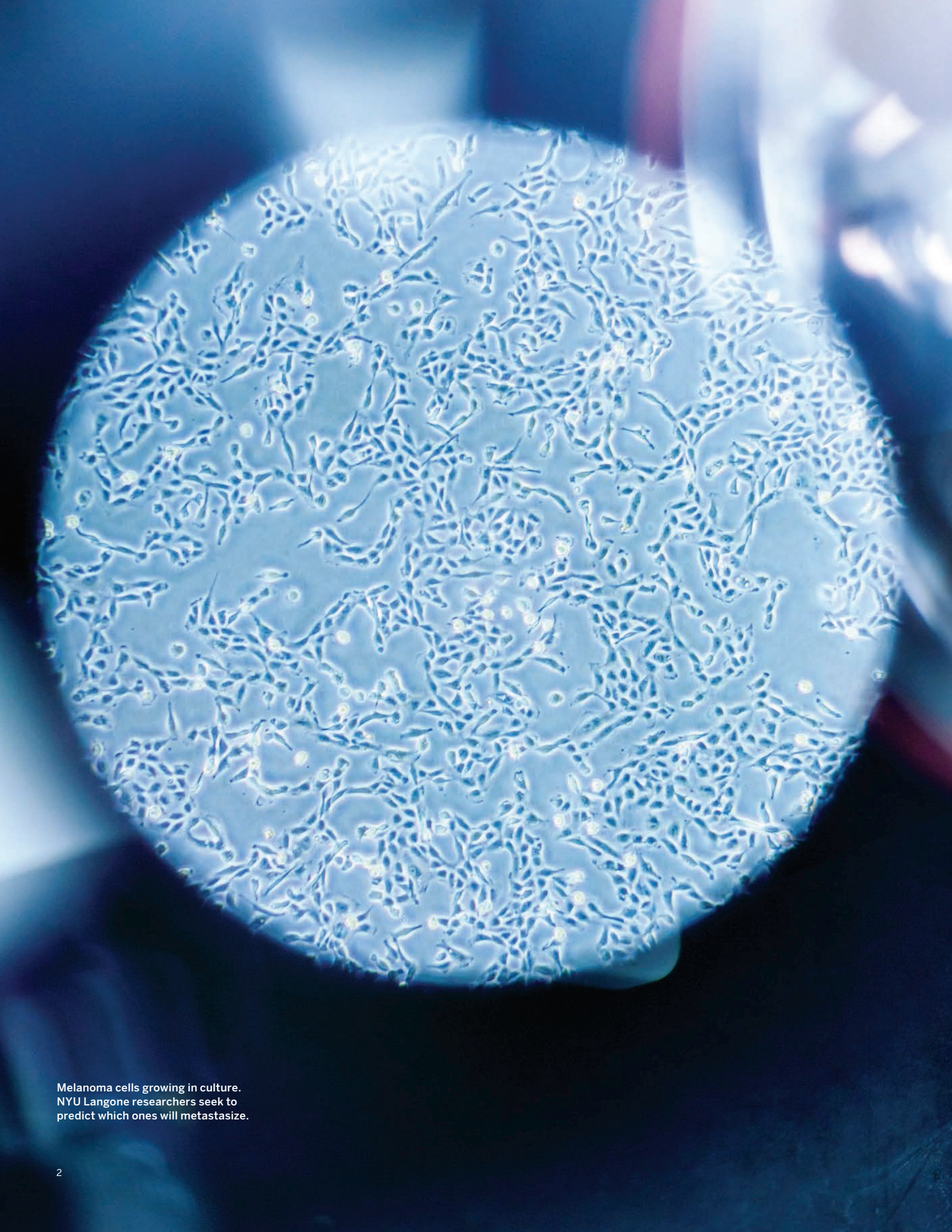
NYU School of Medicine
NYU LANGONE MEDICAL CENTER

TURNING POINTS

2015 RESEARCH REPORT

TURNING POINTS



Melanoma cells growing in culture. NYU Langone researchers seek to predict which ones will metastasize.

THE ROAD TO SCIENTIFIC DISCOVERY WOULDN'T BE QUITE AS THRILLING WITHOUT A FEW DETOURS AND UNEXPECTED TURNS.

As the distinguished researchers profiled on the following pages will tell you, progress rarely follows a straight trajectory. It's the surprising twists along the way—the new clues, the unconventional experiments, the serendipitous collaborations—that yield some of the most profound insights in science. At NYU Langone Medical Center, we embrace a culture of spontaneous interactions and free thinking because we wholeheartedly believe it's the mainspring of medical breakthroughs.

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DEAR COLLEAGUES

Turning Points in Scientific Discovery

Welcome to the *2015 Research Report,* an intimate snapshot of the people and events that help put NYU Langone Medical Center at the forefront of basic, translational, and clinical research. This year's report celebrates notable turning points in our ongoing scientific efforts to transform medicine. As one of the country's preeminent academic medical centers, NYU Langone provides fertile ground for our gifted investigators, who continue to set the bar high for biomedical research.

As we spoke with the inspiring researchers profiled on the following pages about the pivotal events that have launched their research to new levels, a common theme emerged: our institutional values. At NYU Langone, we pride ourselves on a culture of collaboration and exploration. We encourage our investigators to search for answers in unexpected places, and we embrace the scientific surprises born of spontaneous interactions and serendipitous connections. Why? Because it's a philosophy that yields extraordinary results.

Take Daniel Sodickson, MD, PhD, a pioneer in the field of magnetic resonance imaging, whom you will meet in this report. When he wanted to bring more powerful imaging technology to the clinic faster, he established a collaborative new center that brings together researchers, industry partners, and clinicians to test and develop new ideas. Then there is Eli Rothenberg, PhD, a physicist and biochemist, also profiled here. For him, an entirely new line of inquiry sprang from a chance encounter with a colleague over lunch. Now, the two researchers are collaborating on a new diagnostic tool for sudden cardiac arrhythmias. These and other scientists embody a vibrant culture of imagination and ingenuity at NYU Langone, and we hope you enjoy learning about the turning points in their research.

This report also celebrates a major milestone in our ongoing Campus Transformation. The 16-story research facility now under construction along East 30th Street and the FDR Drive Service Road will bridge the Joan and Joel Smilow Research Center and the Medical Science Building. When it opens in 2017, it will allow researchers, clinicians, and students to intermingle, creating the sort of "casual collisions," to borrow a phrase from Silicon Valley, that so often advance scientific discovery.

It will also enable our researchers to carry the momentum of our recent successes well into the future. This year, we received $245 million in funding from the National Institutes of Health, a significant increase over the previous year. At the same time, our ranking in NIH research funding jumped to number 16, up from number 21 last year. Meanwhile, our faculty continues to publish an impressive volume of seminal work in many of the most prestigious peer-reviewed science journals.

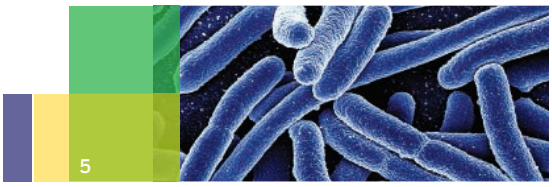
It's all part of our broader mission to provide the very best in patient care, scientific research, and medical education. We hope our singular dedication to this worthy goal shines through on the pages that follow.

ROBERT I. GROSSMAN, MD

The Saul J. Farber Dean and Chief Executive Officer

DAFNA BAR-SAGI, PhD

Vice Dean for Science and Chief Scientific Officer



Our Blueprint for Success

NYU Langone Medical Center has long been an incubator of transformative medical discoveries. Our researchers have helped eradicate polio, stymie tuberculosis and yellow fever, advance vaccines for hepatitis B, cancer and malaria, and develop Remicade®, a potent anti-inflammatory agent that has helped millions of people worldwide.

As we carry this strong tradition of excellence into the 21st century, our talented team of investigators has never been better prepared to shape new milestones in science and medicine. Our expertise in obesity, heart disease, autoimmune diseases, cancer, diabetes, and other pressing health areas is forging a new understanding of chronic disease and laying the groundwork for new treatments.

It's no surprise that we spend a lot of time thinking about how to help our researchers achieve an uncommon level of success and efficiency. What we've learned over the years makes our research programs truly unique. First, we place a premium on interdisciplinary research. We encourage it at every opportunity, through innovative new programs, funding, and forums for sharing information. It's even built into our infrastructure. The new biomedical research facility now under construction on our rapidly expanding campus will connect two existing research centers, allowing investigators, clinicians, and students to freely intermingle. Serendipitous collaborations, after all, yield some of the most profound insights in science.

1 Dr. Jan Vilcek, celebrated biochemist and alumnus of NYU School of Medicine, receives the National Medal of Technology and Innovation from President Obama. 2 Malaria parasites infecting red blood cells 3 Dr. Martin Blaser at a gala hosted by Time magazine, which name him among the top 100 most influential people of 2015. 4 Dr. Vilcek in 1969. His pioneering work led to the anti-inflammatory drug Remicade. 5 Gut bacteria 6 Dr. Severo Ochoa, Nobel Laureate and esteemed alumnus of NYU School of Medicine 7 Dean Grossman at Dean's Honors Day in 2009 with honorees Drs. Ruth and Victor Nussenzweig, and Dr. Gerald Weissmann. 8 Drs. Albert B. Sabin and Jonas Salk, alumni of NYU School of Medicine whose vaccine research helped eradicate polio.

We also strive for "full spectrum" research. That is, we tackle disease from the ground up, starting with basic research and advancing all the way to the clinic and beyond, into communities and even the halls of government. We look for root causes, we pioneer treatments, we study health trends, we test behavioral interventions, and we advocate for smarter health policies. Our work to stem the obesity epidemic is a good example. On the molecular level, our award-winning scientists are uncovering the hidden influence of gut bacteria on metabolism. In the clinic, we are equipping our patients with modern tools and techniques to achieve long-lasting weight loss. In communities hardest hit by the epidemic, our population-health experts are breaking down cultural barriers to quality healthcare.

Finally, we recognize that significant turning points in medicine come from significant resources. At NYU Langone, we're innovating powerful tools and support systems, including a new on-campus data-management resource that helps researchers harness the power of massive data sets. It's one of more than 20 state-of-the-art core facilities we make available to our researchers. You'll read about some of them on the following pages.

All of this helps us retain and attract the very best minds in science. "We've hired 100 new researchers in the past five years and plan to hire 100 more in the next five years," says Laura Ahlborn, vice president of science strategy. To accommodate our growing team, our laboratory capacity will double over the next five years, and as our talent and resources grow, so, too, will our funding for groundbreaking science. Already, our portfolio of grants from the National Institutes of Health has grown faster than that of any other academic medical center in the nation.

Physicist Niels Bohr once quipped that predictions are difficult, especially about the future. He's right, of course. No one can truly predict the next big turning points in medicine. But at NYU Langone, our ability to save lives and alleviate suffering through research depends not on the ability to see the future, but rather to prepare for it.

DANIEL SODICKSON, MD, PhD

Professor and Vice Chair for Research,
Department of Radiology;
Professor of Neuroscience and Physiology;
Principal Investigator, Center for Advanced
Imaging Innovation and Research;
Director, Bernard & Irene Schwartz Center
for Biomedical Imaging

Pioneering Better Body Scanners

A physicist's fresh idea puts NYU Langone at the forefront of groundbreaking medical imaging.

Since the birth of magnetic resonance imaging and computed tomography in the early 1970s, the field of medical imaging has dramatically transformed the way physicians diagnose and treat disease. Yet the process by which imaging innovations reach clinical practice has traditionally been glacially slow and cumbersome, says Daniel Sodickson, MD, PhD, professor of radiology, and neuroscience and physiology, and vice chair for research in the Department of Radiology.

The problem is that every promising idea in the field faces a long, arduous journey on the road to the clinic. First, it must be published and proven. Then, researchers must convince an imaging company of its potential clinical benefit. After that, the company will often redevelop the idea from the ground up and throw it back to a medical center as a prototype for clinical testing. "A year or two later, you're finally ready for the regulatory approval phase, which can take another year or more, and only then does the gradual process of clinical adoption begin," Dr. Sodickson explains. "Such time lines are expected in the pharmaceutical industry, but in many cases, the imaging products in question are software products. When judged by the standard of modern software development, the process is ridiculously long."

A turning point for Dr. Sodickson and his team at the Bernard and Irene Schwartz Center for Biomedical Imaging came last October, when they founded the Center for Advanced Imaging Innovation and Research (CAI^{2}R) at NYU Langone Medical Center. CAI^{2}R, directed by Dr. Sodickson, champions a bold new model of interdepartmental and academic-industrial collaboration. Rather than passing the baton to different players along each long leg of the development process, CAI^{2}R brings together researchers, industry partners, and clinicians right at the scanners to test and develop new ideas. Where new imaging hardware or software might take the better part of a decade to get into the hands of interested clinicians, the CAI^{2}R model promises to produce the same innovations in a small fraction of the time. "It dramatically accelerates the development cycle," says Dr. Sodickson.

Drs. Daniel Sodickson (right) and Ryan Brown examine a mannequin, dubbed an "imaging phantom," used to test prototype MRI detectors and transmitters.

NETFLIX FOR RADIOLOGISTS: STREAMING MRI SETS A NEW STANDARD FOR MEDICAL IMAGING

Daniel Sodickson, MD, PhD, has nothing against art photography. He just doesn't believe it's a particularly modern paradigm for magnetic resonance imaging. Yet for the past 40 years, he says, the process of acquiring clinically useful MRI imagery has borne a strong resemblance to staging a photoshoot. "It's as if we're telling a model, 'OK, look here, act natural, now freeze!" says Dr. Sodickson, professor of radiology, and physiology and neuroscience, and vice chair for research in the Department of Radiology. "We're framing the shots very, very carefully. It can take longer than an hour." For patients, even a few moments lying stock-still in an MRI tube can feel like an eternity. Now, Dr. Sodickson and his colleagues are innovating a far better alternative: streaming imagery. "Instead of taking shot after shot, we want to acquire images in a rapid, continuous stream," explains Dr. Sodickson. Think Netflix for radiologists.

The trick is compressing vast amounts of data. To do this, the researchers are developing a technology called compressed sensing, which is a clever way to dramatically reduce the amount of data required to generate images.

On a practical level, streaming MRI means a radiologist can request multiple views of the body from virtually any angle and at any point in time. "Let's say a radiologist wants to see the heart in a particular phase of contraction," Dr. Sodickson says. "No problem, we can go back to the data and mine it for new images." For patients, it means no more than 10 minutes in a tube, and the freedom to cough or scratch an itch, for instance. There's no staging, no uncomfortable posing. "If the patient moves, we can use new algorithms to capture and correct the movement," explains Dr. Sodickson, whose team at the Center for Advanced Imaging Innovation and Research has used early versions of the technology to image more than 4,000 patients at the Medical Center.

Streaming imagery is a welcome advance for both clinicians and patients, and just one of the ways that Dr. Sodickson and team at NYU Langone are reshaping the field of medical imaging.

CAI^{2}R is one of just 14 centers in the country designated by the National Institute of Biomedical Imaging and Bioengineering as a national resource center. This rarefied designation recognizes groups of innovators who are developing the most advanced technologies, techniques, and methodologies in the biomedical sciences today. Indeed, Dr. Sodickson and his colleagues are pursuing several new technologies at the heart of a genuine renaissance in medical imaging. Among them is a process called rapid continuous imaging. Simply put, it allows radiologists to continuously stream images instead of painstakingly framing shot after shot. "It's like the difference between a fax machine and a digital video camera," Dr. Sodickson explains.

That speed boost makes all the difference in the clinic. Faster imaging delivers sharper, clearer pictures of disease, resulting in better diagnostics. It also translates to a more comfortable experience for patients, since it eliminates the need to lie stock-still in an MRI tube for long periods of time. Finally, speed saves money, as slow scanning is expensive scanning.

The challenge is controlling the data deluge that results from streaming imagery. Here, the researchers are advancing a technology called compressed sensing (see box at left). It works similarly to the way your phone does when it compresses images for text messages or emails. But unlike the software in your phone that strips away unnecessary elements from an existing photo, compressed sensing randomly excludes data points as the shot is being taken. It then uses software to regenerate the missing information and render a complete image. It's a bit like a musician who can perfectly reconstruct a song after hearing just a few signature notes. "Compressed sensing is a clever way of precompressing data," Dr. Sodickson explains.

Another speed-driven project led by Dr. Sodickson is the development and evaluation of a new breed of scanner that combines both MRI and PET imaging for faster and more robust diagnostic power. NYU Langone is home to one of the first integrated MRI/PET scanners in the world, the focus of an ongoing collaboration between Dr. Sodickson's team and a major manufacturer of medical-imaging machines.

Combing MRI and PET images into one scanner offers several advantages. For starters, a patient only needs one exam instead of two. Second, clinicians get complementary information. "It delivers a fingerprint of disease that's much more robust than a single scanner alone," Dr. Sodickson explains.

Take epilepsy. An MRI scanner might lack the contrast to see certain subtle developmental abnormalities in the cortex of the brain that predispose to seizures. The PET scanner, meanwhile, might see a blush of contrast, but it lacks the necessary spatial resolution to localize the abnormality. Combine the scans and suddenly you can see the contrast overlapping a suspicious area on the MRI. "The two scans together make the diagnosis," Dr. Sodickson says.

> "The field of biomedical imaging is in the midst of a genuine renaissance, and NYU Langone is very much leading the way."
>
> DANIEL SODICKSON, MD, PhD

Dr. Sodickson learned the value of speed early on in his career. During a rotation with a cardiologist and cardiac imaging researcher at Harvard Medical School, he got stuck on a seemingly naive question: Why can't we image the heart faster? After reading stacks of articles about incremental improvements in the speed of magnetic resonance imaging, the physicist-clinician hit upon an idea that would change the arc of his career. Instead of using a single detector to take images, why not wrap multiple detectors around the body? That insight was the birth of parallel imaging, a revolutionary method of accelerating the acquisition of MRI data through detector arrays.

Dr. Sodickson has earned numerous accolades and honors over the years for his innovations. In 2006, he received a Gold Medal from the International Society for Magnetic Resonance in Medicine, the organization's highest honor, for his contributions to parallel imaging, among other achievements. He credits his success in the field to his background in physics and math. "There's a lot of basic physics in the construction of next-generation imaging machines," says Dr. Sodickson, who holds a doctoral degree in medical physics from the Massachusetts Institute of Technology. "And there's a lot of mathematics in the algorithms used to take the raw data from those machines and turn them into clinically relevant images."

But his true inspiration is medicine. "I love being part of a team that cares for patients, and developing tools that will improve their care in times to come," he says. "I love having a stake in people's lives."

CENTER FOR ADVANCED IMAGING INNOVATION AND RESEARCH: A NEW VISION FOR TRANSFORMING IMAGING RESEARCH

The Center for Advanced Imaging Innovation and Research, or CAI^{2}R, champions a new standard of academic-industrial collaboration, bringing together researchers, industry partners, and clinicians to test and develop new ideas. Under this new model, clinicians can offer researchers instant feedback. A physician might inform the team that she needs a better view of a cartilage lesion in the knee, for example. "Instead of waiting six months to collect feedback and modify the software, the developers can fix the glitch that night and try again the next day," explains Dr. Sodickson.

The center, designated a national resource center by the National Institute of Biomedical Imaging and Bioengineering, employs more than 80 basic researchers and engages a large number of clinical collaborators. It focuses on three general areas of high public health impact: cancer, musculoskeletal disease, and neurologic disease. At the top of its research agenda are projects to develop rapid continuous image acquisition (see "Netflix for Radiologists" opposite page) and to merge PET scans and MRIs into a single comprehensive imaging examination. "The field of imaging is in the midst of a genuine renaissance," says Dr. Sodickson, "and NYU Langone is very much leading the way."

Unlocking the Mysteries of Human Immunity

For this immunologist, bacteria and B cells offer tantalizing clues to the molecular puzzle of lymphomas and chronic inflammation.

The linchpin of adaptive immunity, B lymphocytes, or B cells, are capable of producing antibodies to recognize more than a billion different foreign invaders. Sergei Koralov, PhD, assistant professor of pathology, studies the genetic shuffling that underlies this remarkable adaptability, and explores what happens when it goes wrong—and it often goes wrong. The problem is that the splicing and dicing of gene segments required to adapt to such a mind-boggling number of pathogens is a highly error-prone process. The result can be lymphomas, or cancer of the immune cells, and chronic inflammation. "The recombination process is inherently dangerous," says Dr. Koralov.

Since setting up his laboratory at NYU School of Medicine in 2010, Dr. Koralov has had a number of insights into B cell development that point to novel treatments for these illnesses. In mice, for instance, he and his colleagues have found that microRNAs, a type of noncoding genetic material that regulates gene expression, play a critical role in the survival and proliferation of B cells. "We've shown that B cells die without these microRNAs," says Dr. Koralov.

While Dr. Koralov's historical strengths lie in decoding the raw mechanics of B cell development, his work has taken on a new dimension since engaging with NYU Langone Medical Center's vibrant community of experts on the human microbiome, the 100 trillion bacteria that live in and on our body. Like so many of his peers, he has found inspiration in the pioneering work of Martin Blaser, MD, the Muriel G. and George W. Singer Professor of Translation Medicine, and director of the NYU Human Microbiome Program at NYU School of Medicine, and Dan Littman, MD, PhD, the Helen L. and Martin S. Kimmel Professor of Molecular Immunology and a Howard Hughes Medical Institute Investigator. He also routinely collaborates with microbiologists Ken Cadwell, PhD, assistant professor of microbiology at the Skirball Institute of Biomolecular Medicine, and Victor Torres, PhD, associate professor of microbiology, to explore the intricate relationship between bacteria and immunity. Using a novel animal model recently generated by his lab, Dr. Koralov and his colleagues have discovered that both friendly and pathogenic bacteria influence the onset of steroid-resistant asthma. They are also helping elucidate the role of microbiota in psoriatic arthritis and in cancer.

"The sheer number of diseases driven by immune dysfunction is astounding," says Dr. Koralov. "A better understanding of how bacterial communities influence immune function can help us develop more effective treatments."

Another turning point for Dr. Koralov—and for science in general—is the advent of a game-changing technology known as Crispr-Cas9, which allows scientists to easily edit the genes of any organism. Where it once took Dr. Koralov years to genetically engineer an animal model, it now takes only a few months with Crispr-Cas9. "This revolutionary technology has transformed how we do science," says Dr. Koralov, "and few places are putting it to better use than NYU Langone to advance our basic understanding of disease."

> "My work has taken on an entirely new dimension since joining NYU Langone's vibrant research community."
>
> SERGEI KORALOV, PhD

IMMUNOLOGY

SERGEI KORALOV, PhD

Assistant Professor of Pathology

MOLECULAR PATHOLOGY

EVA HERNANDO-MONGE, PhD

Associate Professor of Pathology,
a Member of the Helen S. Kimmel Center
for Stem Cell Biology, and the Perlmutter
Cancer Center

Unmasking Melanoma

For this cancer biologist, interdisciplinary research reveals fresh clues to the evolution of deadly skin tumors.

Eva Hernando-Monge, PhD, investigates the molecular basis of metastatic melanoma, a deadly form of skin cancer that kills more than 9,000 people in the U.S. every year. One fundamental question guides her research: How does a tiny tumor originating in melanocytes, the cells that produce skin pigment, so aggressively spread to other parts of the body?

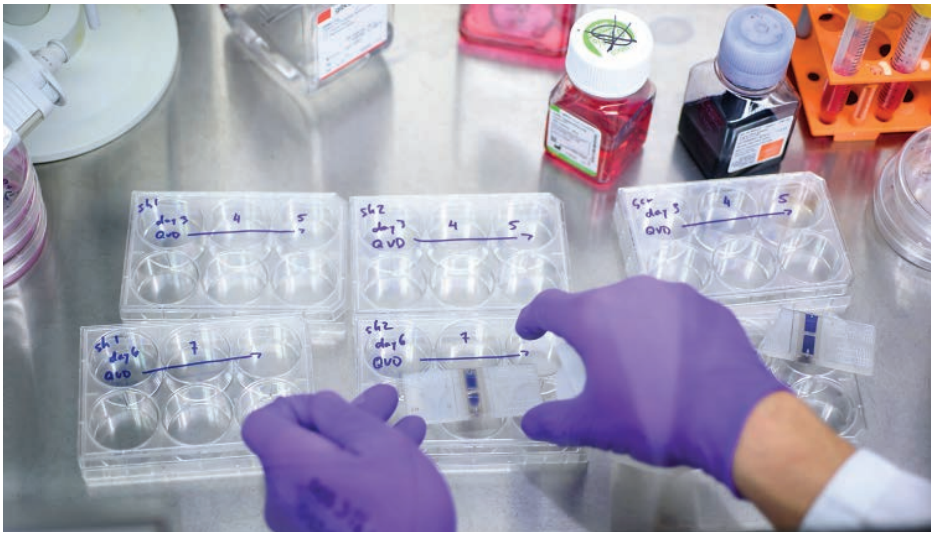
Dr. Hernando-Monge's search for answers took a critical turn in 2006 when she joined the Laura and Isaac Perlmutter Cancer Center's Interdisciplinary Melanoma Cooperative Group (IMCG) at NYU Langone. The IMCG is a multidisciplinary translational melanoma research program founded in 2002 by Iman Osman, MD, PhD, professor of dermatology, medicine, and urology. The prospect of collaborating with researchers across a broad range of disciplines was a big draw. "We never work in isolation," says Dr. Hernando-Monge, associate professor of pathology and a member of the Perlmutter Cancer Center at NYU Langone.

> "Joining NYU Langone's multidisciplinary melanoma research group gave me a new perspective on skin cancer."
>
> EVA HERNANDO-MONGE, PhD

"We focus on different aspects of melanoma biology but with the main goal of understanding what makes tumor cells spread and how we can use that information to identify and treat patients who are at highest risk for aggressive melanoma."

Current diagnostics fail to reliably predict which melanoma cells will metastasize, but once the cancer spreads to other parts of the body it becomes very difficult to treat. While the survival rate for melanoma is higher than 92 percent if caught early, the life expectancy of people with the most advanced stages of melanoma is less than a year.

The IMCG's unorthodox model of research brings a fresh perspective to the problem, and new hope for novel treatments. Cancer research often begins in vitro or in mouse models and progresses to human tissue samples. "Our approach is completely the opposite," explains Dr. Eva Hernando-Monge. She and her colleagues explore the IMCG's bank of 17,000 human tissue specimens for questions most relevant to patients and then design the experiments to answer them. The resources available at the IMCG afford Dr. Hernando-Monge and her team the ability to explore the cellular underpinnings of melanoma at all stages of the disease. "The big question is whether we can look at the primary stage of melanoma, when the tumor is still confined to the skin, and predict whether it will metastasize," Dr. Hernando-Monge says.



Dr. Hernando-Monge's research so far points to rogue stem cells in melanocyte cells that fail to differentiate into mature cells. In a paper published in 2013, Dr. Hernando-Monge and her team described how melanoma cells overexpress BRD4, a protein known to fuel tumor growth. Inhibiting BRD4, the researchers found, inhibited melanoma growth. Last year, her team published another paper describing how the same protein helps stem cells retain their near-magical ability to replicate daughter cells rather than mature into adult cells.

> "The big question is whether we can look at the primary stage of melanoma, when the tumor is still confined to the skin, and predict whether it will metastasize."
>
> EVA HERNANDO-MONGE, PhD

In yet another promising finding, Dr. Hernando-Monge and her team have found that more aggressive melanomas overexpress a specific group of microRNAs, a class of molecules that modulate protein levels. This insight holds important prognostic value. This year, her group published a paper describing a clinical study in which microRNA signatures were found in nearly 300 patients. The study is a big step toward a new diagnostic assay. "The same microRNAs that confer aggressive features to melanoma cells can tell us which patients are at higher risk of developing more metastatic tumors," says Dr. Hernando-Monge.

As part of an exciting new initiative that takes NYU Langone research to a new continent, Dr. Hernando-Monge and others at the Medical Center are now collaborating with the Technion-Israel Institute of Technology in the fight against cancer (see page 29). The partnership, funded by a $9 million gift from philanthropists and NYU Langone trustees Laura and Isaac Perlmutter, bridges two world-class research enterprises and marks a turning point in the Medical Center's commitment to international collaboration.

This page: Eva Hernando-Monge, PhD, (third from right) collaborates with a wide range of researchers as part of the Laura and Isaac Perlmutter Cancer Center's Interdisciplinary Melanoma Cooperative Group. Opposite page: An investigator seeds cells in an experiment to find new therapeutic targets against melanoma.

Seeing the Unseen

A biophysicist capitalizes on the latest microscopy tools to visualize new markers of disease.

When Eli Rothenberg, PhD, first developed an interest in microscopy in the mid 2000s, he knew nothing about biology. "Zilch, nada," he confesses. "I was versed in physics, math, and chemistry." But the more he read about biology, the more intrigued he became.

"The questions were so complex," recalls Dr. Rothenberg, assistant professor of biochemistry and molecular pharmacology. In 2010, after finishing his postdoctoral training in biological physics at the University of Illinois (Urbana-Champaign), Dr. Eli Rothenberg faced a dilemma: should he aim to set up a laboratory within a traditional physics department or pursue his growing interest in biomedical research at a medical school? Dr. Rothenberg chose NYU School of Medicine, a move he now considers a major turning point in his career. A serendipitous partnering with Mario Delmar, MD, PhD, professor of medicine in the Leon H. Charney Division of Cardiology, at a faculty lunch in 2010 soon led to an unexpectedly fruitful collaboration. Using single-molecule fluorescence microscopy, a tool capable of nanometer resolution, the two have discovered that slight changes in proteins situated between cardiac cells can trigger potentially lethal cardiac arrhythmias. Their research has broken new ground—it's the first technique to visualize the molecules populating the juncture between cardiac cells—and has led to several seminal papers.

> "The interdisciplinary culture of NYU Langone has allowed me to ask deeper, more meaningful questions about my work."
>
> ELI ROTHENBERG, PhD

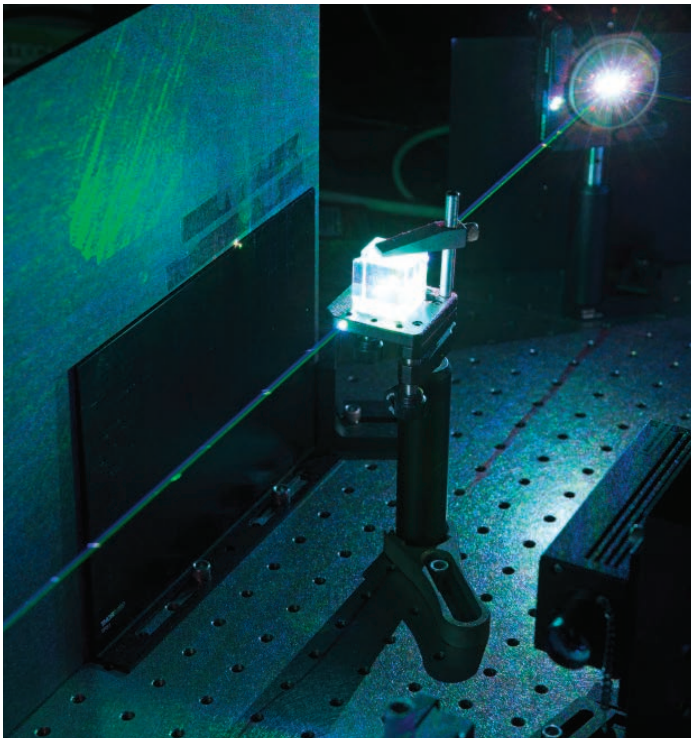
Dr. Rothenberg and his team are applying similar imaging techniques to visualize the cellular machinery responsible for DNA repair. (Dr. Rothenberg's forte, the mechanics of DNA repair, was among the main subjects of his postdoctoral training.) In his research, Dr. Rothenberg examines the vast array of proteins and enzymes that cells employ to help DNA endure stress from a host of factors, from environmental radiation, radiation treatment, and chemotherapeutics to the rigors of replication. Using single-molecule imaging technology to track living cells, his team recently published the first visual evidence of how molecules organize themselves to repair damaged DNA. The findings hold important implications for cancer therapeutics. "When DNA repair mechanisms function poorly, cancer cells take advantage and develop resistance to cancer therapies," explains Dr. Rothenberg.

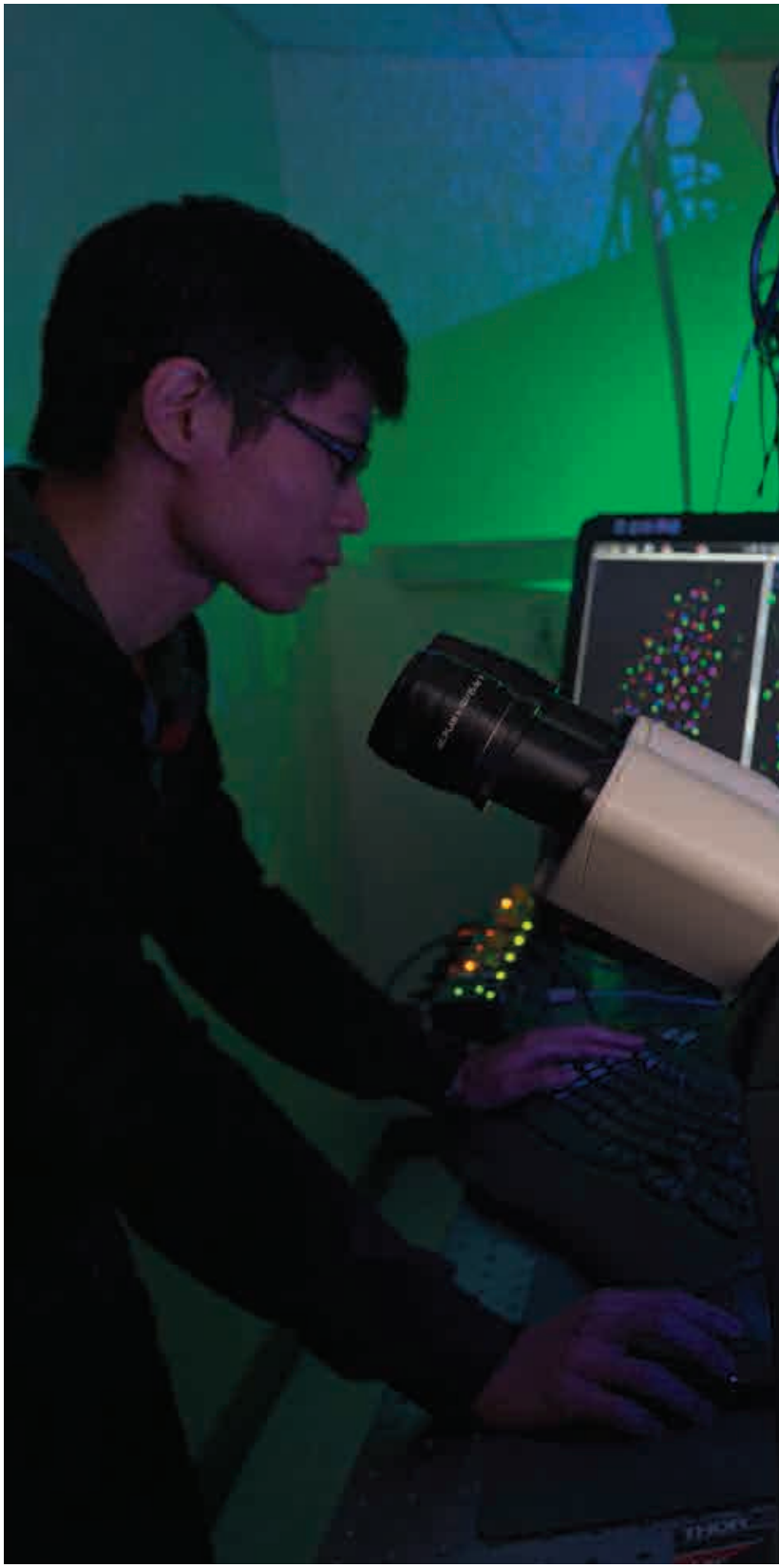
Dr. Rothenberg believes the interdisciplinary culture of NYU Langone Medical Center has allowed him to ask deeper, more meaningful questions about his work. "Communication is so important," he says. With the right questions in hand, he's unafraid to venture off the beaten path and innovate new methods to find the right answers. "I never do anything by the book," says Dr. Rothenberg. "It's more fun to write the book yourself."

MICROSCOPY

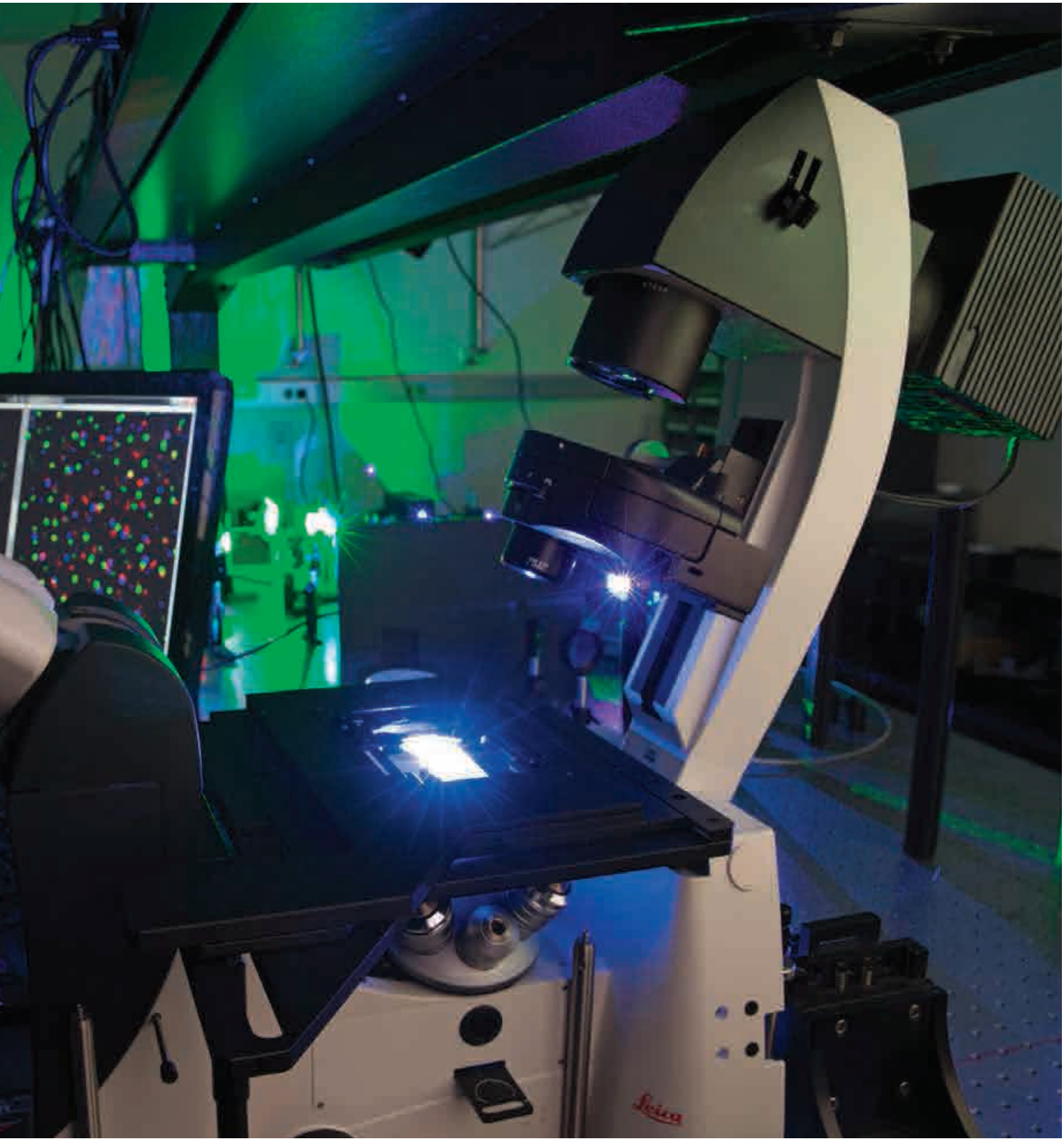
ELI ROTHENBERG, PhD

Assistant Professor
of Biochemistry and
Molecular Pharmacology





The laboratory of Dr. Eli Rothenberg houses a suite of custom-built microscopes designed to visualize individual molecules. Laser light, seen here guided by jigs, reflects off fluorescent tags expressed within a single cell, revealing a level of detail that would be impossible to see with a conventional light microscope.



Yandong Yin, PhD, a postdoctoral researcher in Dr. Rothenberg's lab, using a single-molecule microscopy system to acquire a remarkably clear image of proteins linked to cancer inside the nucleus of an individual cell, as seen on the computer monitor.

PUBLIC HEALTH

DONNA SHELLEY, MD

Associate Professor of Medicine and Population Health;
Vice Chair for Research and Codirector of the Section on Tobacco, Alcohol, and Drug Use in the Department of Population and Medicine Health

Changing the System

A public-health expert discovers that often the best way to improve patient care is to improve the systems that deliver it.

Donna Shelley, MD, MPH, spent years investigating how physicians could best help their patients quit smoking. The more she scrutinized how doctors were attempting to implement the latest smoking-cessation guidelines, the more she realized that it wasn't the doctors who needed the most help, but rather the systems in which they worked.

"We advise doctors on best practices for improving quality and patient outcomes, but what we find is that they don't always have the tools or expertise to implement them," says Dr. Shelley, associate professor and vice chair for research in the Department of Population Health and codirector of the department's Section on Tobacco, Alcohol, and Drug Use.

That insight sparked Dr. Shelley's long-standing fascination with the "science of implementation," a field more commonly applied in the corporate world that examines how organizational change can impact the delivery of quality—in the case of medicine, quality of care. "I wanted a deeper understanding of the multilevel factors that impact quality of care, including patients, providers, and systems," Dr. Shelley says.

"Not just for tobacco use but for other cardiovascular risk factors, such as hypertension, cholesterol, and diabetes."

Dr. Shelley's pioneering work in this emerging field has attracted national attention. Last June, her team at NYU Langone Medical Center became one of only seven nationwide chosen to participate in a $15 million, three-year study, funded by the federal government's Agency for Healthcare Research and Quality (AHRQ), to help primary care practices implement the latest interventions to improve heart health across America. "External support is a vague term," says Dr. Shelley. "How do you define it, test it, prove that it works, and scale it up? The AHRQ is making a significant investment to find out."

As part of the study, Dr. Shelley and her team are examining dozens of factors that influence care providers' ability to successfully implement federal guidelines for reducing cardiovascular risks. "We're addressing every component of clinical practice that affects patient outcomes," Dr. Shelley explains. "We're looking at work flow, patient visits, educators, dashboards, registries, electronic health records—everything."

> "NYU Langone's data-management resources have been a transformative part of my research."
>
> DONNA SHELLEY, MD

Among the puzzle pieces, Dr. Shelley believes electronic health records may be the most important. "Electronic health records have changed the whole landscape of this work," she notes. Part of her research is to figure out how to improve the technology and leverage the data to make the delivery of quality care more efficient.

NYU Langone, in particular, is well poised to help. Last year, the Medical Center's Clinical and Translational Science Institute debuted an on-site data-management service called DataCore (see page 27). For Dr. Shelley, the resource has been transformative—a true turning point in her research. Based in the Medical Center's IT Department, DataCore helps researchers collect, process, and manage the torrents of data that so often threaten to overwhelm research projects. In Dr. Shelley's case, the service is helping her team manage the electronic health records of over 100,000 patients from 250 small to medium-size primary care practices in the AHRQ study. "Before DataCore we would often have to outsource all of our management," notes Dr. Shelley. "Now we have a resource right here on campus. It's helping us measure outcomes more efficiently."

With the help of DataCore, Dr. Shelley's research will also shed light on ways to make electronic health records more physician friendly. "We want to make providers' jobs easier, not harder, and we can do that by helping them do what they really want to do," says Dr. Shelley, "which is provide excellent care."

Rethinking Oxytocin

A neuroscientist sees the "hug hormone" in a whole new light.

Robert Froemke, PhD, has long been fascinated by the human brain's capacity to learn and change. "The concept of brain plasticity is one of civilization's most amazing ideas," says Dr. Froemke, assistant professor of otolaryngology, and neuroscience and physiology, and a member of the Skirball Institute of Biomolecular Medicine at NYU Langone Medical Center. "The decisions we make, the experiences we have, the things we ingest, the lives we lead—it can all change our neural circuits." Dr. Froemke is particularly interested in how the potent hormone oxytocin shapes the brain during motherhood, a time of tremendous neurochemical upheaval. "We're not talking about a protracted learning process," Dr. Froemke says. "Motherhood unleashes a major transformation that takes place in a very short span of time."

In recent decades, oxytocin has earned a reputation as a "hug hormone" or "love drug" for its well-documented role in infant bonding and facilitating trust between humans. Now, Dr. Froemke and his team of investigators are challenging that stereotype, bringing about a major turning point in our understanding of oxytocin. "Increasingly, evidence shows that it's neither a hug hormone nor a love drug," Dr. Froemke says.

In an influential paper published last April in *Nature,* Dr. Froemke showed how oxytocin acts on neurons in the left auditory cortex of new rodent mothers to help them respond to the ultrasonic distress calls of lost pups. The hormone even sensitized mice without offspring that would have otherwise ignored the plaintive cries. Oxytocin, the research found, amplifies the neuronal circuits and molecular cues that control vocal communication between rodent mothers and their offspring. "Oxytocin is more like a chemical volume control," explains Dr. Froemke. "Turning it up allows us to pay more attention to relevant social cues." The study is among the first to elucidate the cellular underpinnings of maternal bonding.

Dr. Froemke's explorations of neurochemical changes in the auditory cortex—a brain region that governs auditory perception and language processing—hold important clinical implications. A sharper understanding of the rules and mechanisms that govern these changes stands to inspire a new wave of therapies for a wide range of disorders from social anxiety to schizophrenia. It will also help Dr. Froemke advance his efforts to build so-called neuroprosthetics to bridge damaged areas in the brain. Two years ago, his laboratory was one of just two teams selected from 32 applicants to receive the NYU Grand Challenge's $250,000 prize, seed money that is now helping the researchers bring such brain implants to the clinic. "The clinical potential of neural implants is quite astounding," says Dr. Froemke.

While some researchers might limit their questions to the resources immediately available to answer them, Dr. Froemke innovates new tools when existing ones fall short. When he and his team wanted to know exactly where oxytocin is released in the auditory cortex, for instance, they developed a novel antibody that binds to and illuminates oxytocin receptors. Their findings revealed that oxytocin receptors concentrate in the left side of the auditory cortex, suggesting that this brain region traditionally associated with language processing may also underlie our ability to process social information.

For Dr. Froemke, the power to heal is a powerful motivator, but so, too, is the ability to help everyone, young and old, become better learners. "The brain never stops changing," he says. "It's true that it's easier to learn certain things when you're younger, but we learn our whole lives. Our lab wants to know what it takes to engage the neural mechanisms that make that possible."

"The decisions we make, the experiences we have, the things we ingest, the lives we lead—it can all change our neural circuits."

ROBERT C. FROEMKE, PhD

NEUROSCIENCE

ROBERT C. FROEMKE, PhD

Assistant Professor,
Skirball Institute of Biomolecular Medicine;
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Growth and Expansion: Creating a Turning Point for Biomedical Infrastructure

Conducting world-class biomedical research demands not only world-class talent, but also world-class infrastructure. On the following pages you will read about some of our efforts to forge strategic partnerships, introduce powerful core resources and dramatically expand laboratory space.

DataCore

Empowering clinical research with the tools of big data.

Biomedical research is increasingly dominated by data. The explosion in *omics*—genomics, proteomics, metabolomics—combined with an avalanche of demographic data from electronic health records and social media have brought an unprecedented level of complexity to data management.

If science is to mine insight and meaning from large data sets, it must posses the tools to store, organize and analyze them. That's precisely the mission of DataCore, a recent Research IT initiative in partnership with the Clinical and Translational Science Institute and the Office of Science and Research.

"DataCore offers technical support for the entire spectrum of clinical research happening at NYU Langone, from very small single-center observational studies to large multicenter clinical trials where people all over the world are entering data," explains Judith Hochman, MD, MA, the Harold Snyder Family Professor of Cardiology and senior associate dean for clinical sciences.

Dr. Hochman, a chief architect of DataCore, understands the value of expert data management. She has been running data-intense clinical trials for two decades. Her latest study, funded by an $84 million grant from the National Institutes of Health, compares two treatment strategies for coronary artery disease in over 8,000 patients. It involves more than 150 medical centers in the U.S. and hundreds more abroad. "It takes a huge infrastructure to run a large multicenter clinical trial," she says.

At NYU Langone, DataCore serves a critical part of that infrastructure by offering researchers a suite of IT tools and services to collect, store, track, and analyze vast collections of data. Alexander Bragat, director of DataCore, likens the resource to GPS, an analogy that applies to finding and routing data to and from researchers. "We help the investigators decide how best to capture clinical data and guide them through the complex electronic medical record structure to extract it," Bragat says.

Since it launched last year, DataCore has helped more than two dozen investigators develop grant applications for clinical trials. Services range from helping to prepare budgets for the data-management portion of a project to coordinating the transfer of data between trial sites. Among these projects is a three-year study run by Donna Shelley, MD, MPH, associate professor of medicine and population health, to investigate factors that influence care providers' ability to successfully implement federal guidelines for reducing cardiovascular risks (see page 23). Dr. Shelley's study, supported by a $15 million federal grant, involves 200,000 patient records from the NYC Department of Health's Primary Care Improvement Project and the Community Health Care Association of New York State practice networks that feed directly into DataCore.

Michael Cantor, MD, director of Clinical Research Informatics, sees such a robust data-management resource as a true turning point in NYU Langone's ability to rise to the challenges of 21st century biomedical research. For one, it's a powerful draw for top-tier investigators whose work depends on cutting-edge data management. Says Dr. Cantor, "DataCore gives us a strong institutional strategy for making the most of our research data."

Center for Large-Scale Clinical Studies

A new resource aims to put NYU Langone at the forefront of clinical research.

Planning and running a major clinical trial is a daunting task that often involves hundreds of steps, years of planning, and spiraling costs. For researchers, the logistical burden can be overwhelming. NYU Langone Medical Center's new Center for Large-Scale Clinical Studies, or CLCS, aims to streamline the process, offering researchers centralized support for multicenter trials.

The brainchild of Judith Hochman, MD, MA, the Harold Snyder Family Professor of Cardiology and senior associate dean for clinical sciences, the CLCS performs a wide range of services, from assisting investigators with protocol development and grant applications to identifying clinical sites, training staff, and overseeing all institutional and federal regulatory approvals involved in clinical trials.

"The National Institutes of Health wants to know you have the infrastructure to lead large national clinical trials," says Jacqueline Arciniega, director of the Office of Science Research's Strategic Initiatives and Programs. "The CLCS helps us prove that administratively we have what it takes."

Patricia Corby, DDS, MS, the CLCS's director, has a keen understanding of the demands of clinical trials. She has spent nearly two decades running her own clinical trials, as well as those of other investigators, most recently at the NYU College of Dentistry's Bluestone Center for Clinical Research. Dr. Corby's experience as a principal investigator and research administrator helps her understand both sides of the process required to succeed when developing new ideas.

"By offering a new level of support and resources, we hope to inspire our investigators to pursue larger and more influential clinical trials," Dr. Corby says. "And once we attract funding for those trials, we hope to help our investigators succeed in running them by ensuring a seamless, less burdensome process."

In the last year, the CLCS has helped organize and submit funding applications for several large multicenter clinical trials that, if funded, will investigate everything from shingles infections in the eye to post-traumatic psychopathology.

As a core resource, CLCS supports NYU Langone's broader mission of advancing excellence in clinical research. "NYU Langone is very much at the forefront of clinical research," Dr. Hochman says, "and running multicenter trials is one way of saying we're recognized as a leader in clinical research."

Crossing Borders

An international partnership marks a turning point in NYU Langone's strategic approach to cancer research.

NYU Langone's dedication to interdisciplinary collaboration extends far beyond its bustling New York City campus. Last February, the Medical Center announced an ambitious new collaboration with the Technion-Israel Institute of Technology to advance cancer research.

The intercontinental partnership, funded by a $9 million gift from philanthropists and NYU Langone trustees Laura and Isaac Perlmutter, bridges two world-class academic research institutions. "NYU Langone and the Technion have a shared, long-standing commitment to advancing cancer research," says Dafna Bar-Sagi, PhD, senior vice president and vice dean for science at NYU Langone, chief science officer at NYU School of Medicine, and a principal architect of the NYU Langone-Technion collaboration. "This partnership marks an exciting turning point in our approach to cancer research as it deepens our expertise in fields like engineering and physics and allows us to explore cancer from new vantage points."

Among the research projects supported by the partnership is a novel approach to targeting melanoma tumors that have spread to the brain, the leading cause of death among patients with malignant melanoma. Led by Dr. Hernando-Monge, associate professor of pathology and a member of the Perlmutter Cancer Center at NYU Langone, and Marcelle Machluf, PhD, a professor of biotechnology at the Technion-Israel Institute of Technology, the study will explore the use of nanotechnology to target brain tumors with therapeutic micro-RNAs, molecules that modulate protein levels in the body and can suppress metastatic cancer.

The inability of most therapeutic agents to penetrate the blood brain barrier represents a major hurdle in the treatment of brain tumors. And even when therapeutic micro-RNAs do manage to pass this formidable barrier, the therapy is often too diluted by the time it reaches tumor cells. It can also accumulate in the liver, creating dangerous toxicity.

Dr. Hernando-Monge combines her expertise in microRNAs and metastatic melanoma (see page 15) with Dr. Machluf's expertise in nanotechnology-delivery systems. "Bringing together the unique expertise of researchers from both NYU Langone and the Technion will hopefully enable us to overcome some of the most difficult challenges in treating cancer patients," said Technion Distinguished Professor Aaron Ciechanover, MD, the 2004 Nobel Prize Laureate in Chemistry, and Distinguished Research Professor and head of the David and Janet Polak Cancer and Vascular Biology Research Center at the Technion Faculty of Medicine.

The Office of Therapeutics Alliances

Pioneering a New Model of Academic Drug Discovery

For years, Robert Schneider, PhD, had been struck by a startling trend in the pharmaceutical industry. Funding for the research and development of new medications had jumped from $15 billion to a staggering $50 billion annually over the past three decades, and yet the number of new FDA-approved drugs had flatlined. "Big Pharma was investing nearly twice as much as the annual budget for the National Institutes of Health and had very little to show for it," says Dr. Schneider, the Albert Sabin Professor of Molecular Pathogenesis in the Department of Microbiology and Professor of Radiation Oncology at NYU Langone Medical Center.

To save time and money, the pharmaceutical industry began shifting its investments in basic research and early drug discovery to the later stages of drug development, leaving hundreds of industry scientists out of work. In a twist that would ultimately favor NYU Langone, newly unemployed chemists skilled at developing drugs then formed small companies known as contract research organizations, or CROs, and sold their services right back to pharmaceutical companies. For Dr. Schneider, the reorganization represented a prime opportunity. "The rise of chemistry CROs leveled our playing field," he explains. "It meant that we could also outsource drug discovery."

Nadim Shohdy, PhD, then in NYU Langone's Office of Industrial Liaison, or OIL, meanwhile had a similar insight. In 2013, he and Dr. Schneider partnered to found NYU Langone's Office of Therapeutics Alliances, or OTA, an academic "virtual biotech" drug discovery program.

OTA's approach to drug development breaks new ground. Unlike most other academic medical centers, which attempt to develop new drugs in house, OTA focuses exclusively on translating the earliest stages of basic research, where NYU Langone scientists thrive, to early-stage drug discovery in the same way that much of Big Pharma now does. "By outsourcing drug development to CROs and painstakingly evaluating research projects for their commercial potential, we save time and money, and reduce risk," says Dr. Shohdy.

The average drug takes about a decade to develop, fails 90 percent of the time, and can cost up to $1 billion by the time it reaches FDA approval. "Our model is entirely different," adds Dr. Schneider. "Our goal is to reduce the risk in drug discovery, make a project much more attractive for partnership, and then hand it off to industry to take to FDA approval while focusing on the rest of our existing portfolio."

A growing team, OTA evaluates research projects at the Medical Center for their therapeutic potential. It also works with OIL to develop funding partnerships with venture capital firms, disease foundations, pharmaceutical companies, and other funding sources to advance the science from basic research to the translation phase, a traditionally underserved stage of development dubbed the Valley of Death. "We are building an engine to increase our share of potential revenue and maximize our success rate," says Dr. Shohdy.

In the past two years, OTA has developed a robust pipeline of more than 17 new drug discovery and development projects in oncology, inflammation, metabolic diseases, and neurodegenerative diseases. Among them is an early-stage drug that could lead to a new treatment for multiple sclerosis, an autoimmune disorder that attacks myelin, the fatty substance insulating nerve fibers. The molecule, advanced with James Salzer, MD, PhD, professor of cell biology, and neurology and neuroscience, helps repair damaged myelin and provides clinical benefit in relevant animal models. "Other drugs tamp down the immune system and slow the progression of the disease, but there's nothing that actually restores function to the nervous system," says Dr. Schneider.

Meanwhile, OTA has also attracted significant extra funding for NYU Langone researchers. Among those efforts, it helped secure a $2 million grant from the National Institutes of Health to help Ann Marie Schmidt, MD, PhD, the Iven Young Professor of Endocrinology and director of the Diabetes Research Program, develop drug candidates targeting a cell receptor known as RAGE, or Receptor for Advanced Glycation End Products, which is a key driver of vascular complications in diabetes such as nephropathy, retinopathy, and neuropathy.

"What makes the OTA model so satisfying is that it allows researchers to capitalize on a lifetime of research and see their work benefit patients," says Dr. Schneider. "It's what researchers live for."

The OTA team (left to right): Anne Koralova, PhD, Robert Schneider, PhD, and Nadim Shohdy, PhD

Illustrations: Ennead Architects. Photograph: Rene Perez.

Building for the Future

The Dramatic Expansion of Laboratory Space Marks a Decisive Turning Point in NYU Langone's History

1 New lab space in the West Tower of the Alexandria Center. 2 Artist's rendering of the new biomedical research building set to open in 2017. 3 The building will feature spacious, state-of-the-art lecture halls and 4 a light-filled lobby with ample seating.

The signs of growth are hard to ignore on the southeast corner of the NYU Langone Medical Center campus. There, along East 30th Street and the FDR Drive Service Road, the steady thrum of construction work signals progress on one of our newest additions: a 16-story facility for biomedical research. Set to open in 2017, the expansive 365,000-square-foot building is part of a historic campus transformation set to dramatically reshape biomedical research and clinical care at NYU Langone over the coming years.

Combined with 120,000 square feet of gleaming new laboratory space in the West Tower of the Alexandria Center for Life Science, the new construction will house 160 principal investigators and their research teams, boosting laboratory capacity at the Medical Center by 25 percent. "It's all part of our goal of becoming among the top five research institutions in the nation," says Laura Ahlborn, vice president for science strategy.

The opening of the new research building coincides with the completion of the Helen L. and Martin S. Kimmel Pavilion, an 800,000-square-foot facility that will connect to the fully refurbished Tisch Hospital. The Kimmel Pavilion will add 374 private inpatient rooms, 30 procedure rooms, and the Hassenfeld Children's Hospital, the only one of its kind in New York City to offer all private rooms.

In many ways, the design of the research facility mirrors the culture of research at NYU Langone: inventive, forward thinking, and collaborative. The building completes the Medical Center's research quad, connecting the Smilow Research Center and the Medical Science Building. This integration, core to the design, facilitates the physical interaction of researchers, clinicians, and students. Each of the 10 floors of wet-bench laboratories will feature shared space and equipment, and a bridge will unite conference centers in the new research building and Smilow. "The idea is to encourage the spontaneous interactions and interdisciplinary collaborations that so often seed scientific discovery," says Vicki Match Suna, senior vice president and vice dean for real estate development and facilities.

The new building will support all aspects of biomedical research. A state-of-the-art vivarium will occupy a floor and a half. Another two floors will be devoted to seminar rooms, multipurpose classrooms, conference rooms, and other facilities that support academic programming at the Medical Center. Meanwhile, the building will also house the NYU Neuroscience Institute. Led by Dr. Richard Tsien, DPhil, the Druckenmiller Professor of Neuroscience, and Chair of the Department of Physiology and Neuroscience, the Neuroscience Institute brings together more than 250 basic and translational scientists with clinicians to tackle some of the most pressing challenges in neuroscience, from Alzheimer's disease to epilepsy to multiple sclerosis and malignant brain tumors.

With LEED Gold certification from the U.S. Green Building Council, the new building will showcase the Medical Center's commitment to sustainable infrastructure. The facility will draw most of its energy from a new cogeneration plant on campus, known as the Energy Building. A glass curtain wall with louvered sunshades will cut glare in the laboratories while reducing thermal heat and conserving energy. A highly efficient HVAC system will dramatically reduce energy costs, while a graywater system will harvest rainwater for flushing fixtures.

Finally, the new building's dramatic double-height lobby, flooded with natural light, will provide an attractive new entrance to NYU School of Medicine, which welcomes the space as a means to accommodate a growing number of recruits and projected growth in funded research.

HONORS

7
Howard Hughes Medical Institute
Investigators

10
Institute of Medicine
Members

11
National Academy of Sciences
Members

9
American Academy of Arts and Sciences
Members

17
American Association for the Advancement of Science
Fellows

STUDENTS

79
MD/PhD

272
PhD

25
PhD Recipients
in 2015

RESEARCHERS

400
Research Faculty

38
New Faculty
in Calendar Year 2014

400
Postdoctoral Fellows

FACILITIES AND PEOPLE

550,500
Square Feet
of Research Space

220
Laboratories

55
Countries
Represented in Research Labs

PUBLISHED RESEARCH

4,053
Original Research Papers
That Appeared in Science and Medical Literature in Calendar Year 2014

339
Publications
That Had an Impact Factor of at Least 10

OFFICE OF INDUSTRIAL LIAISON

NYU School of Medicine Figures*

+$1B
Total Amount Raised
by Startups

705
Patents Issued

52
Startups
Formed

#1
in License Income

24
Biomedical Products
brought to Market

58%
Increase in School of Medicine Licenses
in FY14

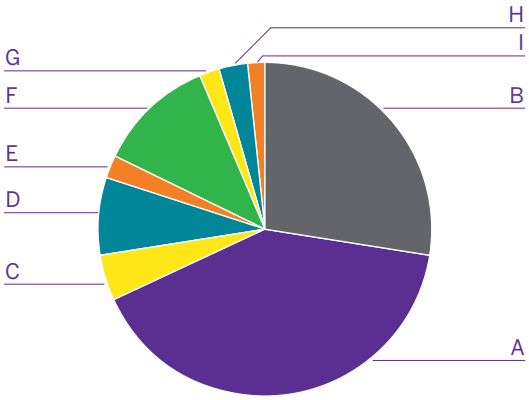
* These numbers are cumulative and do not include activities from other NYU Schools.

FY2014 GRANT REVENUE

$284,463,000

FY2014 AWARDS BY SOURCE

1,452 Total Number of Awards

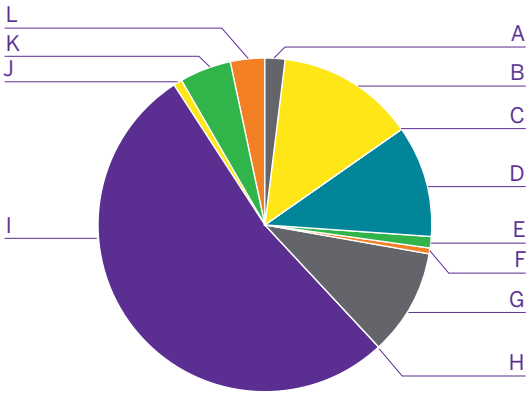


A	NIH: Non–Sandy Relief	40.8%*
B	NIH: Sandy Relief	27.6%
C	NIH: Subcontract	4.2%
D	Federal: Non-NIH	7.5%
E	Federal Non-NIH: Subcontract	2.4%
F	Foundation/Not-For-Profit	11.4%
G	Industry/For-Profit	2.0%
H	State Government	2.7%
I	Nonfederal: Subcontract	1.5%

*Percentages by dollar amounts

FY2014 NIH AWARDS

603 Total Number of Awards



A	Career Development	2.2%
B	Construction	13.1%
C	Contract	0.2%
D	Cooperative Agreements	10.7%
E	Institutional Training and Director Program Projects	1.2%
F	International Research Training Grants	0.4%
G	Program Project/Center Grants (P Series)	10.3%
H	Research Development Center	0.1%
I	Research Grants	52.8%
J	Research-Related Programs	1.0%
K	Resource Grants/Programs	4.9%
L	Training and Fellowships	3.2%

New Nonfederal Funding of $100,000 and Above*

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Alex's Lemonade Stand Foundation
Alfred P. Sloan Foundation
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American Association for Cancer Research
American Brain Foundation
American Cancer Society
American Heart Association
American Medical Association
American Society of Hematology
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J. Weinstein Foundation, Inc.
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Anonymous (1)

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