malaria to HIV and HPV. We have the opportunity to help shape global policy in terms of who gets vaccinated, availability, and informed consent. I'm interested in ethical issues relating to poor research subjects—exploitation, how to use drugs, interventions in ways that we may not feel comfortable doing in the developed world.

***How does the practice of bioethics in American medical research differ from that in the rest of the world?***
Medical research in the United States is very focused on individual autonomy. It must be a patient's choice to participate in a clinical trial of new drugs or treatments, and patients must fully understand the possible benefits and risks they face. I'm not sure the rest of the world sees it that way. In poor countries, where people may not be able to read or write and leaders may not have the expertise to review the research in great detail, autonomy is not as important. Instead, they'll say, "What we want to know is whether we can get access to medical care that can help us." The risk-benefit ratio won't be weighed as critically as it is by Westerners, who have the luxury of living pretty safely and pretty well.

***As longtime director of the University of Pennsylvania's Center for Bioethics, what lessons did you learn that you plan to apply at NYU Langone?***
It's very important to make sure that a bioethics curriculum meets the interests of both faculty and medical students. I'm proud of the stellar master's program in bioethics we created at Penn, and I think we will move to design an equally impressive one here. But there are intermediate steps to come first: certificate programs, weekend and online courses, ethics rounds, continuing education.

***What should students expect from the new division you've been hired to lead?***
It's important that they be exposed to research ethics, clinical ethics, and policy issues. You want to make sure those three areas are adequately represented. We'll try to organize monthly grand rounds on topics like how to deal with an anorexic woman who refuses to eat but is old enough to refuse treatment. These are bedside-driven, day-to-day dilemmas. I'll be knocking on the doors of our chief residents in different departments to ask them to present a case each month.

***You've served on numerous governmental committees. How big a role does politics play in medicine?***
Huge. In one sense, the whole conservative values debate in America is one big bioethics debate along political lines. Part of this comes out of the abortion debate, part of it comes out of arguments about embryonic stem cells and fetal tissue. Whether you're arguing about contraception, assisted suicide, or embryonic stem cell research, you're smack in the middle of the culture wars, which by definition are political.

***When bioethicists tackle a knotty issue, how often do they reach a consensus?***
It depends on the issue. With embryonic stem cell research, I think the field has a

lot of consensus, along with some very strong dissent. There's a lot of consensus around medical records and protecting privacy. But should we use drugs to enhance our intellectual performance? You get a lot of fighting about that one. Some issues are sort of settled. In other areas, there isn't a framework yet, so people debate to develop one.

***What are the three most critical medical issues today?***

For the United States, number one is figuring out how to get all Americans affordable access to basic healthcare. You can't be the only modern country in the world to speak about equality of opportunity and have uninsured people who can't get basic medical and dental care. That is a huge moral problem. Second is our aging population, which is straining our resources. The current debate about cost containment is going to get much worse in the next 10 years. Third, advances in neuroscience. Interesting questions will be raised about how far you can go to change your mental state. Let's say I have a drug that can erase recent memories. If you got raped or witnessed an act of violence, maybe you don't want to remember it. But how are you going to show up in court to testify without a memory of the event? And there are issues around brain physiology. For example, the early appearance of Alzheimer's. It's one thing to say, "My Mom's forgetting things." It's another thing to scan someone at 40 and say, "It looks like you've got an early Alzheimer's brain."

***How has bioethics evolved?***

In the U.S., it's a field that's almost completely driven by technological evolution, beginning way back with kidney dialysis to the Baby Fae baboon heart transplant, the first test-tube baby, new drugs for AIDS, cloning Dolly the sheep, and embryonic stem cell research. Sometimes that's good; sometimes it gives bioethics the appearance that it's running after the latest crisis, like a fire department to a fire. Bioethics started as very American, around the mid-1970s. It is quickly becoming very international, where the issues are less technology-driven and more access-driven. There are more concerns about the poor. That's a positive, notable, and appropriate shift. Also, when bioethics started, you could be an amateur. Anybody could say anything and get into the debate. Slowly, it's becoming more professionalized. You can see the field maturing from a kind of lively adolescence into a respectable middle age.

***Are you pleased with how far the field has come?***

I'm amazed. When I started, I thought it would be a fad that lasted three years at most. There was no money, no foundations, no support. Doctors didn't like it, scientists didn't like it, journal editors didn't like it. I'm pleased because it has really taken hold. I've tried hard in my career to push bioethics into the public arena by talking to the media and writing for wide-circulation journals and more popular publications. I think bioethics should have a strong public presence to let people engage in these issues. I think that's happened. ●

**"You can't be the only modern country in the world to speak about equality of opportunity and have uninsured people who can't get basic medical and dental care. That is a huge moral problem."**

Arthur L. Caplan, PhD

# All in the Family

## After a father saves the life of his infant son, the child does the same for his parents, older brother, and other relatives.

BY GARY GOLDENBERG

From left: Cardiologist Dr. Steven Fishberger, Nadia Arif and her husband, Arif Mahmood, with their sons Saheer and Sarim (in his father's arms), geneticist Dr. Silvia Priori, and otolaryngologist Dr. J. Thomas Roland.

PHOTOGRAPH BY JOHN ABBOTT

"HE'S NOT BREATHING! He's not breathing!" shouted Nadia Arif to her husband, Arif Mahmood. Bolting from the bedroom of their Morris Plains, New Jersey, home, he saw his infant son, Sarim, limp and lifeless in his wife's arms. Though he knew nothing about CPR beyond what he had seen on TV, Mahmood began applying rhythmic compressions to the baby's chest. Two minutes later, Sarim opened his eyes.

The same day, Sarim was transferred from a local medical facility to NYU Langone Medical Center, where Steven Fishberger, MD, a cardiologist and clinical associate professor of pediatrics, inserted an implantable cardioverter-defibrillator (ICD), a pocket watch–size device that will shock the baby's heart back to life should it ever miss another beat.

"I don't know how it happened," Mahmood recalls. "I just started doing the first thing that came to mind." If those few minutes are a blur, so too are the last several years. Since late 2009 Mahmood and his wife have been on a medical odyssey that first involved Sarim but eventually touched the whole family, even relatives in their native Pakistan. It began 20 months before, when Sarim experienced a ventricular arrhythmia and a routine screening revealed that he was profoundly deaf. The family was advised to consult not only

a hearing specialist, but also a geneticist and a cardiologist, since Sarim's condition was probably genetic in origin, and many such problems are associated with heart disorders.

Dr. Fishberger found Sarim to have long QT syndrome, a condition in which the cardiac muscle takes longer than usual to recharge between beats. He prescribed a beta-blocker to reduce Sarim's chances of developing a potentially fatal arrhythmia, or abnormal heartbeat. There was more medical sleuthing to be done, however. "Any one of 13 different genetic mutations can cause long QT," Dr. Fishberger explains. "It needs to be sorted out with genetic testing." At NYU Langone's Cardiovascular Genetics Center, tests uncovered the source: a mutated form of *KCNQ1*, a gene that controls the flow of potassium ions in the inner ear and in cardiac muscle. Aberrations in this gene result in both deafness and long QT, a combination of ailments known as Jervell and Lange-Nielsen syndrome (JLNS), affecting just 1 to 6 infants per million worldwide.

With that one test, the family's odyssey took a stunning and unexpected turn. Mahmood and Arif learned from the center's director, Silvia Priori, MD, PhD, professor of medicine, that JLNS is inherited in an autosomal recessive pattern, which means that Sarim has two copies of the defective gene and each of his parents has one—putting both of them at risk for a dangerous arrhythmia, but not hearing loss. Sarim's older brother, Shaheer, was also found to be a carrier. All three were put on medication, and the family was advised to tell relatives to seek care as well. "There's an old saying that if a child is sick, the whole family is sick," says Sharda McGuire, FNP, the family's nurse practitioner. "This is truly the case here."

Meanwhile, the family began to explore the best treatment for Sarim's hearing loss. It turned out that his cochleas—snail-shaped structures that convert sound waves into electrical impulses—were irreparably damaged. The only solution was a cochlear implant, a sophisticated electronic substitute for the real thing. Sarim received his first implant in October 2010, just as he turned one year old, and his second, five months later. "He's close to being on par with normal hearing for kids his age," explains J. Thomas Roland, MD, the Mendik Foundation Associate Professor of Otolaryngology and chair of the department, who performed both implant surgeries. "Early implantation, often below the age of one, puts children on a trajectory of normal language development."

Save for the small external components of his cochlear implants, Sarim looks and acts much like any other 20 month old—a squirming, babbling bundle of energy. He'll need intensive speech and language therapy for a couple of years and occasional implant tune-ups, and parts of his ICD will need to be replaced periodically. Otherwise, his doctors expect him to have a long, active, normal life. ●

## Genetic Testing for Long QT

Long QT syndrome (LQTS) was first documented in 1856 by a German doctor who described the case of a young deaf girl who collapsed and died while being scolded by a teacher. When the child's parents were informed of her death, they "evinced no surprise," noting that her older brother, also deaf, had died after a "terrible fright." (In retrospect, these were probably the first descriptions of Jervell and Lange-Nielsen syndrome, which includes long QT and congenital hearing loss.) Since the concept of DNA was still a century away, the doctor couldn't even begin to imagine the biological flaw linking those unfortunate siblings.

The mystery of long QT began to unravel in 1995, when researchers discovered the first of 13 known genes that can disrupt the structure of the proteins that form ion channels in cardiac muscle and dangerously elongate the electrical recovery of the heart, also called QT interval, setting the stage for sudden cardiac death.

Testing for mutations in the LQTS-related genes and using genetic results to guide patients' management is now routine at NYU Langone Medical Center and a handful of sites around the nation. Dr. Silvia Priori, director of the Cardiovascular Genetics Center, would like such testing to be commonplace. "While most cases of long QT can be diagnosed with an electrocardiogram, genetic testing can, in three out of four cases, identify the underlying genetic mutation. This information is critical for defining the patient's risk profile and guiding management," she explains.

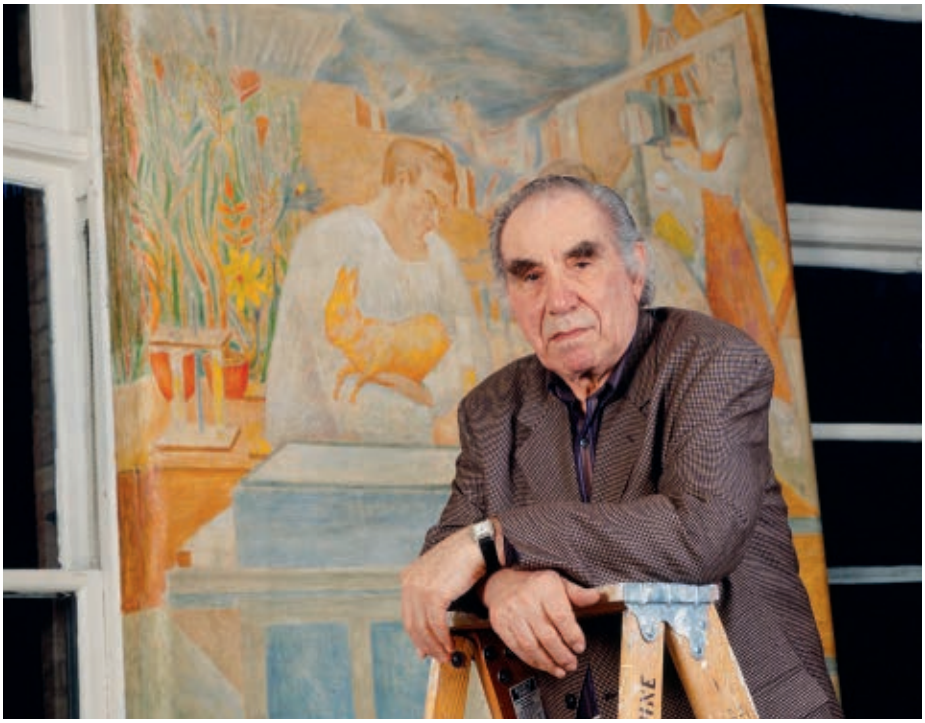
"For example," she continues, "if the defect is traced to the *KCNH2* gene, we'll know that the arrhythmia can be triggered by emotional distress and auditory stimuli, like loud noises. We'll also know the patient would probably partially respond to beta-blockers and might benefit from an implantable defibrillator."

Once a child tests positive, Dr. Priori recommends that the mother and father get tested too, since at least one parent is likely to be a carrier and therefore at considerable risk for sudden cardiac death—even if his or her heart has never so much as skipped a beat. And if a parent tests positive, then other children in the family and close relatives should be screened as well.

Genetic testing for long QT syndrome is expensive and insurance coverage is spotty. However, more and more insurers are coming to recognize the role that such testing can play in improving treatment and saving lives, Dr. Priori says.

# If These Walls Could Talk...

ONE DAY IN THE EARLY 1980S, a maintenance worker at Bellevue Hospital was assigned the task of applying a fresh coat of paint to the first-floor rotunda. But before he could put roller to wall, he had to scrape off several coats of cracked, peeling orange paint. As he chipped away, figures of people and animals began to emerge. Realizing that he had discovered the work of an entirely different kind of painter, the man stopped what he was doing. An art expert confirmed that one of the lost murals of Bellevue had been found.



David Margolis

During the Great Depression, the Works Progress Administration, better known as the WPA, hired artists to paint eight murals in Bellevue's various pavilions. In time all were painted over or lost as buildings were renovated or demolished. The rediscovered treasure was the work of David Margolis, who created it from 1937 to 1941, when the rotunda served as the waiting room for Bellevue's TB clinic.

The semicircular mural, entitled *Materials for Relaxation*, comprises nine panels that depict the story of human progress. Margolis earned $26.50 a week for his work, which adhered closely to the Social Realism style of the day made famous by Diego Rivera, with whom Margolis collaborated on a doomed mural at Rockefeller Center. Rivera's notorious mural featured Soviet leader Vladimir Lenin leading a May Day parade, and it was destroyed after he refused to remove Lenin's image.

The Bellevue artwork barely escaped a similar fate. By the late 1940s the hospital needed space, so the rotunda was partitioned into storage areas. The mural was painted over, though it remains unclear whether it fell victim to disregard or disrepute. It was, after all, the beginning of the anti-Communist Red Scare, and Margolis, a native of Odessa, was known for the socialist overtones of his work. In 1956 the space was converted into a snack bar, Bel-Snacks, adding insult to injury in the form of layers of grease. In later years, the area served as the thrift shop for the Bellevue Auxiliary.

The mural was forgotten by all but those with the longest memories. When it was rediscovered, the hospital obtained government funding for a restoration, which was completed in 1995. Margolis, then 83 years old, was brought in to assist. Visitors today can see what people first glimpsed in 1941. A wilderness scene with animals and Native Americans farming. A scientist at work with a microscope and rabbit. Families fleeing natural disasters. Workers laboring in factories. Citizens participating in democracy. People relaxing in a park, a library, a nightclub.

David Margolis died in 2005, but not before seeing his labor of love preserved, even if in faded glory. "It is like finding out that what you thought was dead is alive," he told *The New York Times*. "It is like tasting the wine of your youth. It is like finding lost friends." ●

PHOTOGRAPH: GREGORY MINK

# Change

## the world…

**One patient at a time.** When you include a bequest in your will to NYU Langone Medical Center you help us deliver outstanding health care to the many patients and families who rely upon us to improve their lives. Superb physicians, an award-winning nursing staff and internationally ranked scientists make the difference. **Join our community, and create your legacy today.**

To learn more about making your planned gift to NYU Langone, please contact Marilyn Van Houten at 212.404.3653 or marilyn.vanhouten@nyumc.org.


Sasha Nialla

NYU Langone
MEDICAL CENTER

www.NYULMC.org

NYU School of Medicine
NYU LANGONE MEDICAL CENTER

Office of Communications and Public Affairs
550 First Avenue, New York, NY 10016