

NYU PHYSICIAN

THE MAGAZINE OF NEW YORK UNIVERSITY SCHOOL OF MEDICINE

SPRING 2014

TAKING IT ON FAITH

Community-based programs are reducing the burden of hypertension in minority populations



PLUS

THE MYSTERIOUS CHANNELS BETWEEN BRAIN CELLS
HIGH-TECH VESTS FOR THE BLIND
THE FUTURE OF FACE TRANSPLANTATION

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.**



**Thank you for
your generosity.**

NYUPHYSICIAN

New York University

Martin Lipton, Esq.
Chairman,
Board of Trustees

John Sexton
President

Robert Berne
Executive Vice President
for Health

NYU Langone
Medical Center

Kenneth G. Langone
Chairman,
Board of Trustees

Robert I. Grossman, MD
Dean and Chief
Executive Officer

Kathy Lewis
Senior Vice President
Communications
and Marketing

NYU PHYSICIAN

Steven B. Abramson, MD
Anthony J. Grieco, MD
Editors, Science
and Medicine

Marjorie Shaffer
Editor

Nicole Dyer
Contributing Editor

Sherry Zucker
Print Production
Coordinator

Segal Savad Design
Art Direction

Nancy E. Sherman
Copy Editor

ON THE COVER:
ILLUSTRATION BY
LYNDON HAYES



COVER STORIES

6 Taking It on Faith
In churches, barbershops, and other gathering places around New York City, researchers at the Center for Healthful Behavior Change are partnering with lay advisers to bring down soaring rates of hypertension in minority populations.
By Bryn Nelson

14 The Spaces In Between
Charles Nicholson's pioneering studies of the slender channels around brain cells could lead to better drug delivery and new treatments for neurodegenerative diseases.
By Nicole Dyer

20 Stick Shift
Driven by his own battle with a vision-destroying disease, Dr. John-Ross Rizzo is devising better alternatives to the white cane for the blind.
By Kenneth Miller

Black-owned barbershops in the city are neighborhood centers for healthcare outreach.

DEPARTMENTS

02 From the Dean
Addressing Health Disparities

03 News From Medicine

- A Surprising New Role for Immune Cells in the Brain
- DNA's Surveyors
- A Virus Exerts Unusual Control Over Its Host Cells

24 Faculty Conversation
Dr. Eduardo D. Rodriguez, the new chair of plastic surgery, discusses face transplantation.

26 Faculty News

- Dr. Jef Boeke Joins NYU Langone as Director of New Institute for Systems Genetics
- Dr. Ruth Lehmann Named Chair of Cell Biology
- Dr. Andrew D. Rosenberg Appointed Chair of Anesthesiology
- Dr. Edward Fisher Awarded Memorial Lectures
- Dr. Rodolfo Llinás Honored

28 Medical Education
Dr. Steven Abramson, chair of the Department of Medicine, revives a beloved teaching tradition: Saturday morning rounds.

30 Patient Story
Solving a case of facial paralysis by tapping into a nerve from the tongue.

32 Obituary
David S. Baldwin, MD

Addressing Health Disparities

Hypertension among minority populations, particularly African Americans, is devastating. High blood pressure killed nearly 52 out of 100,000 black men in the United States in 2009, for example, triple the mortality rate for white men.



The statistics are almost as dire for black women. The condition claimed about 38 lives out of 100,000 black women, more than 2.5 times the rate for white women.

These appalling disparities, tracked by the American Heart Association in its latest survey, have long been a source of great frustration. How can healthcare providers engage minority communities to reduce the burden of hypertension? In this issue of *NYU Physician* magazine, the extraordinary work of Dr. Gbenga Ogedegbe, who founded the Center for Healthful

Behavior Change at NYU Langone Medical Center, provides at least a partial answer. He and his colleagues have established community-based programs that enlist the help of lay health advisers in churches, barbershops, and other gathering places in New York City.

Dr. Ogedegbe's work reveals how creative thinking about an intractable healthcare problem can lead to new approaches with possibly lasting results. The two other features in this issue of the magazine also showcase creative thinkers seeking answers to pressing health problems and scientific conundrums. One story explores the work of Dr. Charles Nicholson, a pioneering neuroscientist whose exploration of the spaces between nerve cells in the brain has yielded some astounding insights. Another describes the innovative work of Dr. John-Ross Rizzo, who is inventing low- and high-tech successors to the cane for the blind. He himself suffers from an incurable disease that is destroying his eyesight.

Altogether, these inspiring stories reveal how tenacity, ingenuity, and creative insight can make a significant contribution to improving healthcare and our understanding of the human condition. That, after all, is a large part of our mission.

DEAN & CEO ROBERT I. GROSSMAN, MD

HYPERTENSION BY THE NUMBERS

42.6%

Percentage of
adult black men
in U.S. with hypertension

—

33.4%

Percentage of
adult white men
in U.S. with hypertension

—

47%

Percentage of
adult black women
in U.S. with hypertension

—

30.7%

Percentage of
adult white women
in U.S. with hypertension

—

69%

The percentage of all
people who have **their first
heart attack** and have blood
pressure higher than 140/90

—

\$51 BILLION

Estimated direct and
indirect **U.S. costs of
hypertension** in 2009

Sources: National Health and Nutrition
Examination Survey (NHANES),
American Heart Association

A Surprising New Role for Immune Cells in the Brain

Researchers reveal that the cells are important for learning and memory.

Microglial cells are best understood as neuronal bodyguards of the brain and spinal cord that patrol for cellular debris and pathogens. For Wen-Biao Gan, PhD, and his colleagues at the Skirball Institute of Biomolecular Medicine at NYU Langone Medical Center, however, the question that has propelled their work for the past decade is not what microglia do when things go wrong, as in disease, but rather what the cells do when things go right.

In teasing out the function of microglia in the healthy brains of mice, Dr. Gan and his team are overturning common assumptions about microglial function and offering compelling evidence in support of the emerging idea that these immune cells, far from being just defensive sentries, play a pivotal role in learning and memory.

“People once believed that microglia just sat around in healthy brains and became functional only in the presence of diseases,” says Dr. Gan. “Now we know that’s not true.” (In 2005 Dr. Gan and his team discovered that microglia cells move constantly in healthy brains.)

In their latest study, published recently in *Cell*, the scientists created a powerful tool to study microglia: the first genetically engineered mouse model that affords precise

control of microglial functions. Researchers inactivate or express specific genes in the microglia of these mice. “Before our mice were generated, there never was a good way to specifically change the genetic expression and function of microglia or control their chemical signaling without affecting related cells elsewhere in the body,” Dr. Gan explains.

Previous studies in mice have shown that manipulating a number of genes expressed in microglia disrupts the development and function of the central nervous system. Yet none of these studies has proved conclusive, since such target genes also express themselves in related cells elsewhere in the body.

The new mouse model—the product of a collaboration with Dan Littman, MD, PhD, the Helen L. and Martin S. Kimmel Professor of Molecular Immunology—overcomes this limitation. Dr. Littman and Christopher Parkhurst, an MD/PhD student who is the first author of the *Cell* paper, turned to a sophisticated genetic-engineering tool that could either remove or express specific genes in microglia using an enzyme called Cre recombinase. The researchers could activate this enzyme at very precise points in the animal’s life by administering an inducing

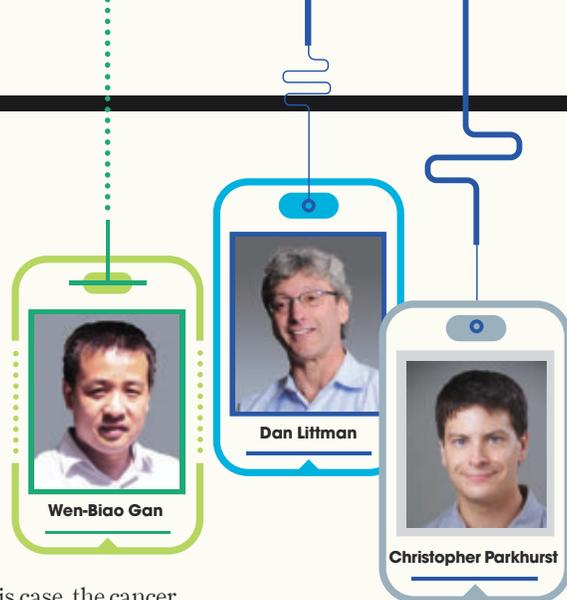
agent, in this case, the cancer drug tamoxifen.

With the ability to target microglia specifically, the researchers found that mice with diminished microglia populations experienced difficulty growing dendritic spines, the treelike extensions of neurons that connect to other neurons and facilitate the passage of information across synapses, the junctions at which neurons meet.

In healthy mice, tests of motor skills, such as balancing on a spinning rod, alter neuronal connections. “When you learn, you make new synapses,” says Dr. Gan. But the microglia-deficient mice showed much-reduced growth of new synapses. So did mice unable to produce brain-derived neurotrophic factor, or BDNF, a

chemical that cements neuronal connections. “We typically associate BDNF with neurons,” Dr. Gan says. “But we know that microglia secrete it too, and that it plays an important part in the formation of synapses.”

The next step is to determine precisely how microglia shape synapses. Do microglia interact with other cells to do the job? Or maybe there are other chemical signals they secrete that somehow influence neurons. “It’s all possible,” Dr. Gan says. “We just don’t know, but we plan to find out.” ● —NICOLE DYER



Microglia carrying a specific gene glow red; others carry a fluorescent yellow protein.

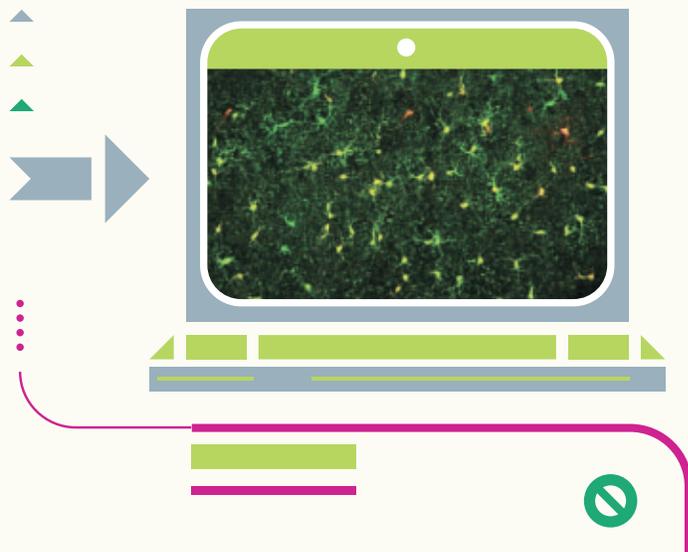


IMAGE COURTESY OF DR. WEN-BIAO GAN

DNA's Surveyors

New findings suggest how molecules collaborate to repair damaged DNA.

All organisms, from bacteria to humans, face a near-constant onslaught of DNA damage from ultraviolet light, chemicals, and other sources. Life depends on the ability of cellular repair specialists to find and fix this damage before it leads to a host of dire consequences, such as cancer, recurrent infections, and premature aging.

Scientists only partially understand how these repair crews do their jobs. Recently, however, Evgeny Nudler, PhD, a Howard Hughes Medical Investigator and the Julie Wilson Anderson Professor of Biochemistry, and his team filled in some significant gaps in our comprehension of the process. The researchers have long studied RNA polymerase, an enzyme that copies DNA into RNA as it slides along tracks of double-stranded DNA. This RNA, in turn, contains all of the information needed to construct cellular proteins.

Their latest study, supported by Timur Artemeyev, suggests that the key to successful DNA repair is a sort of construction supervisor able to literally pull the polymerase backward to point out hidden sites of damaged DNA that need to be fixed. The mechanics of this backtracking, reported in the

journal *Nature*, offer clearer insights into how the repair process works and, most important, how it might be corrected when it goes awry. “Better repair means fewer mutations, which also means slower aging and lower rates of cancer and many other pathologies,” Dr. Nudler says.

According to the study, DNA repair appears to rely on a close association between RNA polymerase and a protein called UvrD. Researchers have long known that UvrD plays a major role in mending damaged bacterial DNA. Inherited defects in the gene encoding the human analog of UvrD, a protein known as XPB, have been implicated in a range of devastating and incurable disorders linked to compromised DNA repair.

A powerful biochemical technique developed by Dr. Nudler’s lab pointed to the unexpected connection between UvrD and RNA polymerase. Even more surprisingly, a series of experiments suggested that UvrD brings RNA polymerase to a grinding halt at frequent intervals along the helical track of DNA. “We proved that

these pauses or arrests are the result of backtracking,” Dr. Nudler says. “So UvrD pulls the polymerase backward, in the opposite direction from the way that it normally goes.”

By doing so, the study suggests, UvrD and a second collaborator, called NusA, help expose damaged DNA sites lodged beneath the polymerase. The two partners then recruit a team of other proteins to patch up the DNA tracks before the polymerase continues on its way.

Dr. Nudler says the new findings also offer a possible justification for a puzzling phenomenon known as pervasive transcription, which he calls “one of the most enigmatic and debated

Our health largely depends on how well DNA is repaired.

subjects of molecular biology.” Why do RNA polymerases transcribe most of our genome, converting vast stretches of DNA to RNA, when only a tiny fraction of those resulting RNA transcripts will ever prove useful? That extensive activity, he says, makes far more sense if the polymerase is simultaneously patrolling our chromosomes for DNA damage and ensuring that its associates help with repairs.

Led by study co-authors Vitaly Epshtein, PhD, and Venu Kamarthapu, PhD, postdoctoral fellows in Dr. Nudler’s lab, the group’s research is dramatically expanding that list of potential polymerase collaborators. ●

—BRYN NELSON



Evgeny Nudler



Venu Kamarthapu



Vitaly Epshtein





Ian Mohr

A Virus Exerts Unusual Control Over Its Host Cells

CMV's tactics could shed light on cancer and other conditions.

With 230,000 letters of DNA, cytomegalovirus is bigger than any other virus known to infect humans. It's also remarkably common, infecting up to 80 percent of adults in the United States. For years, however, researchers deemed this viral giant an infrequent troublemaker that caused disease mainly in babies and in adults with weakened immune systems.

Increasing evidence suggests that the virus may be more dangerous than previously thought. Recent studies, in fact, have investigated the possibility that CMV might assist in the formation of some types of brain tumors.

In a recent study in *Cell Reports*, Ian Mohr, PhD, professor of microbiology, and members of his lab have now found that unlike other viruses, CMV exerts far more selective control over the cells it invades, a technique that helps it flourish. "There's a large extent of this micromanaging," Dr. Mohr says. "Something like this really hasn't been seen before."

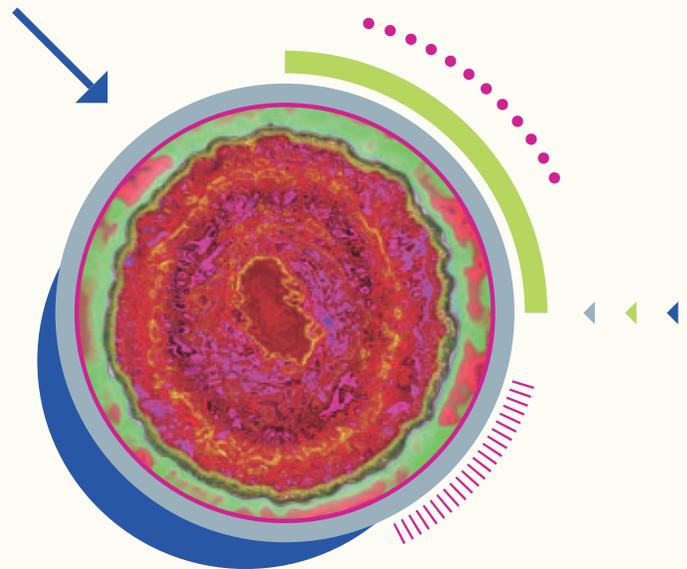
Moreover, the precision of its tactics, he says, may offer new clues about how viral infections and diseases such as cancer can commandeer a fundamental biological process known as translation, which lets cells turn information stored in DNA and encrypted in messenger RNA

into functional proteins.

Most viruses subvert a host cell's normal protein-making apparatus, globally suppressing normal production and forcing the cell to manufacture only viral proteins. Dr. Mohr's lab discovered that CMV uses a different strategy: Instead of shutting down all regular production by the host, the virus reprograms the entire cell and selects which cellular proteins can still be manufactured. In this way, the virus blocks the synthesis of many proteins but actually stimulates the production of thousands of others.

In the translational system, cells recruit molecular engines known as ribosomes to decipher instructions embedded within RNA transcripts for protein production. "Clearly, the virus has the capacity to manipulate this code, and it may be a powerful tool to help teach us how different RNA transcripts are selected for translation by ribosomes," Dr. Mohr says.

Deciphering this code could have profound implications for understanding how other diseases can hijack protein production. For example, the researchers found striking similarities between proteins whose production increases after CMV infection and proteins up-regulated within cancer cells. "That was very



This colorized electron micrograph reveals human herpesvirus-5, commonly known as CMV.

surprising," Dr. Mohr says. But the revelation, he adds, fits with the growing body of research linking CMV to gliomas, a kind of brain tumor.

Some scientists have speculated that the virus might promote inflammation or other conditions that can spur cancer and atherosclerosis. Alternatively, CMV's micromanagement might lead to cellular dysfunction and eventually to disease.

For their study, led by graduate student Caleb McKinney, the researchers infected lab-grown human cells with CMV and then examined the changes in

protein production. The virus shut down its host's ability to produce proteins involved in growth and immune defense. This made sense, but CMV infection also turned up the production of other host proteins capable of limiting viral growth, a seemingly counterproductive strategy.

Perhaps, Dr. Mohr speculates, some host defenses can still evade the viral takeover and rise to the occasion. Alternatively, CMV may be lengthening its own reproductive cycle to avoid killing the cell too soon and burning itself out before it has a chance to reproduce and spread. By biding its time within the cell, the virus might gain the upper hand over the long run. ● —*BRYN NELSON*

TAKING IT ON
FAITH

In dozens of churches, barbershops, and other gathering places around New York City, NYU Langone Medical Center researchers at the Center for Healthful Behavior Change are partnering with lay advisers to bring down soaring rates of hypertension in minority populations.

BY BRYN NELSON • ILLUSTRATION BY LYNDON HAYES





The brick façade of Bethel Gospel Tabernacle is glowing red in the evening sun as a dozen parishioners gather for a lesson on better living. While a gardener waters the shrubs and flowers behind a low wrought-iron fence enclosing the churchyard in Jamaica, Queens, three volunteer leaders are tending to the physical health of their fellow congregants in a nearby Sunday school classroom.

The summer evening begins with a Scripture reading, a prayer, and a chorus of Amens. Then the teachers take turns leading their students—all over the age of 50 and all diagnosed with high blood pressure—through a carefully scripted session about increasing their physical activity and improving their diets. After taste-testing a relatively low-calorie mix of pure pineapple juice and club soda, the class learns how to read nutrition labels and choose healthful drink options. A woman in a white head scarf readily admits that she had never before considered the total carbohydrate content when comparing labels.

“Thank God for this class!” she exclaims.

Similar sentiments are ringing out in 32 churches throughout the five boroughs, where parishioners are enrolled in a National Institutes of Health–funded study called FAITH (Faith-Based Approaches in the Treatment of Hypertension). During a 12-week course, congregants learn how to adopt a more healthful lifestyle, and lay advisers follow up for an additional three months to help participants identify and overcome any remaining barriers. “At the end of the study, we’ve empowered the churches to take this on themselves so that it can be sustainable. That’s the beauty here,” says Gbenga Ogedegbe, MD, MS, MPH, professor of population health and medicine.

Dr. Ogedegbe directs NYU Langone’s Center for Healthful Behavior Change

(CHBC). Launched in 2008, the CHBC has reached out to at-risk residents in dozens of churches, mosques, senior centers, barbershops, beauty salons, and other neighborhood centers around New York City with programs like FAITH. At their heart, nearly all of the center’s projects focus on reducing health disparities by helping minority populations adopt lasting lifestyle changes.

The time-intensive strategy depends upon training church members, barbers, and other leaders to be trusted partners in carrying out the studies. Early signs suggest that the CHBC’s investments could be paying off. If successful, they could form the basis for broader outreach efforts in minority communities across the United States. The CHBC is part of NYU Langone’s recently inaugurated Department of Population Health, dedicated to bringing research advances for improving health into everyday use among people at high risk. “Too often we fail to consider shifting the focus beyond the healthcare delivery system to where people live their daily lives—at home, school, work, and places of worship,” says Marc Gourevitch, MD, MPH, chair of population health.



DOCTORS CALL HYPERTENSION the “silent killer.”

High blood pressure can undermine the body for years before any symptoms

materialize. It slowly hardens arteries, weakens vessels, and reduces blood flow and oxygen through increasingly narrow passageways in the kidneys, eyes, heart, and brain. Then, with a sudden blockage, clot, or burst vessel—and often a heart attack, a stroke, or kidney failure—hypertension makes itself known. Often too late.

Like many primary care physicians, Dr. Ogedegbe has witnessed the devastating consequences of untreated high blood pressure. “I found very early on that by the time we see patients in primary care practices, their disease is far advanced,” he says. “They have chronic kidney disease, or they’ve already had a heart attack or heart failure. Some have had a stroke.”

Although many of the consequences of hypertension can be prevented with medication and more healthful lifestyles, far too few of the necessary interventions ever reach minority communities. Dr. Ogedegbe recalls meetings held by an ecumenical council brought together by the New York City Office of Minority Health in 2005. Faith leaders from around the city talked about the most pressing health issues facing their communities, and hypertension dominated almost every discussion. Again and again, Dr. Ogedegbe heard the frustration of leaders who were desperate for help. “I thought, ‘We’ve got to do some studies that allow us to evaluate alternative approaches to providing care and reducing the burden of hypertension in minority populations,’” he recalls.

In 2009, hypertension killed about 52 out every 100,000 black men in the United States—triple the mortality rate for white men. The stark disparity, tracked by the American Heart Association, was nearly as pronounced among women: high blood pressure claimed 38 out of every 100,000 black women that year, more than 2.5 times the rate for their white counterparts.

To close the gap, Dr. Ogedegbe says, clinicians must overcome the mistrust, poor communication, and other barriers that have long prevented many minority



Dr. Gbenga Ogedegbe and
Dr. Antoinette Schoenthaler

patients from seeking out and staying with lifesaving care. Increasingly, he and colleagues at the CHBC are convinced that the answer lies in an approach that is quickly gaining momentum: bringing more personalized preventive lifestyle strategies directly to community settings.

● ● ●
THE IMMENSE POPULARITY of competitive weight-loss shows like *The Biggest Loser* in predominantly black churches may be one way to boost participation. A city-wide program that

uses positive peer pressure to improve blood pressure in at-risk populations, implemented jointly by the New York City Department of Health and Mental Hygiene and the CHBC, enrolled nearly 200 participants from five churches in

just a few weeks. From that pool, the program identified four churchgoers whose blood pressure was so high that they were at imminent risk of a heart attack or stroke. CHBC researcher Antoinette Schoenthaler, EdD, MA, assistant

Like many primary care physicians, Dr. Ogedegbe has witnessed the devastating consequences of untreated high blood pressure.



From left, lay health advisers Ena Davis, Azerean Cameron, RN, and Princess Ramos, RN, in front of Beth Gospel Tabernacle in Jamaica, Queens.

professor of population health and medicine, says that initial screening was critical in helping the congregants receive immediate medical care.

In 2002, Dr. Schoenthaler joined Dr. Ogedegbe's team to address a crucial question: what prevents so many patients from taking lifesaving drugs? Recent surveys by the U.S. Centers for Disease Control and Prevention have underscored the problem. Although black respondents were more aware of their high blood pressure than whites on average, they were significantly less likely to have it under control.

At a community-based clinic in Long Island City, Dr. Schoenthaler began to chip away at this conundrum through one-on-one motivational interviewing. The counseling technique, adapted from clinical psychology, aims to change unhealthful habits by aligning personal values with behavioral adjustments to achieve specific goals. A man who wants to

spend more time with family, for example, may be more inclined to take his blood pressure medicine if he associates that change with improving his chances of celebrating a milestone anniversary or seeing a relative graduate from high school.

To gain the trust of her study subjects, Dr. Schoenthaler moved closer to the clinic so that she could develop stronger ties with the community. For a new project, she is comparing personalized care to standard care in helping 148 high-risk Latino patients with uncontrolled hypertension stick to their medication regimen. "Rather than just using the evidence base that's published and then developing an intervention, we wanted to hear from the patients themselves: what's getting in the way?" she says.



ACCORDING TO FEEDBACK she has received from focus groups, poor communication with doctors often leads

patients to rely on their own problem-solving skills or on the past experience of friends and family.

"We've learned that heart disease is a very treacherous disease for the patients in our study. They're very scared of it, but they really use symptoms as a guide to determine whether or not to take their medications," Dr. Schoenthaler says. If they feel symptoms, the patients take the drugs. If the symptoms persist, however, many consider the medication insufficient and seek relief through herbal remedies and alternative treatments like garlic and vinegar—a practice that is even more pronounced in African American communities.

Well-intentioned interventions, says Dr. Schoenthaler, can be further complicated in minority communities by a pervasive mistrust of medications and healthcare providers and by fatalistic beliefs about unchangeable health outcomes. The CHBC's researchers have found that

many minority patients never admit to being depressed but instead view it as a normal consequence of life. Likewise, the researchers say, blacks and Latinos are less likely to rank a sleep disorder as an important contributor to poor health, to report having a sleep disorder, or to be evaluated for one. Yet obstructive sleep apnea, which is too often dismissed as little more than noisy snoring, has been strongly linked to hypertension.



MORE THAN A FEW of the community-based advisers in CHBC's projects have become beneficiaries as well. Ena Davis, an administrative assistant at Bethel Gospel Tabernacle, who coordinated her church's involvement in FAITH and serves as one of three leaders, says she's been gratified by the enthusiastic response from her adult pupils. She's also taken her weekly lessons to heart after her doctor told her that her cholesterol was climbing. "What I was reading to them, I would go home and say, 'I need to do this.' Not because I had hypertension, but because I wanted to be healthy," she says. "Not only was I helping someone else, I felt like I was helping myself."

Increasingly, the city's barbers are also feeling empowered. Before Joseph Ravenell, MD, MS, joined NYU Langone in 2008, he and his colleagues in Dallas taught barbers at black-owned barbershops how to measure blood pressure and counsel hypertensive customers to seek medical care. After 10 months, significantly more men in those shops had their high blood pressure under control than in shops where customers received only printed educational materials.

In New York, Dr. Ravenell, assistant professor of population health and medicine, and founder of the Men's Health Initiative at the CHBC, has expanded that barbershop-based outreach to include colon cancer screening. Black men in the United

"Too often we fail to consider shifting the focus beyond the healthcare delivery system to where people live their daily lives—at home, school, work, and places of worship," says Marc Gourevitch, MD, MPH, chair of population health.

Pill Bottles and Birth Dates

FOR HER STUDIES ON MEDICATION ADHERENCE, Dr. Schoenthaler often uses an electronic pill bottle with a microchip embedded in the cap, called an eCap. As a proxy tracking whether and when patients are taking their hypertension drugs, the chip records the time whenever the bottle is opened. A more advanced system measures the bottle's weight from the bottom and can tell whenever a pill has been added or removed. If there's no change in weight, the patient receives a text message reminder to take the medication.

But technology can sometimes create problems of its own, especially among minority populations that are inherently mistrustful of doctors and drugs. Dr. Schoenthaler abandoned an even more sophisticated wireless system after the plug-in electronic hub that captured pill bottle data occasionally short-circuited outlets in patients' homes. Even worse, its blinking lights convinced many participants that their privacy was being invaded. "Our primary measure of adherence was causing patients to drop out," says Dr. Schoenthaler. Her team quickly switched to less intrusive technology.

For a separate study called Keep on Track: Insights for Community Health, staff and congregants at predominantly black churches can access password-protected electronic dashboards that show how enrolled individuals are faring in reducing their blood pressure. The project, a partnership with the New York City Department of Health and Mental Hygiene that has received funding from the federal Agency for Healthcare Research and Quality, has already enlisted hundreds of congregants.

Here, too, however, Dr. Schoenthaler learned that technology can lead to unanticipated privacy concerns. "We learned early on that people don't want to give their birth date—that's one of the registration criteria," Dr. Schoenthaler says. Fortunately, the researchers resolved the issue by asking the electronic dashboard designers to make the birth date optional. —Bryn Nelson

States, he says, have higher colon cancer death rates than any other subgroup, largely due to a lack of timely screening.

During free events at about 90 black-owned barbershops throughout New York City, Dr. Ravenell and a team of researchers, community health workers, and coordinators are recruiting men for separate hypertension and colon cancer screening studies. The two randomized controlled trials, collectively known as the Multi-Intervention Study to Improve CRC Screening and to Enhance Risk Reduction in Black Men, or MISTER B, will test the effectiveness of the center's targeted approach.

"One of the things that's been surprising is just how interested men are in their health," Dr. Ravenell says. "I think we're

"Our reception has been remarkable. We actually have churches and barbershops calling us to see whether or not they can participate in the study," Dr. Ravenell says.

often portrayed as being apathetic about our health. But across the age spectrum that we have encountered, people are very willing to get their blood pressure checked and talk about these issues."

In 2010, Jay's Barbershop in Harlem was one of the first neighborhood shops to sign

on to the initiative. Before NYU Langone began holding free screening events at the shop, owner Jay Green says some of his customers had never had their blood pressure checked.

But men tend to listen to their barber, he says. Starting a conversation about hypertension can then open the door to discussing other healthful behaviors, such as which foods to eat or avoid. Green, who serves on the project's community advisory board, discovered that he too had high blood pressure and stood to benefit from the health initiative. "I stopped putting salt on my food, I drank more water, and now I try to exercise a little bit," he says. "I think it's a great program, and it's helped a lot of dads in the community."

The CHBC is also recruiting men from about 80 predominantly black churches for a related study. "Our reception has been remarkable. We actually have churches and barbershops calling us to see whether they can participate in the study," Dr. Ravenell says. Combined, the two projects have provided free screening and information to more than 6,000 black men and enrolled more than 1,000 in the ongoing research. "That's one of the things we're most proud of—the service aspect of what we're doing, which is really necessary for us to accomplish our research aims," he says.

CHBC researcher Girardin Jean-Louis, PhD, professor of population health and psychiatry, and a behavioral sleep specialist, is adopting similar tactics to study how untreated sleep disorders can

Can Storytelling Save Lives?

LAST YEAR DR. OGEDEGBE RECEIVED A \$12 MILLION GRANT

from the National Institutes of Health to create the Center for Stroke Disparities Solutions in New York City. The center, a collaboration with eight other medical centers and healthcare organizations, is focused on reducing disparities in the city's minority population, with a particular emphasis on preventing recurrent stroke.

One innovative research project is using storytelling in churches as a way to improve stroke literacy rates among both blacks and Latinos. In African American churches, professional storytellers will present narrative tales about stroke patients, emphasizing the telltale symptoms and the importance of calling 911. Afterward, each congregation will hear from an actual stroke survivor.

In Latino churches, the storytelling will take the form of a professionally acted telenovela, a limited-run melodrama similar to a soap opera that is wildly popular on Spanish-language television.

For both projects, researchers will measure the congregants' stroke literacy rates before and after the live presentations. The events will be filmed, and twelve-minute DVDs distributed to church members. Six months later, the researchers will conduct a follow-up survey to determine whether improved stroke literacy—delivered here in story form—can be retained within a community. —*Bryn Nelson*



Jay Green, the owner of a barbershop in Harlem, gets his blood pressure checked by Dr. Joseph Ravenell.

exacerbate health disparities in minority populations. Health educators are helping to steer minority patients toward testing and treatment for sleep apnea and other disorders in one project. Another relies on the expanding network of barbers to recruit peer educators. “If the barber tells me, ‘Hey, this snoring thing you’re talking about, you should go get a sleep test done,’ I’m going to go,” Dr. Jean-Louis says. “Why? Because I trust this guy. He’s helped me in the past.”



ALTHOUGH THE CHBC RESEARCHERS cannot yet say whether stronger ties, deeper trust, and newly acquired knowledge will lead to lasting behavioral changes, the positive feedback from participants has given them reason for optimism.

At Bethel Gospel Tabernacle, the dozen FAITH study participants laugh and joke with each other but readily admit to less-than-healthy meals or minimal exercise. Again and again, they encourage each other to take small steps.

Azerean Cameron, RN, a volunteer adviser at the church and a quality assurance manager at New York Methodist Hospital in Brooklyn, says later that the project has been a welcome extension of the health tips her pastors have long shared from the pulpit. One important lesson is that change does not happen overnight. “You can’t just expect someone who’s been eating the same way for many years to stop and change their ways,” she says. “It’s a process.” Even so, Cameron says her pupils have regularly told her how thankful they are to learn nutrition and exercise facts that

no one had ever shared with them.

Princess Ramos, RN, another volunteer adviser at Bethel and a registered nurse at Kings County Hospital Center in Brooklyn, says she’s been amazed at the congregants’ readiness to incorporate those new lifestyle lessons into their daily regimens. “It just makes me feel good that they’re actually putting them into practice,” she says.

During one particularly well-received outing to a local supermarket, the class studied nutrition labels and picked out more healthy alternatives to their normal options. “I think it opens the eyes of everyone, participants as well as leaders, to see that the choices we make, in fact, can make a change,” Ramos says.

By opening their ears to the need for that change, they may be helping to finally loosen the grip of a furtive killer. ●



the spaces in between

Charles Nicholson has devoted his career to studying the slender channels around brain cells. Long ignored by molecular biologists, his pioneering research is now opening new avenues of inquiry that could lead to better drug delivery and new treatments for neurodegenerative diseases and brain cancer.

BY NICOLE DYER

IT'S A COLD, damp Friday morning in Manhattan, but the dreary winter weather makes it feel more like Monday. Charles Nicholson, PhD, professor of neuroscience and physiology, has just arrived at his office at NYU Langone Medical Center when a bright orb of light suddenly pierces his view. The light slowly spreads across his visual field, obstructing his vision for 15 minutes or so, and then mysteriously disappears. The

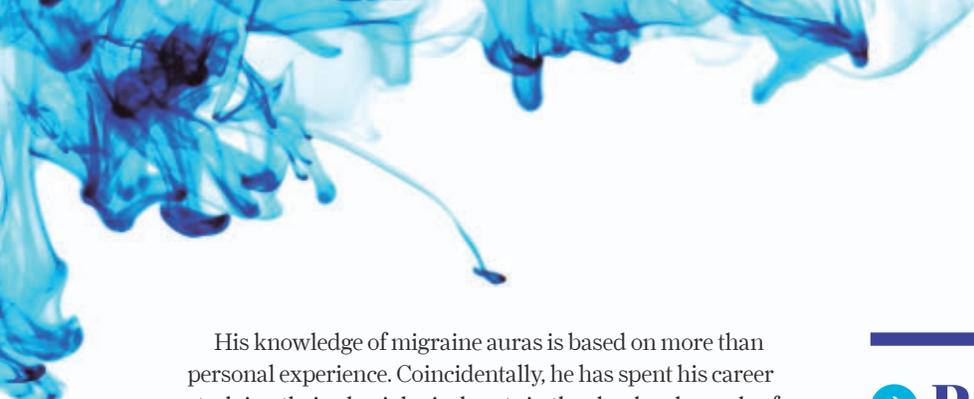
disruption is always unnerving and inconvenient but he never complains; he's one of the lucky ones.

Since the early 1980s, Dr. Nicholson has periodically suffered from a mercifully benign silent migraine, an aura without the classic headache and incapacitating pain that typically ensue. "You recover from it quickly, and it doesn't do you any harm," he says.

PHOTO BY SASHA NIALLA, INK DIFFUSION I STOCKPHOTO



Dr. Charles Nicholson measures the ions that move between brain cells in much the same way that he would measure the diffusion of ink in water.



His knowledge of migraine auras is based on more than personal experience. Coincidentally, he has spent his career studying their physiological roots in the slender channels of fluid that weave between brain cells, called the extracellular space, or ECS. A veritable microenvironment brimming with proteins, polymers, and electrically charged molecules—ions like sodium, calcium, potassium, and chloride—these channels help conduct electric current from one neuron to the next. Migraine auras are thought to arise when something disrupts the diffusion of ions in the channels. As when a circuit breaker is flipped, electricity stops flowing into the cells and the brain can no longer function properly. “We’re almost certain that migraine auras result from ionic imbalances,” he explains.

If ion shifts in the spaces between brain cells can cause visions, what else can they do? Science is only just beginning to understand their clinical significance. Bucking decades-long trends that put neurons at the center of the known universe, Dr. Nicholson has beaten a lonely, persistent path to understand what happens not inside neurons, but rather around them.

With dual degrees in neuroscience and mathematical physics, he has done more over the past four decades to model, measure, and map the ECS than perhaps any other scientist. Along the way he has authored more than 150 peer-reviewed papers and cultivated many of the brightest minds working on the ECS today.

Yet his research remains underappreciated and underestimated, his colleagues say. “The work he does is not understood by most people,” says Rodolfo Llinás, MD, PhD, a longtime mentor of Dr. Nicholson, and the Thomas and Suzanne Murphy Professor of Neuroscience and University Professor in the Department of Neuroscience and Physiology. “It’s mathematically complicated; it’s deep. Yet it’s beginning to flourish because molecular biologists can no longer ignore the extracellular spaces.”

Accumulating evidence—much of it built on techniques pioneered by Dr. Nicholson—suggests the ECS is far more than just cellular padding. As essential to brain function as the cells it supports, the ECS holds vital clues not just to migraine headaches and visual auras, but also to better drug delivery and new treatments for neurodegenerative diseases, brain cancer, and stroke, among other conditions.

Last October a group of researchers at the University of Rochester Medical Center made international headlines with a paper co-authored by Dr. Nicholson and published in *Science* that showed the ECS expands by a remarkable 60 percent during sleep, allowing cerebrospinal fluid to more readily flush away toxins, such as the sticky clumps of protein known as beta-amyloid plaques that accumulate between brain cells during Alzheimer’s disease. The findings offer the first direct evidence for a long-held hypothesis that nightly dips into unconsciousness allow the brain to cleanse itself, an idea that holds broad

➔ Bucking decades—long trends that put neurons at the center of the known universe, Dr. Nicholson has beaten a lonely, persistent path to understand what happens not inside neurons, but rather around them.

implications for the treatment of neurological disorders.

The Rochester scientists spent weeks with Dr. Nicholson learning his trademark technique to measure the volume of the extracellular space. They also relied on his software—now used in labs throughout the world—to analyze the measurements. “We were constantly sending Charles data,” says lead author Maiken Nedergaard, MD, PhD, codirector of the Center for Translational Neuromedicine at University of Rochester Medical Center. “His technique has had a huge impact on our research.”

Eva Syková, MD, PhD, director of the Institute of Experimental Medicine in Prague, has also collaborated closely with Dr. Nicholson. The researchers first met at a conference in the Czech Republic in the early 1980s, when the Czech government, then Communist, forbade Dr. Syková to leave the country. “Charles made several trips to my lab during that time,” she recalls. His software (which she still uses today) has helped her team discover a link between changes in diffusion across the ECS and brain-tumor malignancy. “We can now use diffusion for diagnostic purposes,” she wrote in an e-mail. “For example, the extent of a patient’s operation can be modified according to the degree of malignancy of a tumor, which can be recognized from diffusion parameters.”

It isn’t surprising that Dr. Nicholson’s name commands a special reverence among those familiar with his work. Dr. Llinás calls him the “world authority in his field.” Dr. Nedergaard, who has collaborated with Dr. Nicholson since the late 1980s, considers him “one of the giants of neuroscience.” Robert G. Thorne, PhD, a former postdoctoral fellow of Dr. Nicholson’s, who is now at the University of Wisconsin–Madison School of Pharmacy, marvels at Dr. Nicholson’s enduring influence. “There are a lot of attractive findings published in the best journals that wind up on the scrap heap of history,” Dr. Thorne says. “Charles’s work withstands the test of time.”



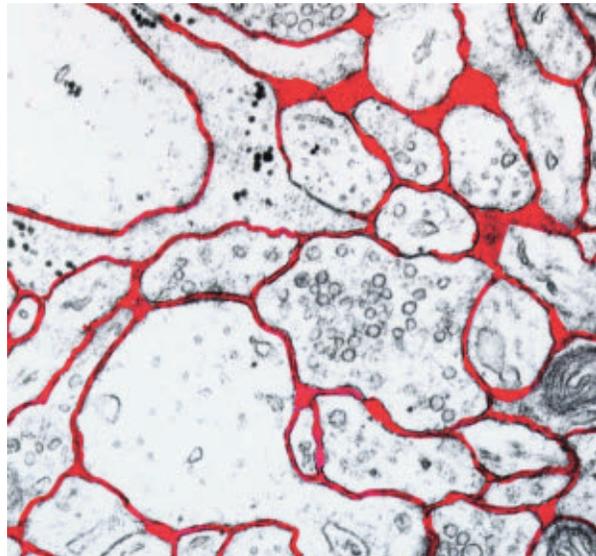
Charles Nicholson's interest in neuroscience began 45 years ago with alligator brains. In 1965 he had just left a post at the Atomic Energy Authority in England, where he had been applying his physics degree to help the government agency understand the energy inside stars. "I had always been torn between physics and biology," Dr. Nicholson says. Growing up in southwestern England, the only child of an accountant and a homemaker, he gravitated toward physics simply because it kept him amused. "I spent a lot of time by myself," he says. He often retreated to the basement to noodle with radio sets and electronics. "I wanted to know how the world worked and I thought physics was probably the best way to do that," he says.

Yet Dr. Nicholson never imagined himself at a university. It was only when he serendipitously encountered a government initiative to encourage more students to pursue higher education that he made his way to college, becoming the first person in his family to do so. There, he fell in love with mathematical physics but received little encouragement. When his physics adviser told him he had no future in academia, he went to work for the government. But the work felt suffocating, so he decided to pursue a PhD in his other area of interest, biology.

Fortuitously, his doctoral adviser happened to work closely with the eminent physiologist Sir John Eccles, who shared the Nobel Prize in physiology in 1963 for his role in elucidating the electric circuitry of nerve cells. Dr. Eccles, then at the American Medical Association's Institute for Biomedical Research in Chicago, needed a graduate student with sharp mathematical skills to help him model the cerebellum, an ancient brain region at the base of the skull just above the brain stem, which coordinates voluntary body movements.

Dr. Nicholson soon found himself in Chicago, thrilled by the opportunity to apply his mathematical mind to the field of biology. However he had no idea what a cerebellum was. If he wanted to model it, he realized he would need to see one, and that's where the alligators come in. Here, too, enters Dr. Llinás, a leading expert on the electric circuitry of the cerebellum who worked for Dr. Eccles. Dr. Llinás wanted to understand the evolutionary origins of the cerebellum and studied alligators because they were among the closest living relatives of the dinosaurs. "We handled them with caution," Dr. Nicholson recalls.

When Dr. Eccles left the AMA Institute in 1968, Dr. Nicholson stayed on to work with Dr. Llinás and finish his PhD in Chicago. "An eight-month visit to the United States turned into 45 years," he says, his British accent still evident. For the two researchers, those early days in Chicago were the beginning of a lifelong friendship.



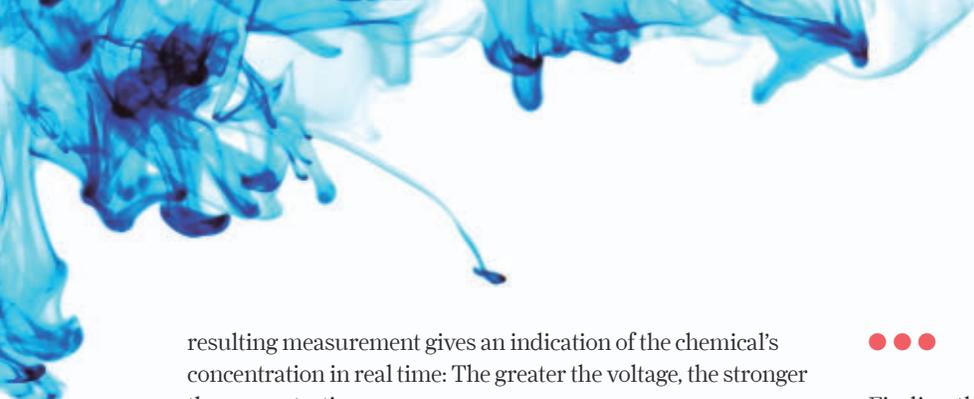
An electron micrograph of a rat brain shows the convoluted network of fluid-filled channels (red) that weave between brain cells. In humans, these extracellular spaces account for 20 percent of the brain by volume.



In 1970, after the AMA Institute closed, Dr. Llinás and Dr. Nicholson, along with about 10 other researchers, moved as a team to the University of Iowa. There, Dr. Nicholson expanded his research to small catfish and took serious interest in the electric currents that flowed between brain cells.

It was also in Iowa that the young researcher began wrestling with a question that would shape the rest of his career: What was carrying the electric current between brain cells? At the time, it was understood that negatively and positively charged ions move in and out of brain cells, creating voltage spikes or "action potentials" that send current zipping down a cell's long, slender projection called an axon. As the current exits the cell, it travels through the extracellular space to complete the electric circuit. But precisely which chemicals were carrying the current and how?

No microscope on earth was yet powerful enough to peer inside the mysterious channels between brain cells, but Dr. Nicholson reasoned he could draw an indirect picture by measuring the molecules that move through them. Happily, he had at his disposal a recent invention called the ion-selective microelectrode, a glass sensor small enough to dip between cells. Still widely used today, the sensor works like a kind of ion trap, using a liquid membrane at its tip to allow passage of a specific ion. As an ion flows through the sensor, a sophisticated voltmeter measures the electric charge. The



resulting measurement gives an indication of the chemical's concentration in real time: The greater the voltage, the stronger the concentration.

"You put a tiny amount of liquid in the tip that binds the ion you're looking at," Dr. Nicholson explains. "The trick is to find the specific liquid membrane and get it to stick in the tip."

It was while using the ion-selective microelectrode in catfish that Dr. Nicholson began to notice that sometimes the voltage in the ECS would just disappear. He suspected the disappearance was connected to a poorly understood phenomenon called spreading depression. Discovered by Brazilian biologist Aristides Leão in 1944 while researching epilepsy in rabbits, spreading depression refers to a wave of electrical disruption in the brain. Like a rolling brownout, the condition knocks out electricity cell by cell, restricting blood flow as it spreads and possibly causing migraine auras like those that occasionally strike Dr. Nicholson.

But what caused the electrical imbalance in the first place? Through meticulous sensor adjustments, Dr. Nicholson and his first graduate student, Richard Kraig, now a professor at the University of Chicago, discovered the source was a massive increase in extracellular potassium ions, along with decreases in sodium and chloride ions. "Other people had suggested some of this, but no one had measured it," Dr. Nicholson says.

The finding offered compelling evidence for a small but growing suspicion that the extracellular space had profound clinical consequences. "People tend to forget that the nervous system is a system and not just a bunch of neurons," Dr. Llinás says.



After six years at the University of Iowa, the British native bid adieu to the heartland and headed east. In 1976 Dr. Llinás and his team, including Dr. Nicholson, moved to NYU School of Medicine, where Dr. Llinás became chair of the neuroscience department.

Settled in New York, Dr. Nicholson began to dig deeper into the mystery of how ions diffuse through extracellular space. When a prominent group in Germany made a splash with one of the first calculations of ionic diffusion through the ECS, Dr. Nicholson suspected a subtle but serious flaw in their technique. For starters, they were using potassium ions to make their measurements. Potassium, Dr. Nicholson realized, disappears into cells nearly as soon as it enters the ECS. "This was confounding their results," he recalls.

So he developed a better probe, using a small molecule called tetramethylammonium, or TMA, that resists cellular uptake, and got a very different answer, the right one as it turned out. "It was a very exciting time," he recalls.



Finding the right molecules to study diffusion in the ECS soon led to another critical insight. In 1981 Dr. Nicholson published a landmark paper in the *Journal of Physiology* (his most frequently cited one today) that showed how a modified version of a classic physics principle, called the diffusion equation, could predict how ions move through the ECS. Dr. Nicholson likens diffusion to a cocktail party: "If you herd people into a corner, they will eventually disperse throughout the room. No one wants to be crowded."

The trick was to mathematically account for two factors. One was the concept of hindrance or tortuosity, which refers to the winding, random path that ions take as they diffuse through extracellular space. Like the person at a cocktail party trying to find the restroom in an area crowded with tables, an ion inevitably bumps into obstructions as it travels, zigzagging randomly from point A to point B. "Tortuosity is one of Charles's most important concepts," says Dr. Llinás. "The distance between two points is rarely a straight line."

The other factor was the size, or volume, of the space through which the ions move. Taking into account these two parameters, tortuosity and volume fraction, Dr. Nicholson developed a mathematical formula that, in conjunction with the new TMA probe applied to anesthetized rodents, was able to do what no microscope could: accurately measure the volume of brain tissue occupied by the ECS in real time. By his calculations, the space accounted for a startling 20 percent of the brain.

The figure was initially met with skepticism. In the 1960s, esteemed Harvard Medical School scientist Sanford L. Palay, pioneer of the electron microscope and former chief of neurocytology at the National Institutes of Health, used his high-powered scope to arrive at an estimate of just 5 percent.

While Dr. Palay's estimate was widely accepted, it gnawed at Dr. Nicholson. He suspected something was off. As with the German research, that something turned out to be a technical oversight. In order to see the spaces between brain cells beneath an electron microscope, Dr. Palay had to first euthanize the rodents he was studying and then fix the brain samples in formaldehyde. But killing the animal cut off the oxygenated blood flow to the brain, causing cells to swell, which in turn reduced the volume of the ECS. And the formaldehyde procedure dehydrated the brain samples, further shrinking the ECS.

Dr. Palay defended his technique for years. "He finally admitted to me on a bus at a conference that my estimate was probably right," Dr. Nicholson says. The 20 percent figure still holds today, although the work of the University of Rochester team in slumbering rodents adds a new twist.

➔ No microscope on earth was yet powerful enough to peer inside the mysterious channels between brain cells, but Dr. Nicholson reasoned he could draw an indirect picture by measuring the molecules that move through them.



By the late 1990s, Dr. Nicholson had turned his attention to the diffusion of larger molecules like albumin, dextran, growth factors, and other proteins in the ECS. It was a particularly important line of inquiry for drug delivery. Even if an oversize molecule could penetrate the blood-brain barrier, the selective membrane that keeps pathogens in the blood from contaminating the brain, it would still need to squeeze through the extracellular channels to reach its target. A chunky medication aimed at brain tumors would never make it.

No one had yet figured out a way to track and measure so-called macromolecules, but Dr. Nicholson and his long-time colleague Lian Tao, PhD, soon came up with a solution. In 1993 they developed a breakthrough technique called integrative optical imaging. It took advantage of newly invented fluorescent tags that could make certain macromolecules glow under a microscope. The researchers loaded the tagged molecules into a miniaturized dropper and used a short pulse of nitrogen to disperse them into the ECS. Then they used a fluorescence-detecting microscope and digital camera to photograph the molecules as they spread out like a cloud of ink in water. Dr. Nicholson and Dr. Tao wrote software to quantify the cloud dispersion.

But the technique had its limits. For one, it relied on brain slices bathed in a physiological solution; these were living tissue as opposed to the fixed slices used by Dr. Palay, and so the ECS was preserved, but the blood flow was absent. Plus, the fluorescent tags were only available for certain size molecules.

In 2002 Dr. Thorne, a postdoctoral fellow in Dr. Nicholson's lab at the time, suggested quantum dots, man-made nanoscopic crystals that glow under ultraviolet light. A new door opened.

Unlike conventional fluorescent tags, quantum dots come in a variety of sizes, allowing the researchers to explore how big a molecule can be before it stops moving through the ECS altogether. Another advantage is that the dots could be coated with an electrically neutral chemical, which would keep them from reacting with other molecules in the ECS. "It's a beautiful tool," Dr. Thorne says.

Moreover, Dr. Thorne devised a way to view the dispersal of the dots in living, anesthetized rats, using what's called a cranial window, which is essentially a tiny sunroof implanted in the skull that affords a view into the living brain. "It's becoming increasingly clear that the physiological state of the animal has a big effect on the ECS," he says.

Using this modified form of integrative optical imaging, along with quantum dots about 35 nanometers in diameter, the researchers discovered the width of the extracellular channels to be about 40 to 60 nanometers, one seventeenth the diameter of the average human hair, and twice as wide as the previous estimate. "We overturned decades of dogma that said the ECS was about 20 nanometers wide," Dr. Thorne says. After all, how could a 35-nanometer-wide dot squeeze through a 20-nanometer-wide channel? Their resulting paper, published in *The Proceedings of the National Academy of Sciences* in 2006, has become a citation classic.



One could measure the success of a scientist by tallying up the number of papers published, honors bestowed, grants earned. At 72, Dr. Nicholson has plenty of all of those. But he also has something even more telling: the trust, respect, and admiration of a large circle of accomplished collaborators who credit part of their own success to his techniques, software, and intellectual support. Two members of the NYU School of Medicine faculty—Mitchell Chesler, MD, PhD, and Margaret Rice, PhD, both professors of neurosurgery and physiology and neuroscience—trained with Dr. Nicholson. "We all benefit from Charles's techniques," Dr. Thorne says.

But it's not just about his technical savvy. Dr. Nicholson's generosity and humility have also made a lasting impression on his colleagues. Dr. Nedergaard, lead author of the recent *Science* paper, remembers calling Dr. Nicholson a few years ago to tell him that her group had found evidence of convective flow in the extracellular space during sleep. Unlike diffusion, flowing particles move like a river, directed by some external force. "We had never seen that in the extracellular space before," Dr. Nicholson recalls. Although the idea surprised him and challenged existing notions of the ECS, he dove in to help. "He was really excited and supportive," Dr. Nedergaard says. "It's never about him, it's about the research." ●



Dr. J. R. Rizzo shows how CumbaCane, a low-tech successor to the old-school cane, could help avoid obstacles or changes in terrain without swinging.

Stick SHIFT

DRIVEN BY HIS OWN BATTLE WITH A VISION-DESTROYING DISEASE, DR. JOHN-ROSS RIZZO IS DEVISING BETTER ALTERNATIVES TO THE WHITE CANE FOR THE BLIND.

BY KENNETH MILLER • PHOTOGRAPHS BY JOHN ABBOTT

FOR THOUSANDS OF YEARS, blind people have used sticks, staffs, or canes to navigate the pedestrian world. Such devices have changed little over the millennia, except to become more uniform. In 1921, as motor traffic became a growing peril, a Briton named James Biggs, who'd lost his sight in an accident, painted his cane white to alert drivers; by the 1940s, that color had been adopted almost everywhere. During World War II, a veterans rehabilitation specialist in Pennsylvania, Richard Hoover, developed a new technique using a long white cane to probe the path ahead; by sweeping it from side to side, the user could better detect obstacles and drop-offs. The "Hoover method" became the universal standard and remains so to this day.

Yet even lightweight modern canes are relatively primitive instruments. They can miss up to 50 percent of tripping hazards, such as potholes, curbs, or uneven sidewalks, and the constant swinging can cause damage to the back, shoulder, elbow, and wrist. For John-Ross Rizzo, MD—clinical instructor and associate research scientist at

NYU Langone Medical Center's Rusk Rehabilitation—those flaws are a source of intense and very personal, frustration.

The 32-year-old physician suffers from an incurable disease that is gradually destroying his eyesight. At present, he's hobbled by severe tunnel vision, cataracts, and difficulty adjusting to changes in lighting; stepping from sunshine into shadow or vice versa can leave him entirely sightless for minutes at a time. You might not guess any of this watching him stride around the hallways of the Ambulatory Care Center at NYU Langone Medical Center. Dr. Rizzo, who prefers to be addressed as J.R., is friendly and voluble, and talks enthusiastically about the topics that obsess him. He has a black belt in karate, and in familiar surroundings he moves with an athlete's confidence. On city streets, however, he proceeds slowly—and despite his caution, he stumbles at least once a day. Eventually, he knows, he'll need a white cane of his own.

Before that happens, he's determined to create a better alternative. "My mission is to make a commercially viable product and get it into users' hands," he says. "I'm not going to rest until that's done."

THE FIRST SIGNS of Dr. Rizzo's illness emerged in early childhood. Growing up in northern New Jersey, he loved to climb trees, practice martial arts, and explore his suburban neighborhood. But after sunset, while the other kids kept playing, he would retreat to the sidelines or run home. In a dimly lit movie theater, he'd cling to his mother as they headed for their seats. By the time he reached his teens, his parents had begun to wonder why their son was so uncomfortable with darkness. A peripheral-vision test provided a hint: the boy scored so poorly that his pediatrician thought he must have fallen asleep. "I said, 'The test was boring, but I swear I was awake,'" Dr. Rizzo recalls. "That's when we knew something was seriously wrong."

For the next year, he bounced from one specialist to another, undergoing endless diagnostic procedures. The verdict arrived when he was 15: choroideremia, a rare inherited disorder that destroys capillaries in the choroid (the layer just beneath the sclera, or white of the eye) and in light-sensitive tissue in the retina. Carried on the X chromosome, the disease strikes an estimated 1 out of 50,000 to 100,000 people—almost exclusively males. The first symptom is usually impaired night vision; over the years, a patient's visual field narrows and his visual acuity diminishes until by his 50s or 60s, he's completely blind.

The diagnosis plunged Rizzo into a deep depression. Within a few months, however, he'd transformed his misfortune into a driving force. He began devouring ophthalmology textbooks and interviewing eye doctors to learn more about choroideremia and related disorders. Soon, he decided to become an ophthalmologist himself. Although his worsening vision made reading a challenge, he graduated from NYU (magna cum laude) with a BS in neuroscience and earned his MD (with honors) at New York Medical College. When it came time to choose a specialty, however, he learned that his ailment put his intended profession, which requires good eyesight, out of reach. After another period of mourning, he settled on a field that addresses a broader range of disabilities: physical medicine and rehabilitation, also known as physiatry.

Dr. Rizzo began his residency at Rusk Rehabilitation in 2009. While conducting research in areas ranging from exercise-induced kidney damage to how the brain plans movement, he treated patients as a physiatrist at several hospitals affiliated with Rusk, including the New York Harbor Veterans Affairs Medical Center. "I was seeing vets coming back from Iraq and Afghanistan with all kinds of injuries," he recalls. "If they lost a limb, the government would pay for a \$50,000 robotic prosthesis. But if they lost their sight, we gave them a stick. I said, 'This is insane.' The dearth of mobility devices for people with visual handicaps

“THE DEARTH OF MOBILITY DEVICES FOR PEOPLE WITH VISUAL HANDICAPS WAS VERY UPSETTING TO ME.”

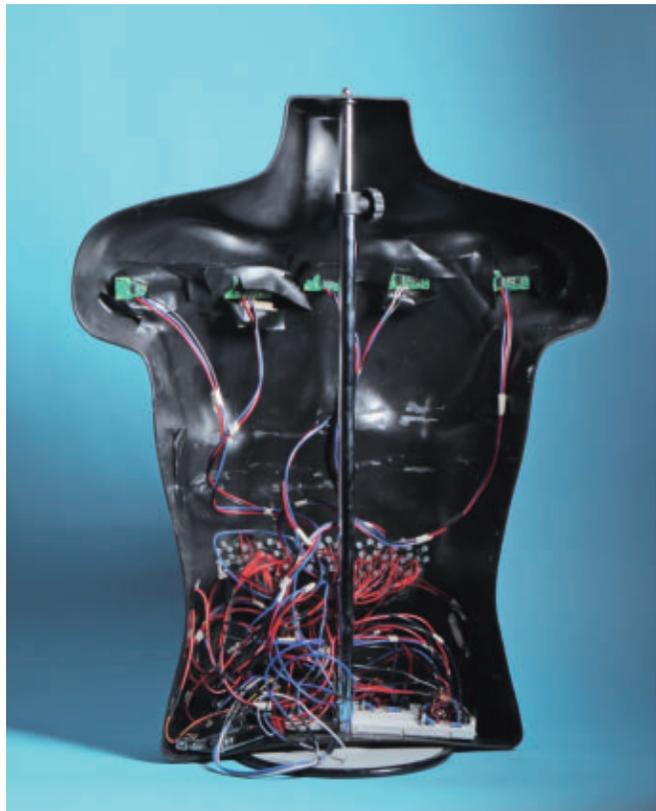
was very upsetting to me.” In his spare time, he began sketching ideas for gadgets that could fill the gap.

By 2012, Dr. Rizzo had been appointed chief resident; he joined the faculty later that year. In addition to his teaching duties, he became codirector (with Tamara Rusk, MD) of Rusk's new Residency Research Program and founding director of the Visuomotor Integration Lab, which studies how brain injuries affect hand-eye coordination. He also started a company called Tactile Navigation Tools to turn his sketches into products that could make the traditional cane obsolete.



OTHER INVENTORS have pursued that goal for decades, with little success. Since the 1960s, a small number of canes or handheld obstacle detectors using sonar or lasers have hit the market, but none took off commercially; they were too bulky and difficult to operate to justify their high cost. Only recently have advances in microelectronics and computer technology made a truly user-friendly sensor-equipped cane a practical possibility. Few such gadgets, however, have reached the manufacturing stage, and they remain dauntingly expensive.

Dr. Rizzo and his team—including business partner Todd Hudson, PhD, a computational neuroscientist at the NYU Center for Neural Science—are developing both high- and low-tech successors to the old-school cane. Their most basic device is the CumbaCane, which has two legs angling out from the lower portion of the shaft, each with a small wheel mounted on springs. (The extensions are collapsible, like an umbrella.) The wheels roll along the ground, a body-width apart, allowing the user to detect obstacles or changes in terrain without the need for swinging. At a planned price of less than \$100, this product would be affordable to a large proportion of the estimated 4 million Americans—and 150 million others worldwide—who are visually disabled. "It



doesn't have to be plugged into an outlet," Dr. Rizzo notes, "so it can be used anywhere on the planet."

The digital version of the cane, the Deyenamic, was inspired, in part, by Dr. Rizzo's studies of the natural world. "Animals with poor vision have some amazing navigation methods," he says. "Paddlefish can sense electric fields; snakes use thermal imaging; bats echolocation." He also took a cue from auto-industry research into driverless cars, which use combined input from a variety of sensors to avoid collisions. The Deyenamic will be fitted with technologies such as LiDAR (light detection and ranging) laser, infrared and ultrasound, each of which functions best under a different environmental condition and will supplement the others. Dr. Rizzo's company is also developing a lightweight vest, the Eyeronman, containing similar sensors. These devices, used together or separately, will be connected wirelessly to an undershirt made of e-textiles, fabrics that can seamlessly incorporate microprocessors and other components. Data transmitted from the cane or vest will trigger actuators in the shirt, creating vibrations whose position and intensity will correspond to the direction and proximity of obstacles. "It's an intuitive platform," says Dr. Rizzo. "If the object is on your left, you feel a tickling on your left side. If it's taller, you feel it higher up. If it's shorter, you feel it lower."

This system is designed to provide more precise and detailed information than existing electronic canes, which

A lightweight vest would incorporate various sensors and other components seen in the model above. Drs. Rizzo and Hudson named their prototypes Edgar and Ethyl.

typically use just one kind of sensor and transmit vibrations to the handle. But transforming the vision into reality will be a complex process. The CumbaCane is in its third prototype; Deyenamic and Eyeronman are in earlier stages of gestation. Dr. Rizzo is busy filing patents, raising capital, and refining his designs. He expects to bring the devices to market within the next two years.

That would be an ambitious aim for any inventor-entrepreneur, let alone one with a severe disability. But those who know Dr. Rizzo have little doubt that he'll make his deadline. "I constantly forget he's visually impaired," says Dr. Hudson. "Nothing gets him down. Whenever we have a setback, he drives right through it. It's that way with everything in his life. He just sets his mind on the goal and keeps on going."

For Dr. Rizzo, there's no time to waste. "I'm trying to make people with a specific weakness as strong as possible," he says. "There's nothing else I'd rather work on. This is my *raison d'être*." ●

Face to Face

The new chair of the Department of Plastic Surgery discusses the present and future of face transplantation.

BY GARY GOLDENBERG



Dr. Eduardo D. Rodriguez

IN 1997 Richard Norris of Hillsville, Virginia, suffered an accidental shotgun wound that nearly obliterated his face. Despite multiple reconstructive surgeries, he remained terribly disfigured and had trouble talking and breathing. His life took another dramatic turn in 2012, when a large team of medical experts rebuilt his eye sockets, upper jaw, teeth, and tongue, plus the nerves, muscles, and skin of his face, using bone and soft tissue from a 21-year-old man who had died in a car accident. Today, Mr. Norris, now 39, can venture outside without drawing stares and ridicule.

More than two dozen people around the world had undergone a face transplant before this 36-hour operation at the R Adams Cowley Shock Trauma Center in Baltimore, but none was as complex as Mr. Norris's.

The surgeon in charge of this groundbreaking procedure was Eduardo D. Rodriguez, MD, DDS, then affiliated with the University of Maryland Medical Center. Dr. Rodriguez brought to the operating table a rare combination of skills in oral and maxillofacial surgery, plastic and reconstructive surgery, and reconstructive microsurgery.

He recently joined NYU School of Medicine as chair of the Department of Plastic Surgery, director of the Institute of Reconstructive Plastic Surgery, and the Helen L. Kimmel Professor of Reconstructive Plastic Surgery.

What brings you to NYU School of Medicine?

I thought I would stay at the University of Maryland and Johns Hopkins Hospitals for a long time, but then one of the giants of craniofacial surgery, Joseph McCarthy, decided to step down as chairman of plastic surgery at NYU. The opportunity to take the helm of this internationally recognized center of excellence was the ultimate dream.

What is your vision for the department?

One goal is to push forward with surgical innovation in tissue engineering and tissue transplantation, including limb transplants as well as face transplants. I would also like to explore the potential role for transplants in the pediatric population. Ultimately, it comes down to limiting the morbidity associated with long-term immune suppression. One of the great benefits of being at NYU is that we have the resources to address every aspect of this issue, from the basic science questions to the ethical questions.

How close are you to doing face transplants here at NYU Langone?

We are already organizing the team. In fact, we just performed our first transplant simulation rehearsal [in January 2014], using cadavers. It far exceeded my expectations. We can't begin evaluating any patients until we receive formal IRB [Institutional Review Board] approval, however, there are plenty of patients who would like to be considered as candidates.

You assembled a team of 150 medical specialists for Mr. Norris's case. Are you recruiting staff from outside the institution for the upcoming surgery?

Most of the key elements already exist here: the surgeons, the anesthesiologists, the radiologists, the psychiatrists, the nurses, the speech pathologists, the nutritionists, the social workers, the blood-typing specialists, just to mention a few.

Could you tell us a little about your background?

I was born and raised in Miami. Both of my parents were Cuban émigrés. An interesting bit of family history is that my father fled Cuba at the beginning of the Castro revolution. He then enlisted in the Bay of Pigs invasion, during which he was wounded and held prisoner until he was eventually released following a negotiation.

You hold a degree from NYU College of Dentistry as well as a degree in medicine from the Medical College of Virginia. What influenced your initial career path?

I had good role models: an uncle who was a physician and a close friend's father who was a dentist. I was torn between the two, but ultimately, I decided that I liked how dentists had more control over their lifestyle.

Were you studious from an early age?

Educationally, I was a bit of a late bloomer. I always wanted to learn more, but it wasn't until my fellowship in oral and maxillofacial surgery that I really became committed to my studies and my future.

“Advances in immunosuppression and surgical techniques made face transplantation possible. We also had a great clinical need, as all these injured soldiers were coming back from Iraq and Afghanistan.”

What turned you around?

Toward the end of my fellowship, when I was applying to medical school, there were some individuals who felt I didn't have the intellectual capacity or the work ethic to go to the next level. That was a good awakening. More than wanting to prove them wrong, I wanted to prove to myself that I could do it.

Why did you decide to study medicine?

I enjoyed oral surgery, but I wanted to be able to do even more and did not want to feel limited. I can point to a particular incident: a patient who had breathing troubles after a surgical procedure. He needed a tracheostomy, but I wasn't trained to do one. The surgical airway team got there in time, but it was touch and go. I felt helpless and I didn't want to be in that situation ever again.

How did you become involved in face transplantation?

About 10 years ago, I came to the realization that there was only so much we could do for patients with what we call central facial injury. We could improve their deformities, but we could never re-create certain parts of the face. Around that time, the chair of surgery at the University of Maryland asked me to participate in an Office of Naval Research grant looking at the possibility of facial transplantation as a treatment for disfigured soldiers.

How did your peers receive this initiative?

There were many naysayers. They reasoned that these patients are medically stable and the potential for death is high, so why risk their lives.

How did you respond?

Yes, these people are stable, but they are extremely disfigured and cannot lead normal lives. Advances in immunosuppression and surgical techniques made face transplantation possible. We also had a great clinical need, as all these injured soldiers were coming back from Iraq and Afghanistan.

What criteria do you use for selecting potential face transplant candidates?

First, they have to have a deformity that cannot be treated by conventional measures. Second, we look at their psychologic state and their level of commitment. Compliance with treatment—especially with taking immunosuppressant medications—is absolutely key.

Are there limits to the age difference between donor and recipient? What about gender?

I would not consider transplanting a 60-year-old's face onto a 20-year-old. But there are no specific limits. As for gender, it's not unreasonable to transplant a female face onto a male. The cosmetic result would probably be acceptable, and it would broaden the potential donor pool. But I don't know if it would work the other way, male to female; just because of facial hair, I would not support it.

How do you prepare a donor's family for the possibility of seeing their loved one's face on another person?

In the Richard Norris case, the family was counseled beforehand through the organ donor system that this could happen—especially since we anticipated substantial media coverage. But I don't know if you can fully prepare anyone for this, especially a parent who has lost a child.

(Continued on page 27)

JEF BOEKE APPOINTED DIRECTOR OF INSTITUTE FOR SYSTEMS GENETICS

RENOWNED GENETICIST JEF BOEKE, PhD, DSc, has been appointed director of the newly established Institute for Systems Genetics at NYU Langone Medical Center. Dr. Boeke, a member of the National Academy of Sciences, joins NYU Langone from the Johns Hopkins University School of Medicine, where he served as professor in the Department of Molecular Biology and Genetics and the Department of Oncology. He also founded the High Throughput Biology Center, an interdisciplinary research facility that leverages automation to rapidly test millions of chemical, genetic, and pharmaceutical compounds.

At NYU Langone Dr. Boeke will oversee a new hub for modern genetics research. "It's the only institute in the world with the words 'systems genetics' in the title," Dr. Boeke says. Spurred by the advent of automated DNA sequencing in the 1990's, systems genetics puts a high-tech twist on genome analysis, tapping data-processing techniques to map the vast networks that connect genes, proteins, and other molecules.

Dr. Boeke's team will use the latest tools and insights from human genetics, systems biology, computational science, and biological engineering. "It's a major initiative to bring together this level of expertise under one roof," says Dr. Boeke, who aims to recruit 12 to 15 faculty members within the next few years. The link for the Institute for Systems Genetics is: <http://research.med.nyu.edu/systemsgenetics>.

Dr. Boeke is a pioneer in the emerging field of synthetic biology, designing microorganisms to produce novel medicines, raw materials for food, and biofuels. His research focuses on the genome of *Saccharomyces cerevisiae*, commonly known as brewer's yeast.

In late March, Dr. Boeke and a team of international researchers announced the synthesis of the first fully functional yeast chromosome. The achievement, published in *Science*, affords researchers an unprecedented opportunity to explore genetic interactions and functions central to biology and human health.

"It's the most extensively altered



chromosome ever built," says Dr. Boeke, who will expand on this work at NYU Langone.

"We have shown that yeast cells carrying this synthetic chromosome are remarkably normal. They behave almost identically to wild yeast cells. Only they now possess new capabilities and can do things that wild yeast cannot."

Dr. Boeke is a native of New Jersey. He graduated from Bowdoin College in Maine in 1976, earned his PhD in molecular biology at Rockefeller University in 1982, and was a postdoctoral fellow in the laboratory of celebrated biologist Gerald R. Fink at the Whitehead Institute/Massachusetts Institute of Technology.

CHAIR OF ANESTHESIOLOGY

ANDREW D. ROSENBERG, MD, professor of anesthesiology and orthopaedic surgery, has been appointed the Dorothy Reaves Spatz Chair of the Department of Anesthesiology. Previously, Dr. Rosenberg had served as chief of anesthesiology at the Hospital for Joint Diseases (HJD) and executive vice chair of the Department of Anesthesiology.

A graduate of Cornell University, Dr. Rosenberg earned his medical degree

as an Alpha Omega Alpha graduate of the State University of New York Upstate Medical Center. He trained at NYU Langone as a resident, chief resident, and cardiac anesthesiology fellow before joining our faculty as a cardiac anesthesiology attending physician in 1984. He served as chair of the Department of Anesthesiology at HJD from 2000 to 2006, when HJD merged with NYU Langone.

Dr. Rosenberg is a leader in orthopaedic anesthesia and is an

innovative educator, developing simulators for teaching ultrasound-guided regional anesthesia. His research focuses on regional anesthesia, outcomes in orthopaedic anesthesia, neurotoxicity of local anesthetics and antiseptics, and infection control.

Dr. Rosenberg succeeds Thomas J.J. Blanck, MD, PhD, who stepped down as the Dorothy Reaves Spatz, Chair of the Department of Anesthesiology last June to devote himself to research at our institution.

NEW CELL BIOLOGY CHAIR

RUTH LEHMANN, PHD, the Laura and Isaac Perlmutter Professor of Cell Biology and director of the Skirball Institute of Biomolecular Medicine and the Helen L. and Martin S. Kimmel Center for Stem Cell Biology, has been named chair of the Department of Cell Biology.

Dr. Lehmann joined the faculty of the School of Medicine in 1996 and has received numerous prestigious honors throughout her career, including election to the American Academy of Arts and Sciences, the National Academy of Sciences, and the European Molecular Biology Organization. She has also been a Howard Hughes Medical Institute investigator. In 2011, she received the Conklin Medal of the Society for Developmental Biology, which recognizes extraordinary research and mentoring.

Dr. Lehmann studies germ cells, the only naturally occurring immortal cells in our body, as they differentiate into sperm or egg and can give rise to a new organism. She is interested in the signals that specify and guide migrating germ

cells to the developing ovary and testis and the mechanisms that control the quality of germ cells as they mature into egg and sperm to assure the health of the next generation.

Dr. Lehmann succeeds David Sabatini, MD, PhD, who joined NYU School of Medicine in 1972 to become chair of the Department of Cell Biology, and in 1975 was named the Frederick L. Ehrman Professor of Cell Biology. He stepped down after nearly 40 years of illustrious leadership and scientific achievements in the fields of organelle biogenesis and intracellular protein traffic.

EDWARD A. FISHER AWARDED

EDWARD A. FISHER, MD, PHD, MPH, the Leon H. Charney Professor of Cardiovascular Medicine, who directs both the Marc and Ruti Bell Program in Vascular Biology and the Center for the Prevention of Cardiovascular Disease, was honored last year as the George Lyman Duff Memorial lecturer, among the most longstanding and prestigious of the American Heart Association awards.

In March Dr. Fisher delivered The 24th Annual Dennis Memorial Lecture in Cardiology at the Baylor College of Medicine/Texas Heart Institute and the annual Frank H. Tyler, MD, Honorary Endowed Lecture in Medicine, University of Utah School of Medicine.

Dr. Fisher, who is also professor of pediatrics and cell biology, and his colleagues have developed models of atherosclerosis regression that have revitalized this area. They have adapted HDL particles to carry imaging agents and therapeutics into atherosclerotic plaques.

DR. LLINÁS HONORED

RODOLFO LLINÁS, MD, PHD, the Thomas and Suzanne Murphy Professor of Neuroscience, received the Ragnar Granit Lectureship in Neuroscience awarded by the Nobel Forum, Karolinska Institutet in December.

Dr. Llinás is a world-renowned neuroscientist who pioneered magnetoencephalography, a highly sensitive, noninvasive technology for measuring the brain's electrical activity.

*Continued from page 25
(Faculty Conversation with Dr. Rodriguez)*

The Norris case was a great success, but is there anything you would do differently next time?

The recipient's side of the operation took longer than we had anticipated. Extensive scarring made it difficult to identify anatomical structures. We delayed the final separation of the donor's face as long as possible. But there were patients waiting for the donor's other organs, so we had to separate the donor's face and place it in a cold preservative solution. No one really knows how long this can be done without affecting the long-term function of the tissue. Next time, we'd probably begin the recipient's operation a bit earlier.

Were there any surprises?

Perhaps the biggest surprise was how

much sensation Richard now has throughout his face. Because of the scarring, we weren't able to connect any of the sensory nerves. The donor nerves were laid in proximity to the recipient nerves, and somehow they connected. We're looking into how that happened.

How committed was Mr. Norris to this operation?

Richard was so courageous. Even at the last minute, we gave him every opportunity to abort the operation. He wanted to do this. He always had—and still has—this commitment to helping others by pushing this work forward.

Now that you've relocated, are you still in touch with Mr. Norris?

We still have a very close relationship. He

comes up to NYU Langone for follow-up care. He can receive all of the services he needs in our comprehensive program, treatments like speech and physical therapy, dental care, and periodic blood work and biopsies to test for rejection.

What do you say to people who say that face transplants are too costly?

They are costly. But you have to keep in mind that without a transplant, these patients would still undergo several major reconstructive surgeries—at no small expense. And they will never be quite right. In that light, a single corrective procedure—a face transplant—isn't much more costly overall. Not only that, it could dramatically reduce the patient's physical, emotional, and psychological stress, which is no small benefit. ●

Stopping the Clock on Saturday Morning

Reviving one of NYU School of Medicine's most beloved teaching traditions, Dr. Steven Abramson, chair of the Department of Medicine, rounds with residents during off-peak hours.

BY GARY GOLDENBERG



FORTY YEARS AGO, Dr. Steven Abramson, freshly graduated from Harvard Medical School, arrived at NYU School of Medicine to begin his internship in medicine. He was delighted to be at NYU Langone Medical Center, one of the nation's top-ranked academic medical centers, and looking forward to his clinical training at Bellevue Hospital Center, NYU's major teaching affiliate and America's oldest public hospital.

Like many residents, the young man was drawn to the extraordinarily diverse patient population and inspired by the

leadership of Saul Farber, MD, the School's longtime dean and chair of the Department of Medicine, who was hailed as one of the most respected physicians in the country and a master educator. A compassionate physician and tireless teacher, Dr. Farber personally led hospital rounds on Saturday mornings, taking advantage of these quiet hours to delve deeper into the art and science of bedside care.

These rounds, which included medical students as well as residents, became legendary for the pearls of wisdom Dr. Farber imparted. The focus was always on

▼
Saturday morning rounds with Dr. Abramson (right), and Dr. Brandon Oberweis, chief resident, and other residents.

the patients and the deep responsibility of the physician as a professional entrusted with their care. These peripatetic off-peak rounds eventually passed into history, but not from memory. When Dr. Abramson, who as chief resident spent many a Saturday morning at Dr. Farber's side, was appointed chair of the Department of Medicine in March 2013, one of his first actions was to revive the tradition

of Saturday morning rounds, this time to include NYU Langone's Tisch Hospital and the Manhattan VA Medical Center, NYU's other primary teaching hospitals.

"One reason we brought back Saturday morning rounds was to slow down the clock at the bedside for trainees, if only for a few hours," Dr. Abramson says. "Because of the changes in hospital care, including the focus on managing acute problems with comorbidities in the outpatient setting, inpatient care gets telescoped. Too often, the clinical questions that get addressed become what, how, where: What is the patient's diagnosis requiring admission? How do we treat it? Where does the patient go next? But in some sense we focus less on the important why.

"For example, if the admitting diagnosis is deep venous thrombosis, why is there a thrombosis, why do the platelets clot excessively in this patient? Asking the why question not only leads to a deeper understanding of the patient's illness that may alter therapy, but also reminds us of how little we often understand about disease mechanisms and how much research remains to be done," he adds.

And the why can make all the difference. "On a recent Saturday morning at Bellevue," Dr. Abramson recalls, "we visited a newly admitted patient, Mr. K.—hungover, disheveled, uncommunicative, relegated to the status of a homeless alcoholic—admitted for head trauma post-fall, and now awaiting placement and being observed for the inevitable delirium tremens. But as we started talking to him, we noticed his tattoo of an Army insignia. When I asked him about it, his face lit up. It turned out he had been a paratrooper in Vietnam and later fell on hard times. Digging deeper, the team began to see the patient not as Mr. K, a street person, but as an individual with a life history, a veteran with perhaps an undiagnosed case of post-traumatic stress disorder, a possible explanation for his current condition."

If the economics of healthcare have put a crimp on residency training, so too

have safety considerations. A decade ago, New York State passed a law limiting a resident's workweek to 80 hours, reasoning that fatigued doctors-in-training—who perform the lion's share of inpatient medical care—put patients in jeopardy.

"When I was a resident, we worked through the night every third day, in addition to our daily shifts," recalls Dr. Abramson. "It was exhausting, but it did have its advantages both for learning and for the continuity of patient care. At night, we could set aside 20 to 30 minutes here and there to talk about this X-ray or that EKG. Those quiet evening moments for learning are uncommon in the new shift-driven restrictions on ward duty, but I think Saturday rounds is a step in the right direction."

Dr. Abramson is also concerned that more and more hospital rounds have moved from the bedside to the conference room, a nationwide trend. It can be more efficient to discuss cases in a conference room. But without that hands-on perspective, we're losing something. The focus becomes discussion, rather than the patient. We need to combine both."

"Over the years," Dr. Abramson continues, "we've created a host of courses and programs in medical humanities and bioethics, which are vital in preparing physicians for practice. But when you're a resident working nonstop for 8 or 10 hours, you can lose sight of all that. We need to reinforce these lessons at the bedside at every opportunity."

As senior vice president and vice dean for education, faculty and academic affairs, Dr. Abramson, in addition to



being a departmental chair, is steeped in administrative responsibilities. Saturday morning rounds, he says, keep him in touch with the clinical side of medicine. "Rounding with residents gives me insights into their daily lives," he says. "It also makes a clear statement that the chief of medicine cares enough about what's happening on the wards to come in on the weekend."

Brandon Oberweis, MD, senior chief resident in internal medicine, appreciates the effort. "Having the chair of medicine round with residents on Saturday morning really emphasizes the approachability of the senior faculty," he says. "Also, it's tremendously helpful for us to see the way a highly experienced physician like Dr. Abramson interviews a new patient and generates a differential diagnosis."

After four decades on the front lines, all of it spent at NYU Langone, Dr. Abramson has his own stories to tell, his own wisdom to share. And now, like his onetime mentor, he has a weekly opportunity to pass both on. ●

Who Are You If You Can't Emote?

Solving a case of facial paralysis by tapping into a nerve from the tongue.

BY AMY ENGELER

FOR ANTON DOLCE, the dull headaches and light-headed moments were all too easy to dismiss. He even came to appreciate the ringing that developed in his right ear after he turned 60—the rhythmic whoosh sounded like the crashing waves of his childhood on the Long Island shore. So it was with shock when Dolce, 64, an architect and mechanical engineer, learned that these mild symptoms came not from age and noisy construction sites but from a golf ball-size brain tumor lodged behind his right ear, growing dangerously close to his brain stem. Like about 2,000 other people in the United States that year, Dolce was diagnosed with an acoustic neuroma, a slow-growing tumor of the nerve that carries sound from the inner ear to the brain. Although such a cancer will not spread outside the nerve, it can crush surrounding nerves and structures as it grows.

At the same time that removing the tumor promised to prevent further damage and perhaps save Dolce's life, it risked injuring his facial nerve, which passes out of the brain stem and close to the ear before it divides into seven branches to control the muscles on the side of the face. Surgeons J. Thomas Roland Jr., MD, the Mendik Professor of Otolaryngology and chairman of the Department of Otolaryngology, and John George Golfinos, MD, chair of the Department of Neurosurgery, worked carefully over eight hours in August 2012 to extract the growth and untangle it from the facial nerve, which had become wrapped around the tumor like ribbon on a gift. After several decades of experience with this delicate surgery, Drs. Roland and Golfinos are able to preserve facial nerve function in 19 out of 20 acoustic neuroma cases, better than the nationwide average.

When Dolce awoke, he learned that while his nerve remained intact, it had been stretched during the surgery. Only time would tell whether the resulting paralysis was temporary or permanent. "The doctors were very hopeful that the nerve would come back over the next few months. I was hopeful too," Dolce says.

But his paralysis persisted. Dolce tried to stay calm as he looked into the mirror. On the paralyzed side of his face, the cheek drooped like that of a jowly old man. The right eye, open and unblinking, looked startled. His right lip sagged sadly. "When I tried to smile," he says, "it just looked like I had gas." Upbeat and gregarious by nature, Dolce became too self-conscious to go anywhere other than job sites. He

injury, viruses, even Lyme disease—to know that the suffering goes beyond vanity and health concerns. "So much of who we are is in our facial expressions," says Dr. Roland. "It's what gives us personality and makes us human. With a flaccid face that is unable to express emotion, it can be difficult to feel whole."

The surgical technique, performed 45 times at NYU Langone since 2003, calls for grafting the damaged facial nerve into a healthy one from the tongue, essentially plugging it into a new power source. In the past, the tongue nerve might be weakened or sacrificed for the added nerve, but Dr. Roland and colleagues found a way to loosen the facial nerve from around a salivary gland

"So much of who we are is in our facial expressions," says Dr. Roland. "It's what gives us personality and makes us human. With a flaccid face that is unable to express emotion, it can be difficult to feel whole."

ate in private, unable to close his mouth, and remained home if his wife went out. "My friends tell me I don't look like a freak show," he said, "but I feel like one."

When electrical tests on the nerve showed no activity beyond the brain stem 12 months after surgery, Dr. Roland proposed a nerve graft, using a technique he had pioneered at NYU Langone 12 years earlier. He had seen enough patients with facial paralysis—from tumor removal, Bell's palsy, traumatic

near the jaw and extend its length by 3 to 5 centimeters. The extension allowed them to graft the nerves together without tension, thus increasing the odds that both nerves would function.

The surgery presented Dolce with some unusual but surmountable challenges. Until his brain adjusted to the rerouted nerves, he might need to think of chewing in order to grin. But Dolce was eager to try anything to regain his smile.

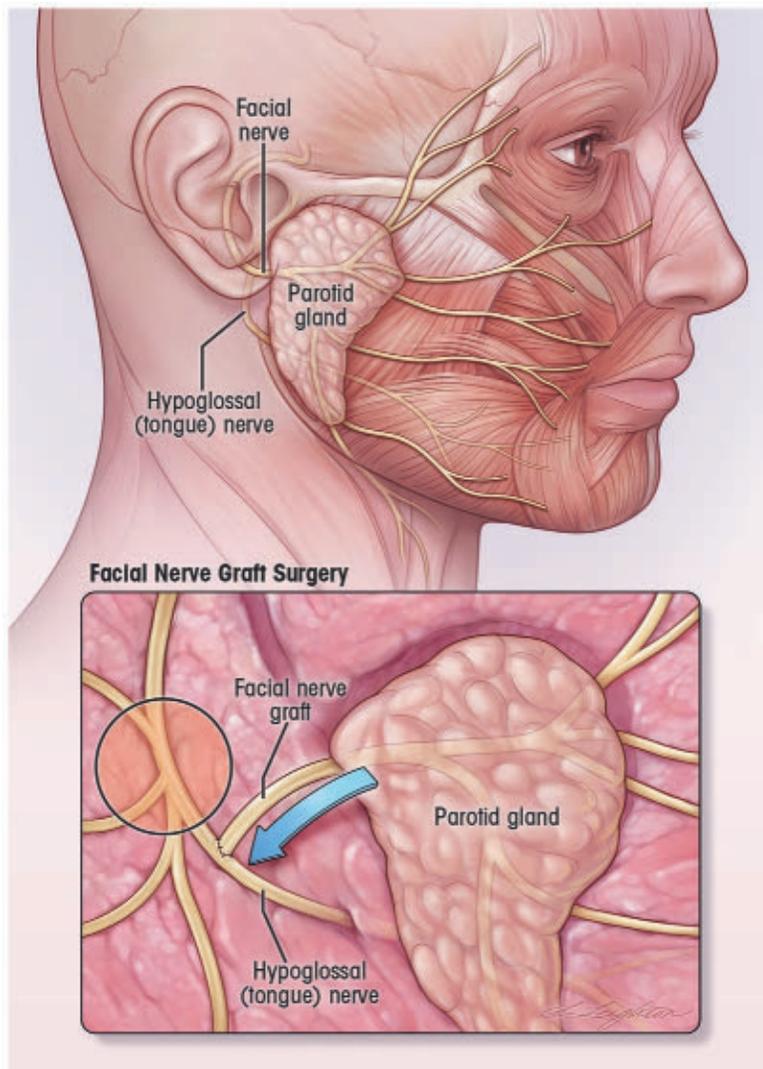
"I can deal with an eye that doesn't

blink,” he said. “But to be able to smile again would be fantastic. If they can fix my mouth, I’ll be happy.”

To ensure the best possible outcome, Dr. Roland recruited the help of facial plastic surgeon Matthew White, MD, assistant professor of otolaryngology-head and neck surgery. On the day of the operation, performed in early November, Dr. White began by implanting a gold weight on Dolce’s right eyelid to help it close. Then he lifted his eyebrow and pulled a tendon from his upper jaw down to the edge of his mouth—a facelift technique that would balance both sides of his face and help him control his lips. “I told him, ‘Don’t make me look like Joan Rivers,’” Dolce recalls, jokingly. When Dr. White finished, Dr. Roland took over and moved the intra-temporal facial nerve down to the hypoglossal (tongue) nerve and grafted the facial nerve to half of the tongue nerve, using tiny sutures under the lens of a microscope. Dolce emerged sore and bruised but thrilled with the results.

For starters, he no longer looked angry. With symmetrical eyebrows and a mouth curved upward he appeared cheerful. Able to smile passably and show his teeth, Dolce felt his old personality returning. “My friends say I’m 80 percent better,” he says, “and the nerve hasn’t even kicked in yet to do the rest of the job.”

As the nerve fully heals over the next year, sensation should first return to the eye and work downward through the nerve branches toward the chin. “In nine months I’ll ask him to push his tongue to the roof of his mouth,” Dr. Roland explains. “If I see something moving in his midface or eye, I will know that he’ll get an acceptable result.” ●



The facial nerve relays messages from the brain to most of the 43 muscles in the face. Dr. J. Thomas Roland Jr. modified a surgical technique to re-establish facial muscle innervation and movement by grafting the temporal facial nerve onto the nearby tongue nerve, also known as the hypoglossal nerve, which acts as a surrogate power source. One key to success is locating the graft below a junction of nerves near the jugular vein, called the ansa hypoglossi, (circled in above inset), a kind of switchboard that connects dozens of nerves originating in the neck with the tongue nerve. A graft above this junction might not be as effective.

Dr. David S. Baldwin

DAVID S. BALDWIN, MD, professor emeritus in the division of nephrology, and former director of the division, died in his sleep December 23, 2013, at his home in New York City. He was 92.

For half a century this meticulous bench scientist and beloved physician trained scores of kidney specialists at NYU Langone Medical Center. He studied and documented the natural history of virtually all forms of glomerular disease, in which infections like strep throat and bacterial endocarditis or conditions such as diabetes and systemic lupus, impair renal function by damaging the glomeruli, the tiny blood-filtering units of the kidney.

Paul L. Kimmel, MD ('76), a researcher with the National Institute of Diabetes and Digestive and Kidney Diseases, remembers his former teacher as a "charming man," polite and engaging, who treated his students and residents as his equals. Dr. Baldwin was the first to establish that acute disease can continue to damage the kidneys even after clinical signs and

symptoms have resolved, Dr. Kimmel says.

In an editorial published in 1977 in the *American Journal of Medicine*, Dr. Baldwin challenged medical wisdom that strep-induced damage to the glomeruli resolved after acute symptoms abated. His follow-up of such patients over 10 to 18 years showed that the hallmarks of the disease—blood and protein in the urine, high blood pressure, impaired renal function, and hardening or scarring of the glomeruli—either persisted or recurred in most patients even years later and, in some cases, progressed to kidney failure. "His ideas, based on patient observations confirmed in the lab in the 1970s and '80s, are at the forefront of nephrology today," Dr. Kimmel says.

Another of Dr. Baldwin's former students, Jerome Lowenstein, MD ('57), professor of medicine, later became his colleague and then his patient. Still later, their roles reversed. The two met in the mid-1950s, when Dr. Lowenstein was a third-year medical student. "He had just gotten out of the Army a few years before. There was only about a 10-year age difference, but

he seemed very much my senior," Dr. Lowenstein says.

In those early days, few physicians made careers in adult kidney disease because no treatment existed. Dr. Lowenstein recalls that Dr. Baldwin came to NYU Medical Center because he "wanted to study with Homer Smith, MD, a giant in renal physiology." At the time, "a lot of textbooks described the signs and symptoms of kidney disease but little was written about the course of the disease." Dr. Baldwin "wrote and published papers that describe every form of glomerular disease—an extraordinary body of information," Dr. Lowenstein says. He was also among the earliest clinicians to use nitrogen mustard, a

forerunner of cyclophosphamide, to produce remissions of symptoms caused by kidney damage.

The son of Russian Jewish immigrants, David Baldwin was born in Rochester, New York, and raised with two older sisters in an orthodox home. He attended college and medical school at the University of Rochester. In 1940 he met Halee, his wife of 68 years. In 1947, after a residency in St. Louis, the couple moved to New York City. Early in his career, Dr. Baldwin worked a second job as a staff physician at the *New York Times*, according to Daniel Baldwin, one of his four sons, who fondly recalls how a boyhood interest in classical music led his father to take him to hear a live string quartet in the studios of WQXR, then owned by the New York Times Co.

"He was the person I turned to for advice when I had important decisions to make," Daniel says. "He was a great listener, which I'm sure contributed to his skill as a diagnostician."

Dr. Baldwin could cut a rug with his wife at dinner dances, too, and he loved Hydrox cookies as much as he did a well-made martini. Although he had worked mornings on the weekends when his children were still living at home, on Sunday afternoons he would take his sons for a drive through Central Park, then open to auto traffic. "It was a big deal," Daniel says. "He allowed us to listen to rock stations, the Beatles."

An avid reader throughout his life, Dr. Baldwin in later years turned to drawing in his spare time. He retired at age 82 in 2004. Two years later he and Halee created a fellowship fund in nephrology at the School of Medicine.

He is survived by his wife; four sons and three daughters-in-law, Neil and his wife, Roberta, Andrew and his wife, Susan, Daniel and his wife, Nancy, and James; seven grandchildren, Nicholas, Allegra, Seth, Laura, Matthew, Joshua, and Julia; and two great-grandchildren, Levi and Emily. ●

—AUBIN TYLER

Dr. Baldwin and his wife, Halee



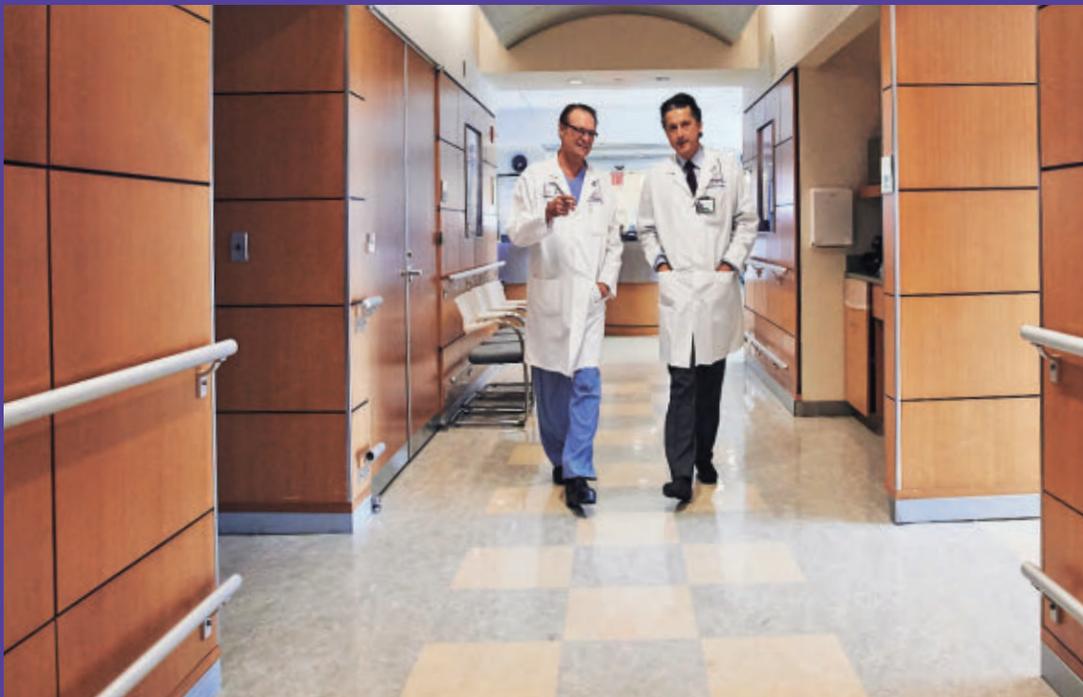
Change

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



www.NYULMC.org



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

