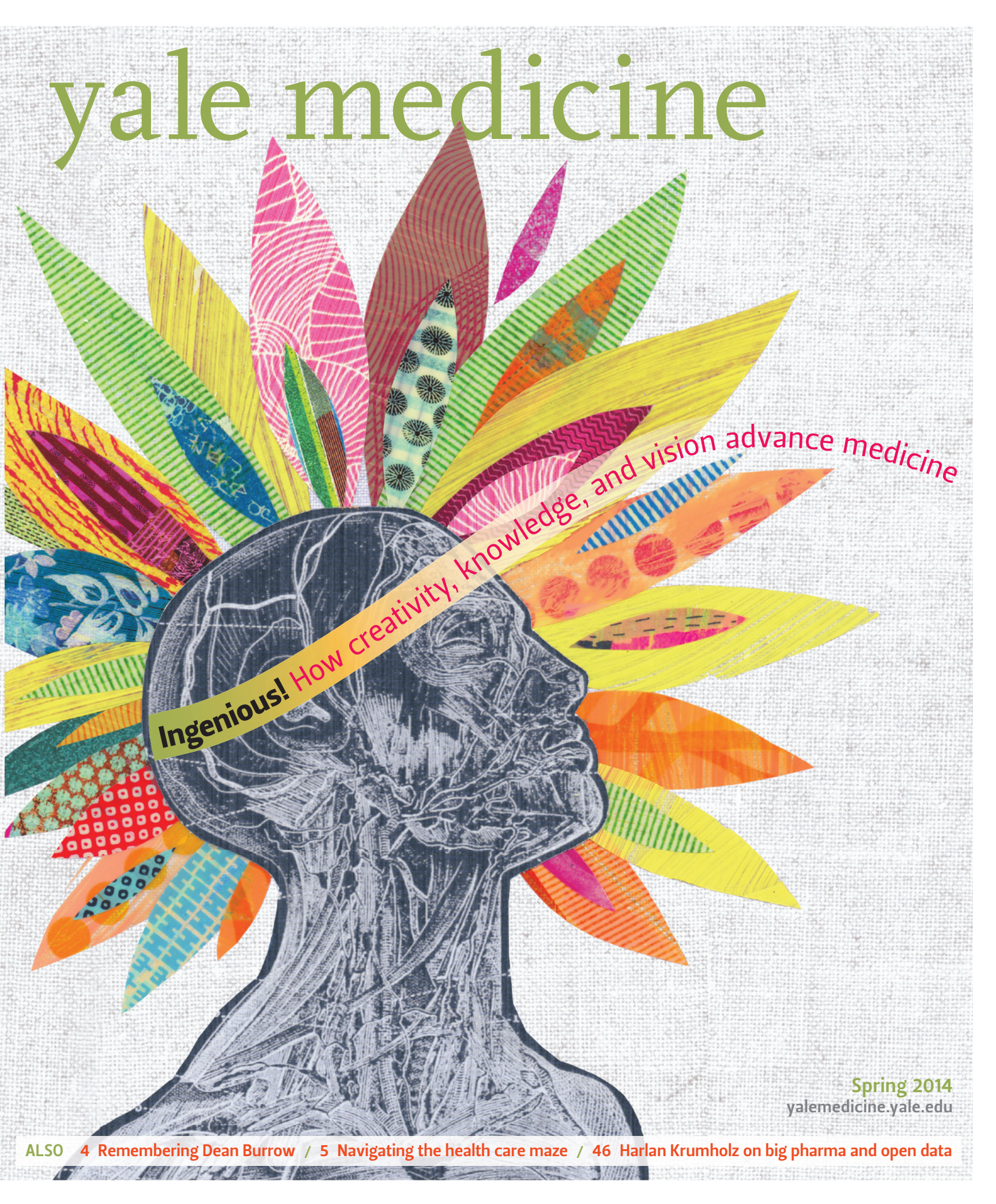


# yale medicine



**Ingenious!** How creativity, knowledge, and vision advance medicine

Spring 2014  
yalemedicine.yale.edu

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## from the editor

### The elusive word

This is the second issue of *Yale Medicine* dedicated to a single theme. But as we edited, revised, and reworked the feature articles, it became clear to us that our initial theme, invention, was not quite right. Our feature on Rong Fan and his microchip does indeed chronicle the invention of a new medical and research tool. And our article on the Yale Center for Biomedical and Interventional Technology describes how scientists from different disciplines converge to craft new medical devices. But the story of how the iPad and the iPad mini are

changing medical education is more about serendipity and a willingness to seize unexpected opportunities. We also tell about a patient willing to undergo a rare heart procedure in order to avoid having a heart transplant or a pump installed in his chest. The last two were not exactly about invention, but they are stories about people who subscribe to the notion that chance favors the prepared mind; about people who are willing to try something new or different. We needed a less trite way to say "thinking outside the box."

We consulted dictionaries and a thesaurus. We looked online for articles and references to creativity and ingenuity. We talked with experts on the subject. Still, that one incisive, inclusive word that would

define the magazine's theme eluded us. Because we are a small shop, we all have other things to do. That allowed us to abandon the search for the missing word from time to time and dedicate ourselves to other tasks. And as we know from experience, as well as from the experts (see our introductory essay on page 10), inspiration often comes when it's least expected; when ideas have had time to germinate in the back of one's mind. We regrouped regularly to check in on the status of the magazine, and at one of those sessions, the word came to us. Not surprisingly, it had long been on a list gleaned from dictionaries and online sources. Ingenious!

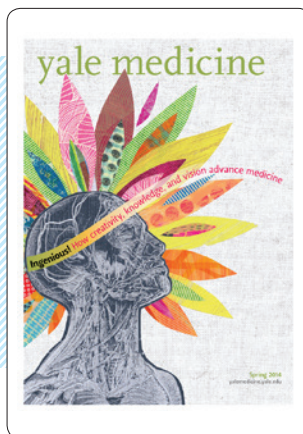
John Curtis  
Editor, *Yale Medicine*

### SECOND OPINION BY SIDNEY HARRIS



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Abbreviations used in *Yale Medicine* include HS to denote the final year of residency for house staff, FW for the final year of a fellowship, and YNHH for Yale-New Haven Hospital.

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## “Successful investigators often have a sixth sense”

INGENUITY AND CREATIVITY, qualities essential to advancing scientific and medical knowledge, are the focus of this issue of *Yale Medicine*. We spoke with Dean Robert J. Alpern, M.D., about how institutions can promote such an atmosphere.

**How does a medical school foster creativity? What are the conditions that make innovation likely?** There are a number of ways to enhance creativity. First and most importantly, you recruit the best people, who have a track record of creativity. Second, you provide an environment with opportunities for significant interactions, and you make certain they receive outstanding mentorship early in their career. Third, you provide access to the best technologies. And then you let them loose and see what they accomplish.

**When you recruit faculty, are you thinking about how they will interact? What do you think makes those interactions creative and productive?** The goal is to recruit people who will have varied skills and knowledge and can facilitate each other’s research. The best collaborations are between people who share a common interest yet have very diverse training. I think that’s the key thing for a medical school, to bring together faculty with different backgrounds, different expertise, but enough of a common interest that they want to talk to each other.

**It has been said that successful people actually fail more than others. Is failure an essential part of the scientific process?** Not necessarily. I think a courageous investigator should not be afraid to fail, and clearly the science that will be of the greatest impact runs the greatest risk of failure. But successful investigators often have a sixth sense that enables them to know what will likely succeed or fail, and to know when to abandon a failing approach.

**Is framing the right question in research a matter of imagination?** I think imagination is one part of it. Like any creative person, whether you’re an artist or do research, you need a knowledge of the tools, some imagination, and a sense of what is likely to be the best path to pursue.

**That last bit is both judgment and maybe a bit of intuition as well.** Yes it is both. There have been times in my research career when I had an idea and I just knew it was going to be positive, even though there was no basis for me to know that. In those cases, it most often turned out to be positive.



## “An honorable person who really cared about Yale”



The late Gerard Burrow, the medical school's 14th dean, is remembered for his kindness, friendship, and medical legacy.

AT A MEMORIAL SERVICE for the medical school's 14th dean on January 17, friends, family, and colleagues honored a devoted academic physician who tweeted about iodine deficiency and cared for a whale with renal failure. They remembered a fun-loving man who cheered the animals at Mystic Aquarium's sea lion shows; sported a fake earring at reunion; and relished sailing and tennis. And they recalled a kind mentor who was unfailingly supportive of colleagues.

Gerard N. Burrow, M.D. '58, HS '66, died on December 14 at the age of 80. He served as dean of the medical school from 1992 until 1997, when he became the David Paige Smith Professor of Medicine Emeritus and professor emeritus of obstetrics, gynecology, and reproductive sciences. He had also published widely in the field of endocrinology. But Burrow is remembered as much for his warmth, humor, and remarkable range of outside interests as for his medical accomplishments.

“He was a brilliant academician,” Dean Robert J. Alpern, M.D., Ensign Professor of Medicine, said in an interview, and “an honorable, gentle, nice person who really cared about Yale.”

Burrow's son Peter put it another way, calling his father “a people's dean.”

When Burrow accepted the deanship, recalled Michael Kashgarian, M.D. '58, HS '63, FW '65, his best friend since medical school, he “brought a new atmosphere to the school.” Burrow worked to improve relations between the basic science and clinical departments, and to strengthen ties to Yale-New Haven Hospital, said Kashgarian, professor emeritus and senior research scientist in pathology.

A strong believer in the Yale system, Burrow wrote in 1999 that modern medicine continues to require a “liberal arts physician.” Such a physician, the

object of the Yale system, he wrote, is trained in science and the values of medicine, prepared for uncertainty, and able to adapt. He had previously expressed concern that medical schools in the 1990s were being forced to “carry out worldly business ... such as industry-directed clinical trials and increasing amounts of purely clinical practice,” potentially blurring their academic focus. “He probably was the last of a group of medical school deans from an era when academic medicine was simpler, more idealistic, and less of a business,” Alpern noted.

Though not always at Yale, Burrow maintained connections to the school throughout his career. He helped to set up a high-risk obstetrics clinic at Yale–New Haven Hospital, raised money for a fitness center in Harkness Dormitory, and led the board of trustees of the Cushing–Whitney Medical Library. He also wrote *A History of Yale’s School of Medicine: Passing Torches to Others*. One of Burrow’s metal sculptures, made when he took up welding as a hobby, resides at Yale–New Haven Hospital.

After completing his residency at Yale in 1966, Burrow joined the faculty and remained at Yale for the next 10 years, leaving for the University of Toronto in 1976. From 1988 to 1992, he served as dean of the UC San Diego School of Medicine, where he oversaw major infrastructure projects and recruited distinguished

scientists—and sat on a stool over a pool of water for the annual Dunk-a-Dean event. (“History does not record,” said his son Peter, “how many times I stood in that line.”)

Burrow was an authority on iodine deficiency as well as on thyroid and other medical disorders during pregnancy. Early in his career, he had studied the prenatal effects of the Nagasaki bombing with the United States Public Health Service in Japan. What he learned there sparked a lifelong interest in maternal and fetal health that led to dozens of publications over the ensuing decades. He co-authored a book on thyroid disease with Kashgarian, and also wrote a popular reference work on medical disorders of pregnancy that ran to six editions.

After retiring from Yale, Burrow chaired the board of the UConn Health Center. He also became president and CEO of Sea Research Foundation, the parent organization of Mystic Aquarium. He helped establish a formal research program there, offering one veterinarian a plastic beluga whale to which he’d attached a clay thyroid gland as a suggestion for a research topic. The aquarium’s Animal Parent program, which invites supporters to adopt a whale, penguin, or other aquarium animal, inspired Burrow to set up an Adopt-a-Rare-Book program at the Medical Historical Library.

An aquarium colleague, Tracy Romano, Ph.D., recalled the day



Burrow took her sailing shortly after she was hired. He handed the inexperienced Romano the helm, showing a faith in her ability that buoyed her. “He made everyone feel important and special,” Romano said. “His biggest contribution was the passion he had for life, and the compassion he had for people.”

—Jenny Blair

Throughout his career, Gerard Burrow maintained strong connections to the School of Medicine, even writing a history of the school.



## Navigating the health care maze

After his service in the 82nd Airborne Division during the Vietnam War, Michael Joseph (not his real name) went into free fall. A one-two punch of PTSD and alcoholism left him chronically homeless and unable to take advantage of the health benefits available to veterans.

In 2012, when emergency room doctors sent Joseph to the VA Connecticut Healthcare



REMEMBRANCE

Throughout his tenure on the faculty of the School of Medicine, when he also served as deputy dean for education, Robert Gifford, M.D., HS '67, was known for the poems he wrote. At the memorial service in January, Gifford remembered his friend and colleague Gerard N. Burrow, M.D. '58, HS '66, in verse:

*I knew him as gentle  
and generously kind.*

*Quite private with his  
points of view.*

*Conservative? Liberal?  
Something combined?*

*His silence at times  
gave no clue.*

System in West Haven for psychiatric treatment, he met Cheryl Eberg, a VA employee and fellow vet who found him shelter, scheduled his medical appointments, and got him bus passes. With Eberg's help, Joseph, 58, is recovering. "She pretty much keeps up with all aspects of my daily living," Joseph said. Without her assistance, he said, "I'd be outside in the streets, drinking."

Patients overwhelmed by illness, bureaucratic tangles, or insurance problems can benefit from a professional companion like Eberg. She is a patient navigator whose job it is to be a human GPS as well as a motivator and cheerleader. As the name implies, patient navigators help patients find their way through the maze of medical care—they help schedule appointments, arrange

referrals for specialty care, and go to bat for patients with Medicare and Medicaid. Navigators are liaisons between patients and health insurers and providers, who, in addition to scheduling appointments, try to ensure that patients have the means to keep those appointments, finding them a ride when necessary. They try to link homeless people, who often suffer from chronic health issues, with agencies that can help them.

Thanks to a program begun at Gateway Community College and inspired by Suzanne Lagarde, M.D., HS '77, FW '80, a Yale physician, Eberg is among the first certified patient navigators in Connecticut. She was one of 15 students who enrolled in Gateway's initial Patient Navigator Training Program, which started in the fall of 2012 with a grant from the state's Department of Public Health. Since then, four more sections of the class have been offered at Gateway, one offering training for work with cancer patients,

two offering general training, and one offering general training with additional training in colorectal cancer screening. This fall the program will offer training in preventive cancer screenings and diabetes.

"You're riding the crest of a huge wave," Lagarde, who became director of the Fair Haven Community Health Center last year, told the students at the first session of the inaugural class. Lagarde, assistant clinical professor of medicine (digestive diseases), recognized the importance of patient navigators when she helped start Project Access-New Haven, which helps the uninsured and underinsured find pro bono specialty care. "Four years ago, I had never heard of the word. I've become a zealot."

Patient navigation is the brainchild of Harold P. Freeman, M.D., who started a program in New York City in 1990 to clear barriers to detecting, treating, and comforting cancer patients. In 2007, with the help of a \$2.5 million grant, the Harold P. Freeman Patient Navigation Institute was opened to establish standards and practices for the growing profession. Health care providers, Lagarde said, have come to understand that navigators are a cost-effective way to promote health. A navigator can help patients find treatment before they show up in the ER. "Save two or three hospitalizations, and you could have a person's salary for a year," Lagarde said.

## Members of a new profession help patients find their way through the complexities of the medical system.



Four years ago, physician Suzanne Lagarde had never heard of patient navigators. Now, she says, she has become a zealot and helped launch a course for patient navigators at Gateway Community College.



Patient navigators can be especially helpful in dealing with patients who have problems above and beyond their medical conditions, such as the homeless. “People who are homeless cost the system three to six times as much,” said David Rosenthal, M.D., the doctor in charge of a patient-aligned care team that serves homeless veterans at the VA. “They’re frequent users. To try to address that from a medical standpoint without a navigator is to work with a hand tied behind your back.”

Clinics also realize savings, because navigators help patients keep appointments so that devices like MRIs aren’t idle, said Christopher Borgstrom, program coordinator of Project Access. The tandem of patient and navigator “leads to amazing compliance,” he said. No-show rates for the program’s patients have fallen from 30 to 40 percent to just 2 to 4 percent.

When Lagarde approached Gateway officials, they thought the class fit well with the school’s mission—addressing the “changing academic, occupational, technological, and cultural needs of a diverse population,” according to the school’s website. Discussions first centered on training people to help cancer patients through their grueling health care maze, but Victoria L. Bozzuto, Gateway’s dean of workforce development and continuing education, also wanted a class for generic navigators. “You may think you only want to

work with cancer patients, but find you want to work with the homeless,” she said. Interest in the class was “viral,” said Erika Lynch, Gateway’s continuing education coordinator for workforce development.

The program consists of three eight-hour Saturday classroom sessions followed by 24 hours of shadowing patient navigators at work. What defines a patient navigator is “broad,” Lynch said. A navigator, said Lagarde, must be creative, caring, and persistent in dealing with problems that are critical but ancillary to medical care, especially with homeless and mentally ill patients. “You’ve got to accept that there will be many closed doors,” she said. In addition to finding a way through those doors, a navigator must also act “like an Aunt Tilly,” and convince reluctant patients to fill out forms, manage finances, take medications, and show up for appointments. Since many navigators aren’t medical professionals, they must also know their boundaries and not make such clinical decisions as helping patients interpret test results.

Navigators often “come from the same community as the patients they serve,” said Kevin Fiscella, M.D., M.P.H., a professor of family medicine at the University of Rochester and the author of studies showing the benefit of navigators. “This enables navigators to establish a rapport and even a trust—somebody who speaks their

language.” Eberg, for instance, served with the National Guard in Iraq in 2006 and 2007. “I don’t need to know anything else about her,” said another VA outpatient who served in the Army in the Iraq and Afghanistan wars. In Iraq, Eberg was in charge of transportation support operations. Like the Radar O’Reilly character in the television series *M\*A\*S\*H*, she’s skilled at procuring things, like a cell phone for the veteran.

Navigators also provide a shoulder to cry on. When a 48-year-old patient from the Dominican Republic had surgery for bladder cancer there, doctors found another tumor and said her best hope was to get treatment in the United States. She spoke no English, didn’t qualify for Medicaid, and any appointments were months in the future. She wound up in the ER. “I had no guidance, no idea of what to do,” she said.

Edna Cruz-Cedeño and Giselle Carlotta-McDonald, patient navigators at Project Access, found physicians who treated her cancer, which is now under control.

“I had two cancers,” the patient said, “one in the body, and one of just thinking and worrying. That kills you faster.”

“As soon as she walked in the door, I could see it in her face,” Cruz-Cedeño said. “At this point it’s not navigating. It’s just listening.”

—John Dillon



ONLINE EXCLUSIVES

Used wheelchairs and walkers find new homes

A furry friend helps students, staff unwind

A new skill for docs: writing for the public

Med students educate public on Obamacare

Full stories and event photo galleries, as well as other online-only content, can be found on our homepage at [yalemedicine.yale.edu](http://yalemedicine.yale.edu).



## Gene mutation linked to Tourette syndrome

So much of what we do, we do on autopilot—whether tying our shoes or driving the same route to work. Functioning on autopilot frees our attention for other things, but it can also entrap us in inflexible and uncontrollable behaviors that assume lives of their own, said Christopher Pittenger, M.D., Ph.D., associate professor of psychiatry and in the Child Study Center and assistant professor of psychology, who studies how the brain’s cortical-basal ganglia circuits help to automate routine behaviors.

In his clinical work and as director of the Yale OCD Research Clinic, Pittenger realized that many psychiatric disorders ranging from obsessive-compulsive disorder (OCD) and Tourette syndrome to drug addiction entail habits turned into compulsions. These disorders are also all associated with abnormalities in the basal ganglia, a brain region critical to motor control and procedural learning. To discover what is out of balance in a specific circuit, how it got that way, and how to fix it, Pittenger studies affected patients; looks for genetic variations that may contribute to their condition; and observes the effect of those variations in mice to learn something new—with the ultimate aim of exploring the broader relevance of those findings in patients.

But discovering such genetic variants is tricky. Tourette



syndrome, for example, is 50 percent genetic, but it may involve perhaps hundreds of mutations that individually have a minuscule effect; thus, geneticists often search for rare genes with large effects to gain new insights about a disorder.

In 2010, researchers at the School of Medicine found such a gene for Tourette, a syndrome characterized by involuntary repetitive movements and vocalizations called tics. A father and his eight children share this syndrome—and a mutation not found anywhere else in a gene called *HDC*. *HDC* normally codes for an enzyme that helps produce histamine, a signaling molecule associated with allergies. Histamine also relays messages between neurons; it was the loss of this neurotransmitter function that seemed to cause Tourette in this family.

Pittenger’s team reported in the January 2014 issue of *Neuron* that the *HDC* deficiency in mice disrupts the basal ganglia,

which increases signaling by dopamine, a neurotransmitter associated with habit formation, Tourette, and other psychiatric disorders. Mice with the mutation twitched their noses, sniffed, and groomed in a “rapid, repetitive and purposeless way, paralleling human behaviors.” But the tic-like behaviors disappeared when the mice received haloperidol, a drug that can lessen Tourette symptoms by blocking some effects of dopamine. When researchers infused histamine into a mouse’s brain in another experiment, the infusion reversed the symptoms.

“That proved that the *HDC* mutation caused the disorder in these mice,” Pittenger said. “The mutation is so rare that it cannot be the cause of Tourette in most people, but it’s a foot in the door for learning more about the disorder.” For example, *HDC* deficiency in mice causes abnormalities in the levels of dopamine receptors. When Pittenger went back to the family with the rare *HDC* mutation, PET brain imaging showed a similar irregularity in dopamine receptors. Now he is asking whether this irregularity occurs in other Tourette patients and if so, what causes it.

“We’re optimistic that using this method again and again, we’ll find previously unknown characteristics of Tourette that we can target with new treatments. We’re not there yet, but it’s an exciting first step.”

—Cathryn Delude

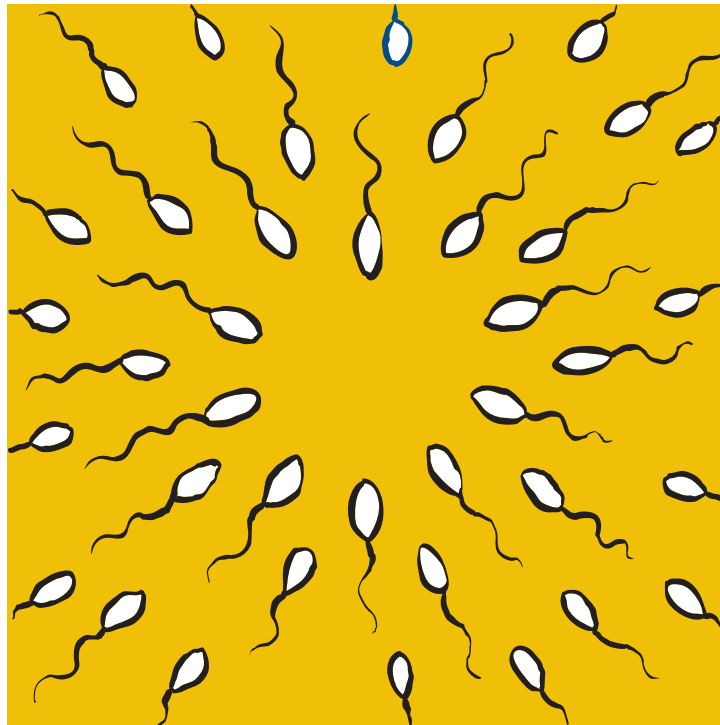
# round up

a collection of recent scientific findings



## WHO'S IN THE IN-CROWD?

Being in with the in-crowd is the result of a couple of simple and well-established psychological principles that govern how we form allies and enemies, according to researchers at Yale and the University of North Carolina. We like people who are nice to us. And we like friends of our friends—and dislike our friends' enemies. The researchers used a computer model—with just 80 lines of code—to show that these two ingredients form the recipe for “us versus them,” and published their findings in the journal *Psychological Science*. David Rand, Ph.D., assistant professor of psychology, economics and management, was a co-lead author of the study.



## MEN'S FERTILITY NEEDS MORE RESPECT

When it comes to reproduction, men just don't get the attention they deserve. How women's health affects fertility has long been studied. Much less, however, is known about how men's health affects reproduction, according to Rene Almeling, Ph.D., assistant professor of sociology, and co-author Miranda R. Waggoner, Ph.D., a postdoctoral research fellow at Princeton. Even though family

history and health habits matter for men as well as women, the only place men are likely to get counseling on the topic is a sperm bank, say the researchers, whose findings appeared in December in the journal *Gender & Society*. This relative lack of attention to men leaves questions unanswered, including how men's reproductive contributions are understood.



## EASING PAIN WITH TARANTULA VENOM

A protein in the venom of the Peruvian green velvet tarantula blunts activity in pain-transmitting neurons, Yale scientists have found. The new screening method the scientists used to identify the protein has the potential to scour through large numbers of spider toxins in search of safe pain drugs and therapies. “The likelihood is that within the vast diversity of spider toxins we will find others that are active against other channels important for pain,” said Michael Nitabach, Ph.D., J.D., associate professor of cellular and molecular physiology and of genetics, and senior author of the paper published in the journal *Current Biology* in March.

## 50 YEARS OF ANTI-SMOKING EFFORTS HAVE SAVED LIVES

Anti-smoking measures that began after U.S. Surgeon General Luther Terry warned of the dangers of smoking 50 years ago have saved as many as 8 million lives, according to a Yale study published in January in *JAMA: The Journal of the American Medical Association*. According to first author Theodore R. Holford, Ph.D., the Susan Dwight Bliss Professor of Public Health (Biostatistics) and professor of

statistics, along with researchers from the National Cancer Institute's Cancer Intervention and Surveillance Modeling Network, the surgeon general's 1964 report was pivotal in changing attitudes and behaviors related to smoking. In addition to the now-familiar warnings placed on cigarette packages, taxes on tobacco have increased, advertising is restricted, and public smoking areas are limited.



# Ingenious!

How creativity, knowledge,  
and vision advance medicine

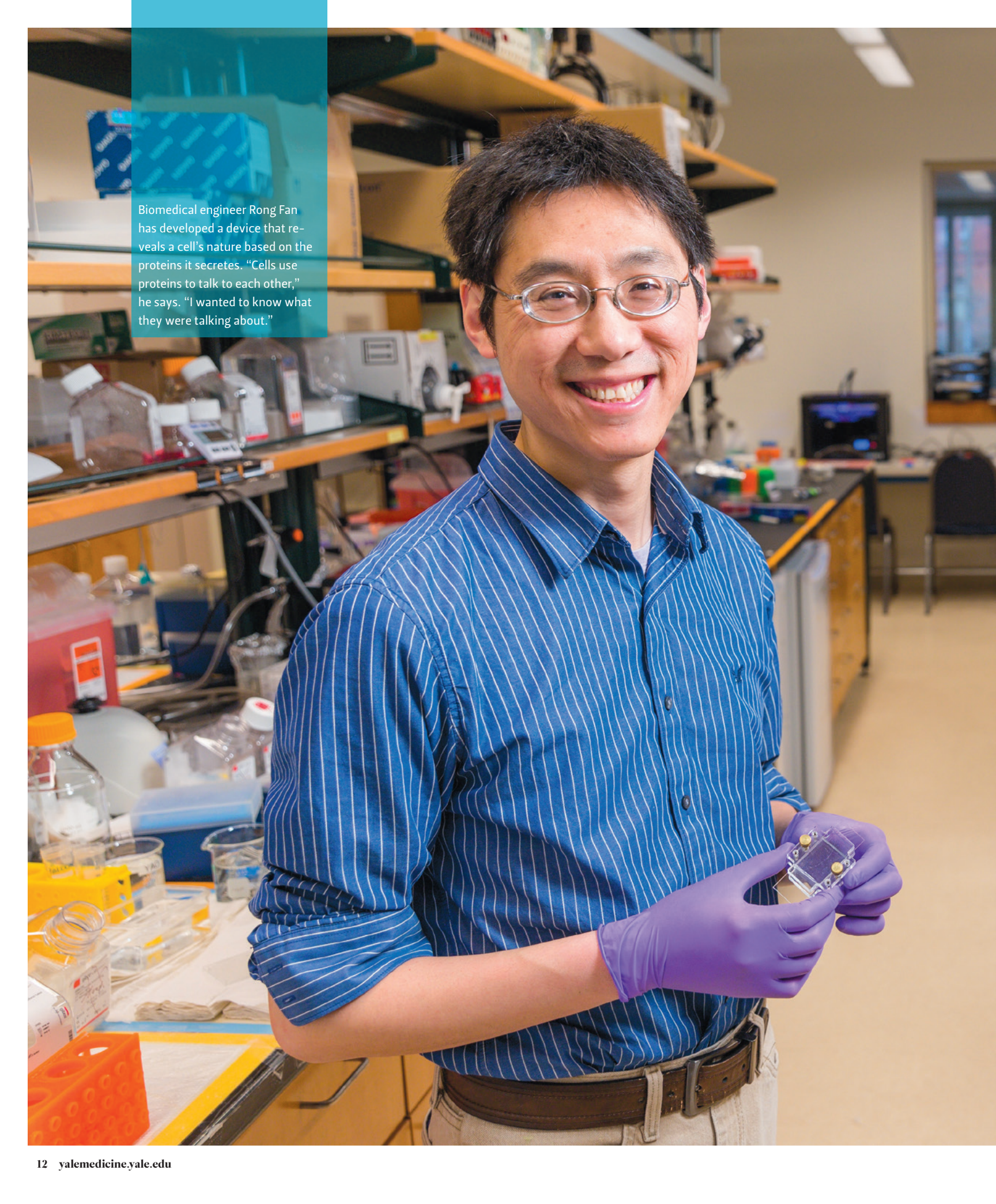
WHEN WE IMAGINE ARCHIMEDES jumping out of his tub, shrieking “Eureka!” and running naked through the streets of Syracuse to celebrate his discovery, we miss the point. His eureka moment was not a sudden inspiration, but rather the culmination of hours, days, weeks, even months of letting a problem gestate in his mind. And it was no accident that the ancient Greek scholar’s epiphany came while he was soaking in a hot bath.

A key to creativity, according to R. Keith Sawyer, a psychologist at the University of North Carolina who studies creativity and innovation, is to follow up periods of intense study and research by letting your mind relax, wander, and imagine. Work hard, take time off, play, get your mind off the problem, and let it incubate. No wonder that Archimedes’ discovery—he saw the water level rise as he sank into the tub and realized he’d found a way to measure the volume of irregular objects—came when he was relaxing. John Lennon once described struggling for hours to write a song before giving up in frustration. He sacked out on a sofa and, in short order, the lyrics and melody to “Nowhere Man” came to him almost fully formed. (As the Beatle would sing in a different song, “Turn off your mind, relax, and float downstream ...”)

Creativity starts with asking the right question, being receptive to solutions all around us, being willing to combine different ideas, and freeing the mind to imagine. In this issue of *Yale Medicine* we look at how clinicians, scientists, and educators at Yale have come up with creative solutions in surprising ways: Tiny machines that can decipher how cells talk to each other; an iPad app that has created a new dynamic in the classroom and in clinical clerkships; and a controversial procedure to treat aneurysms and spare patients a heart transplant. And the new Center for Biomedical and Interventional Technology creates a seemingly unlikely consortium of engineers, clinicians, and scientists to brainstorm new ways of developing medical devices.

**12 A new device deciphers the language of cells / 20 Building a better mousetrap / 26 Medical invention incubator**





Biomedical engineer Rong Fan has developed a device that reveals a cell's nature based on the proteins it secretes. "Cells use proteins to talk to each other," he says. "I wanted to know what they were talking about."

A photograph of a laboratory. A woman in a light blue lab coat is standing at a lab bench, wearing purple gloves and working with equipment. The lab bench is cluttered with various pieces of laboratory equipment, including pipettes, bottles, and a laptop. Shelves above the bench are filled with boxes and other supplies. A window is visible in the background on the left.

# A new device deciphers the language of cells

A biomedical engineer listens in on what  
proteins are saying.

By Bruce Fellman Photographs by Robert Lisak

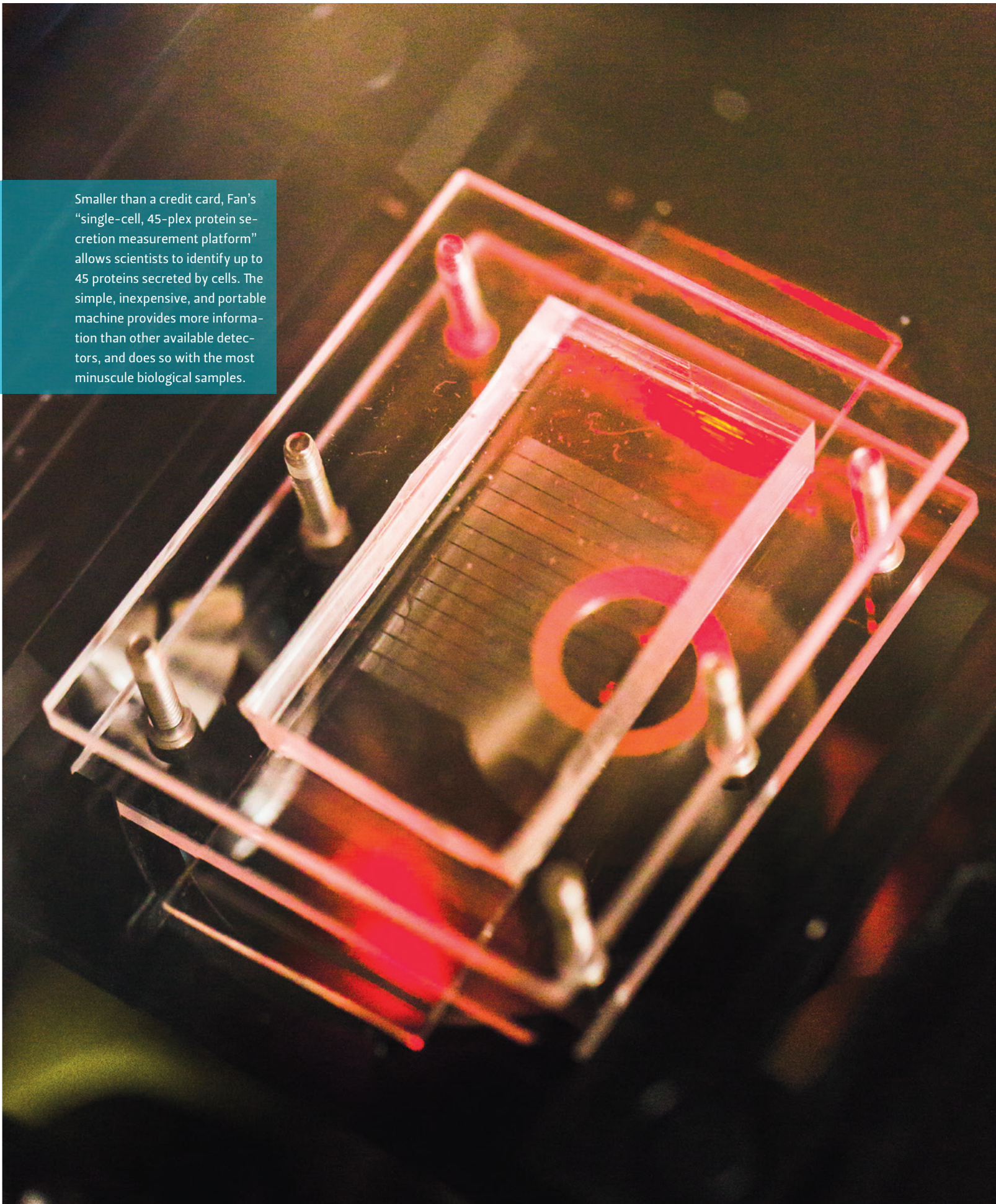


# As inventions go,

Yale biomedical engineer Rong Fan's entry into the innovation sweepstakes is not much to look at. Fan's device, impressively named a single-cell, 45-plex protein secretion measurement platform, seems to be little more than a sandwich of two sheets of clear silicon rubber the thickness of window glass, each sheet a bit smaller than a credit card and bearing a smaller, darker rectangle divided into 14 vertical sections. It has no flashing lights, no intriguing noises, no moving parts, no signs of Applesque high design. Indeed, the object, displayed in Fan's bustling laboratory on the first floor of the Daniel L. Malone Engineering Center, doesn't appear to be doing anything at all.



Smaller than a credit card, Fan's "single-cell, 45-plex protein secretion measurement platform" allows scientists to identify up to 45 proteins secreted by cells. The simple, inexpensive, and portable machine provides more information than other available detectors, and does so with the most minuscule biological samples.



Fan has formed a company, IsoPlexis, to commercialize his device. Kara Brower, a recent Yale College graduate who worked in Fan's lab, is the company's chief technology officer. Collaborators at Yale, other universities, pharmaceutical companies, and government labs are already using Fan's invention.





Appearances deceive. Fan, a soft-spoken wizard of the nanorealm, has crafted an unprecedented way to trap individual cells as they travel highways only a billionth of a meter wide. In that same device, the engineer has incorporated a technology akin to super-market barcodes that enables him to learn and listen to the language of cells. Collaborators at the School of Medicine and other universities, pharmaceutical companies, and government laboratories are starting to use Fan's invention to uncover the hidden details of the cells' stories. These investigations—all in their early stages—could help scientists make medical discoveries that lead to more effective vaccines, precision-targeted medications, a better understanding of autoimmune diseases, and even optimal strategies for diagnosing and treating such perplexing ailments as prostate cancer, glioblastoma, and myeloproliferative disorders.

"The potential applications are very broad," said Fan, who has spun off a company called IsoPlexis to commercialize the device. "We're entering the era of cellular medicine."

#### HOW CELLS TALK TO EACH OTHER

Human cells come in many shapes and sizes. In recent years, scientists have discovered that they can identify and characterize cells in both the immune system and in tumors by the suite of proteins they secrete. This proteomic signature, which may have dozens of individual components, gives researchers and physicians alike important clues that they can use to, say, zero in on the cells that are instrumental in producing the right immune system response or those in a tumor that reveal its intentions, its vulnerabilities, its response to treatment, and its likely future direction. For example, in a patient diagnosed with a myeloproliferative neoplasm (MPN)—a chronic precancerous disorder of the bone marrow—the device could detect which cells in a population are secreting cytokine proteins that signal a high likelihood of MPN's morphing into leukemia. In theory at least, this early warning could help researchers develop effective drugs that doctors could unleash at a time when a cure is most likely.

"Proteins are just like the words of a language," said Fan. "Cells use proteins to talk to each other, and I wanted to know what they were talking about."

Currently available tools like flow cytometers and mass cytometers do at least part of the listening job, but the devices are expensive and generally found only in major research centers like the School of Medicine. And because existing technologies can detect just a few of

the many proteins secreted by cells, they give researchers sentences with many missing words. Filling in the blanks is vital to understanding cancer and other diseases. "A tumor is like a community—it's filled with all sorts of different cells talking to each other," said Fan.

Getting a complete picture of tumor heterogeneity is important, Fan explained, because "what's happening in the tumor microenvironment often determines the progression of the disease." So Fan devised what is essentially a high-tech listening device—a way to isolate individual cells and record the stories they tell through the proteins they secrete—as many as 45 at a time. Not only can the simple, relatively inexpensive, and eminently portable platform provide more relevant information than any available detector, it can do so with the most minuscule of biological samples: a drop of blood or a tiny bit of tissue from a fine-needle biopsy.

"With the handheld device we're refining, we may be on the verge of an important transition in medicine—from qualitative to a much more quantitative analysis of a patient's response to treatment," said Kara Brower, a 2013 Yale engineering grad who worked in Fan's lab and is presently chief technology officer of IsoPlexis.

#### FROM CHEMISTRY TO NANOTECHNOLOGY

It's too early to know whether Fan and his company have a game changer. But the fact that he's in the game at all is something that few people, Fan included, would have predicted when he was growing up in China. "My interest in science was driven simply by curiosity," he said, adding that when he came to the United States as a graduate student at the University of California, Berkeley, he had "very little interest in biology or biomedical research."

At Berkeley, Fan pursued a doctorate in chemistry and focused on better ways to make nanotubes and nanowires. But when he discovered that nature was already working on the scale of a billionth of a meter, Fan became hooked on biology. For his postdoctoral work, he opted for a more applied—and biomedical—career path at the California Institute of Technology and its NanoSystems Biology Cancer Center. There, Fan worked with James Heath, Ph.D., a nanochemist with a penchant for translational medicine and formidable inventive skills. On his lab's website, Heath notes that "we focus on the



fundamental scientific bottlenecks that, if solved, can provide keys toward solving much larger problems.”

Fan would soon find some appropriate bottlenecks to tackle. One came from researchers looking for a better way to evaluate responses to vaccines by putting together a complete profile of the proteins secreted by single T cells. Another came from Fan’s search for devices that could uncover the proteomic fundamentals of cancer cells. In both cases, “the bottleneck was technology,” he said.

Fan realized that the solution lay in the nanotechniques he’d mastered at Berkeley. The proteins secreted by one cell in a normal-size test tube might be too low to detect easily—but put that same cell in a test tube about one-hundred-thousandth the diameter of a human hair, and the concentration of its tell-all secretions increases to the point of readability. “I’m pretty good at making things smaller and smaller,” Fan said.

At Caltech, Fan developed “one sexy-looking machine”—sexy, at least, to a nanoscale engineer adept at crafting minuscule chambers in clear plastic rectangles. The flow of cells was controlled by a pumping system that could handle fluid flow in tiny pipes. The individual cells were then isolated and allowed to interact with specific antibodies in a second micro-chamber to generate what researchers call a barcode, which reveals the individual identities of a multitude of secreted proteins.

The device proved too complicated to use easily, so Fan, who joined Yale’s School of Engineering and Applied Sciences in 2010 as an assistant professor of biomedical engineering, built the proverbial better mousetrap. The new model has some 4,000 micro-chambers, and by rethinking his initial design, Fan eliminated the need for pressure to move cells around. “Now everyone can use this device,” he explained.

#### **NANOBIOTECHNOLOGY REACHES THE CLINIC**

A number of Fan’s colleagues at the medical school are doing just that. Immunologist Joseph Craft, M.D., the Paul B. Beeson Professor of Medicine, professor of immunobiology, and section chief of rheumatology, is working with the engineer to profile the CD4 T cells that play a role in the development of such autoimmune diseases as lupus. Richard Flavell, Ph.D., chair and Sterling Professor of Immunobiology, is using the device to

better categorize cells critical to regulating the immune response. Fan also has developed collaborations with researchers at the Memorial Sloan-Kettering Cancer Center and the National Institutes of Health.

But the partnership with perhaps the most immediate payoff is with Peter Schulam, M.D., Ph.D., professor and chair of urology, and a skilled surgeon who specializes in the treatment of prostate cancer. Fan and Schulam are developing a two-part strategy to better deal with this disease—the most common cancer among men in the United States and the second leading cause of male deaths from cancer.

Prostate cancer poses one of the most difficult health care dilemmas for patients and physicians alike. “Not all, or even most, prostate tumors need to be treated,” said Schulam. “Some are what we call indolent: They won’t grow or spread over your entire lifetime, and they cause no functional problems. But because we can’t currently differentiate the indolent tumors from the aggressive ones—the ones that can kill you—we overtreat.”

Almost every man past 50 has had a digital rectal exam and the controversial blood test that looks for a marker called the prostate-specific antigen or PSA. If the results are suspicious, the patient is sent for a biopsy. If the pathologist assigns what’s called a Gleason score in the intermediate-to-high range to the cellular architecture of the prostate sample, the patient is sent for treatment—typically either surgery to remove the prostate or radiation to destroy the tumor. “But these are not benign procedures, and each has significant morbidities, such as impotence and incontinence, that can radically alter your quality of life,” said Schulam. “So it’s critically important for us to learn how to distinguish patients who need treatment from those who do not.”

The urologist is refining an imaging system that will enable physicians to take targeted biopsies of the prostate, and a subset of those cells will go to Fan’s lab to be placed on the device and characterized. The resulting proteomic profile will, the two researchers believe, enable physicians to more easily—and less subjectively—read the minds of prostate tumors and single out only the bad actors for treatment. “We’re trying to increase our confidence level,” said Schulam. “What excites me most about Rong’s technology is that it gives us the opportunity to address a significant clinical problem and have a potentially great impact.” */yale medicine*

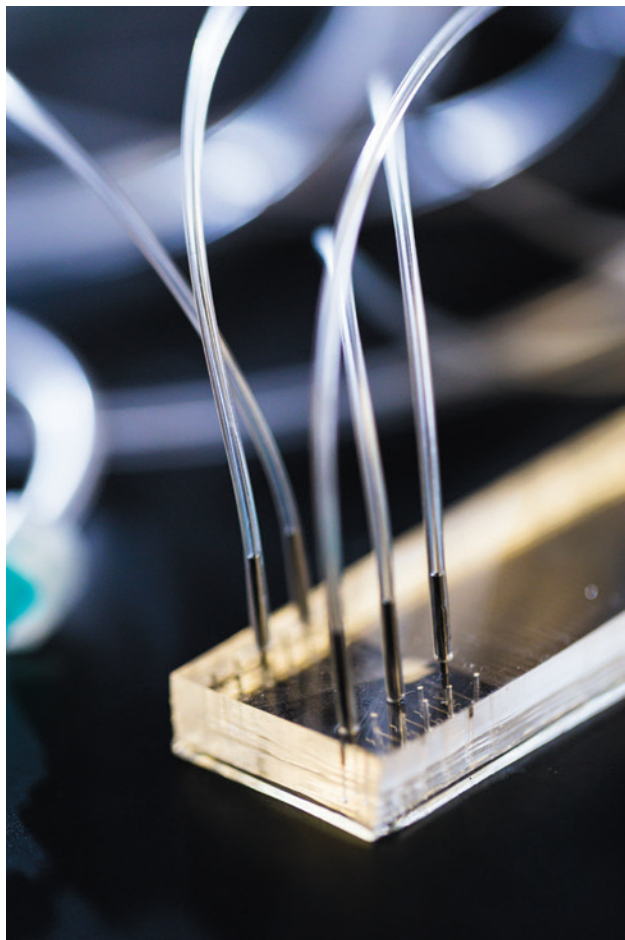
*Bruce Fellman is a freelance writer in North Stonington, Conn.*



In his lab, Fan has multiple manufacturing stations equipped with pressure tubes to make ultra-high-density antibody microarrays. When coupled with a single-cell microchip, a large panel of proteins in individual cells can be measured.

Rong Fan //

“Cells use proteins to talk to each other, and I wanted to know what they were talking about.”



# Building a better mousetrap (and mouse)



The history of innovation in scientific methodology dates to antiquity, with such advances as the astrolabe in ancient Greece and the seismometer in China during the second century C.E. At Yale, it can be traced to the influence of such early figures as Benjamin Silliman, who created the first “modern” science laboratory at Yale in the early 1800s and was one of the founders of the medical school; and Russell Chittenden, who established the first laboratory in the United States for the teaching of physiological chemistry. Both men helped guide the medical school toward a focus on experimental science, uncommon in an era when most physicians received only brief exposure to science during their apprenticeships.

From this environment grew a thirst not only for new knowledge, but also for new tools with which to discover. Over the past 200 years, Yale scientists have devised numerous methods for expanding knowledge and accelerating the accumulation of data—and seeing or measuring things that had been previously beyond comprehension. The milestones that follow are excerpted from the 2010 book *Medicine at Yale: The First 200 Years*, by Kerry L. Falvey, and from other sources including *Yale Medicine* and *Medicine@Yale*. Do you know of an example not on this timeline that could be added to our online edition? If so, write to us at [ymm@yale.edu](mailto:ymm@yale.edu).

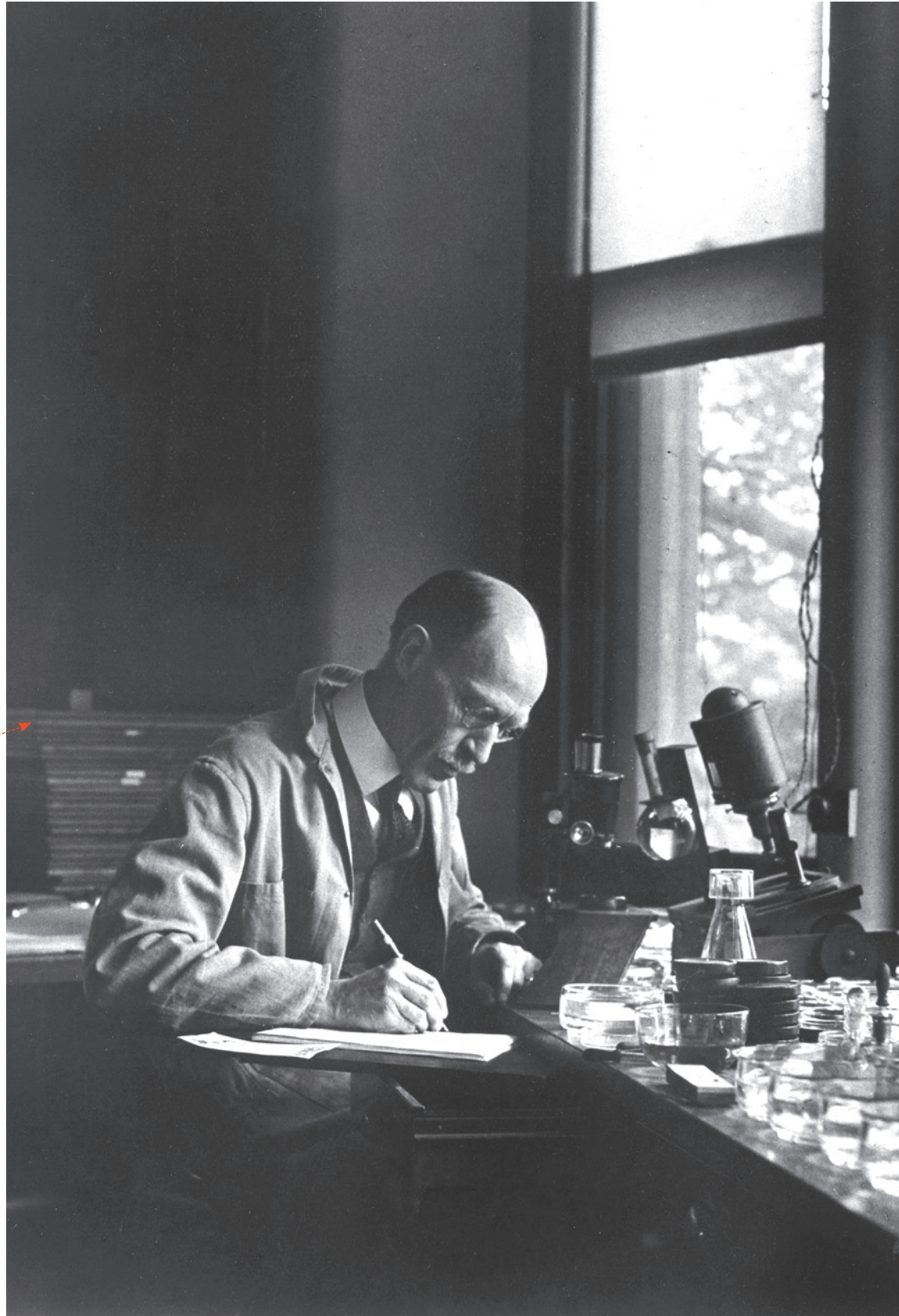
# 1911

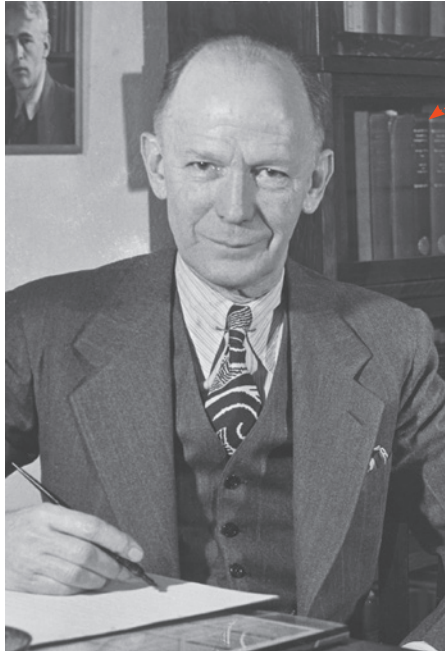
Arnold L. Gesell, Ph.D., M.D. '15, establishes the forerunner of the Yale Child Study Center, and uses a new technique, longitudinal motion-picture studies, to follow child development from infancy through age 6.



# 1917

The Nobel Committee recommends awarding the prize in physiology or medicine to Yale scientist Ross G. Harrison, Ph.D., M.D., but because of World War I, no prize is given. Harrison is recognized for developing the technique of tissue culture, allowing cells to be grown outside the bodies of living organisms. His student, Yale College alumnus John Enders, Ph.D., will win the Nobel decades later for his work growing the polio virus using this method—a development that was crucial to the creation of the polio vaccine (as was work done in the 1940s and 1950s by Yale professor Dorothy M. Horstmann, M.D., FW '43).



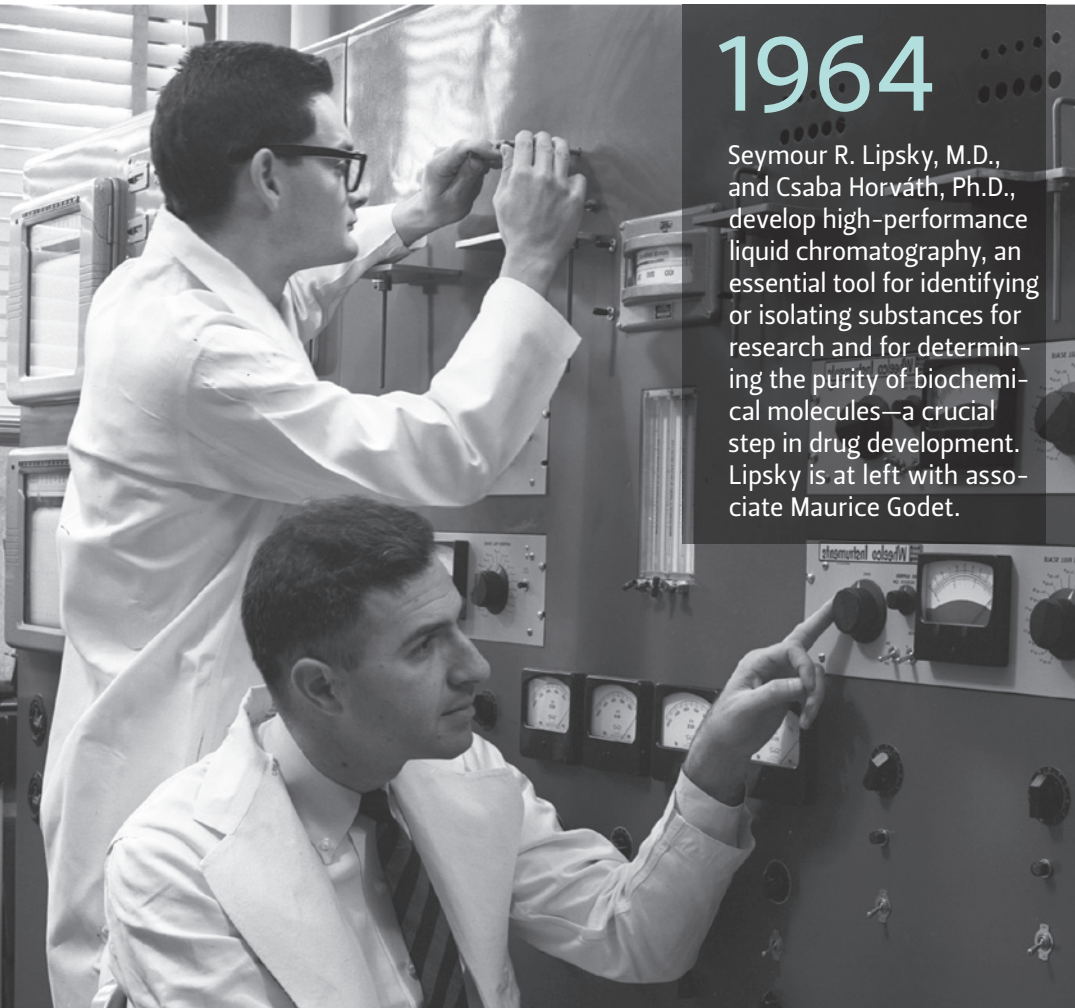


## 1931

John P. Peters, M.D., is the co-author of the text that will become the veritable bible of quantitative clinical chemistry, based on methods he devised to standardize the analysis of blood and urine. As Donald Seldin, M.D. '43, will later write, "The salutary result was a radical transformation of qualitative impressions into precise quantitative measurements."

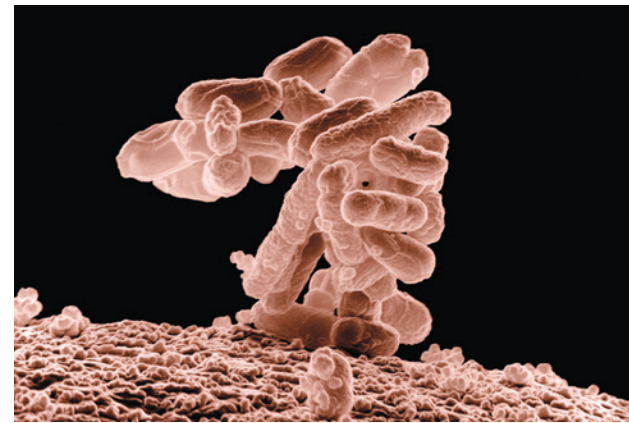
## 1940s

John F. Fulton, D.Phil., M.D., constructs a decompression chamber in his lab during World War II to study the physiologic dangers faced by Allied airmen flying in unpressurized planes at high altitudes. His work leads to better flight suits and education of pilots on the dangers of high-altitude aviation.



## 1964

Seymour R. Lipsky, M.D., and Csaba Horváth, Ph.D., develop high-performance liquid chromatography, an essential tool for identifying or isolating substances for research and for determining the purity of biochemical molecules—a crucial step in drug development. Lipsky is at left with associate Maurice Godet.



## 1963

During his three years as a postdoc in New Haven, Herbert W. Boyer, Ph.D., FW '66, produces two key papers on bacterial genetics that set him on a course as a pioneer in the fields of genetic engineering and biotechnology. Boyer will later team up with Stanley Cohen, M.D., of Stanford to invent methods of genetic recombination for the large-scale replication of human proteins in *E. coli* (above) and establish the world's first biotechnology company, Genentech, in 1976.



# 1967

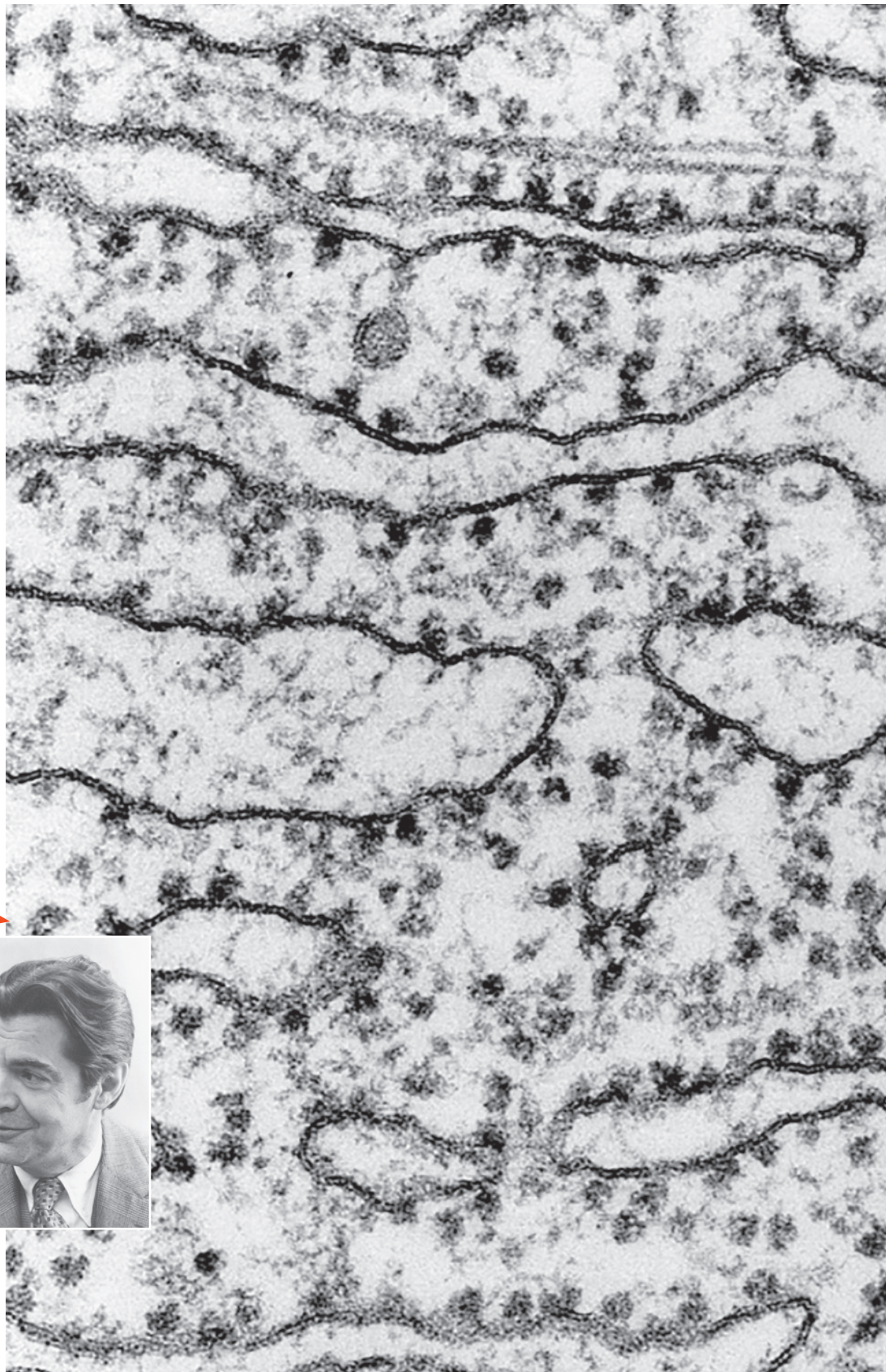
Alvan R. Feinstein, M.D., HS '54, lays out the foundation of the new science of clinical epidemiology in his book *Clinical Judgment*. Feinstein will propose new methods of study design, data interpretation, and the measurement of study outcomes that are the standard in clinical research today.

# 1968

Gerhard Giebisch, M.D., joins the Yale faculty. He and colleagues will devise novel micropuncture and patch-clamp methods to study how the kidney handles potassium—work that is largely responsible for current understanding of the mechanisms underlying regulation of renal potassium excretion.

# 1973

George Palade, Ph.D., comes to Yale from The Rockefeller University, where he created methods that combined electron microscopy with new biochemical strategies to elucidate the fine structure and function of cellular organelles—an unparalleled body of work that laid the foundation of modern cell biology and won Palade the Nobel Prize the following year.





## 1980

Jon W. Gordon, Ph.D. '78, M.D. '80, and Frank H. Ruddle, Ph.D., create the first genetically engineered mouse stably integrating foreign DNA. The so-called transgenic mouse has become an essential tool of biomedical scientists, allowing researchers to add and delete genes in experimental animals in order to observe normal gene function and determine how genetic defects contribute to disease.

## 1992

Richard P. Lifton, M.D., Ph.D., then a fellow at the University of Utah, and colleagues apply the technique of linkage analysis to hunt for genes in the extended families of individuals with rare diseases. This new approach yields one of the first papers showing that a mutation intrinsic to the kidney is critical for blood pressure homeostasis. Lifton will come to Yale in 1993 and identify more than 20 genes associated with blood pressure, cardiovascular disease, and bone density using this method.

## 1992

Robert G. Shulman, Ph.D., and colleagues at Yale turbocharge their outdated MRI system by adding echo planar imaging, enabling one of the earliest functional MRI studies; it will be the first to show the brain responding to individual events, in this case a single visual stimulus. Shulman's team subsequently collaborates with Greg McCarthy, Ph.D., to perform the first fMRI measurements of a person performing a cognitive task.

## 2001

Vincent A. Pieribone, Ph.D., and colleagues identify two corals (*Lobophyllia hemprichii* and *Favites spp.*) that produce fluorescent proteins, which, like jellyfish green fluorescent protein, are used as markers of gene expression. In 2013, they will develop a new molecular probe called ArcLight, which allows one to measure electrical activity of genetically targeted sets of neurons in a living organism, a prerequisite for understanding the complex language of the brain.

## 2005



Tian Xu, Ph.D. '90, and colleagues engineer the *piggy-Bac* transposon in mice. This “jumping gene” makes the mouse a mutant factory: when the animal breeds, the transposon causes random genetic mutations in the mouse’s offspring—one gene per mouse is disabled. Compared to current methods for making experimental mice, known as knockouts, using *piggy-Bac* is 100 times quicker and cheaper. *PiggyBac* also carries a genetic marker to turn the mouse pink for easy identification.

## 2009

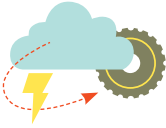
Yale scientists develop a method of whole-exome sequencing that enables the detection of gene variants with a high degree of sensitivity. The approach is also highly efficient in that it examines only complete coding regions, or 1 percent of the human genome. The method is used to diagnose a kidney disorder in a 5-month-old boy in Turkey, the first-ever genetic diagnosis by whole-exome (or whole-genome) screening.

## 2010

A group led by Laura Niklason, M.D., Ph.D., develops a method for creating artificial lung tissue, which succeeds in facilitating gas exchange for a brief period in a rat model. The advance is cited by *Time* magazine as one of the 50 Best Inventions of 2010.

## 2014

Immunobiologists at Yale create a mouse with human versions of genes that are important for innate immune cell development and function: monocytes, macrophages, and natural killer cells. This “humanized mouse model” may be used to mimic the human immune system in scenarios of health and pathology, and may lead to new therapies for human disease.



## Yale debuts an incubator for medical inventions

THINK OF A MORE FORMAL VERSION of a Silicon Valley garage that's also a think tank and fundraiser, and you have an idea of what the new Yale Center for Biomedical and Interventional Technology (CBIT) will do. CBIT is a consortium of engineers, clinicians, and other researchers whose goal is to foster the development of medical devices.

CBIT, said Peter G. Schulam, M.D., Ph.D., chair and professor of urology, is to be “the point of entry for an idea.” He initiated a similar program at UCLA and said that Yale’s center will be a clearinghouse for devices ranging from prosthetic limbs to nanoparticles.

“This center will allow us to have a standard place to go rather than have the faculty hunt around and say, ‘I need a guy with a pump. I need a guy with a circuit board,’” said John Geibel, D.Sc., M.D., vice chair and professor of surgery (gastrointestinal), and professor of cellular and molecular physiology.

Yale has long recognized that inventions cannot live on ideas

alone, and has a veritable alphabet soup of centers to capitalize on them—the Center for Engineering Innovation and Design; the Yale Entrepreneurship Institute; the Office for Cooperative Research (OCR); and the Yale Center for Clinical Investigation. CBIT will partner with all of them, and has also approached the University of Connecticut, the National Institutes of Health, and commercial entities like Eigen, the medical imaging firm in California, and Covidien, the medical technology company located in Connecticut.

The other centers each have areas of expertise, but not the capability to bring a device to fruition, said Thomas Shrader, Ph.D., OCR’s director of strategic corporate alliances. Most importantly, none have the space. Great universities “have lots of good ideas but they’re

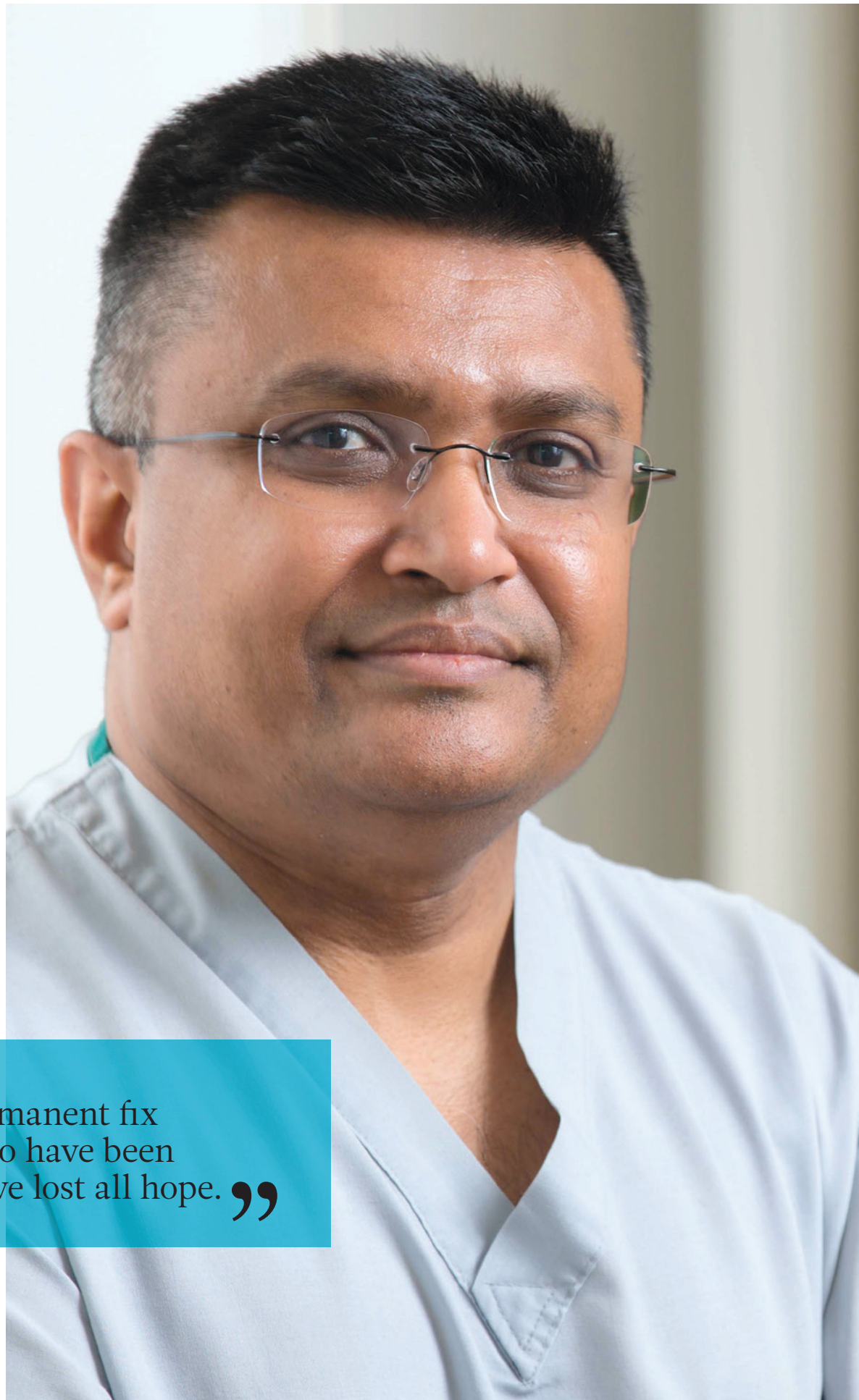
scattered all over the place,” he said. Dedicated lab space will allow engineers to test a physician’s idea to see whether it’s feasible.

W. Mark Saltzman, Ph.D., chair and Goizueta Foundation Professor of Biomedical Engineering, and professor of cellular and molecular physiology and of chemical engineering, said one key aspect is holding workshops with experts from various fields. “That’s hard to do in this field,” said Saltzman, who developed the plan with Schulam. People with skills capable of developing devices “might not be in the same department. They might not be in the same school.”

CBIT will have an executive board composed of experts from the medical, engineering, and management schools that will meet monthly to vet ideas. Once approved, an idea will undergo engineering development. “A lot of ideas get cast aside because you don’t think it’s possible,” Saltzman said. “But a clever engineer might say, ‘This might be possible.’” If the engineers can fashion a prototype, clinicians will put it through clinical or preclinical studies. If it passes these tests, School of Management experts will advise on fundraising and perhaps bringing the device to market. But as Shrader cautioned, “If no one can figure out how to make money on it, it’s not going to be made.”

—John Dillon





Pramod Bonde //

“This can be a permanent fix  
for those patients who have been  
so sick and have lost all hope.”

# Old problem, new tools

Cardiovascular surgeon Pramod Bonde takes an unconventional approach to repairing aneurysms, sparing some patients transplants or implants.

By Colleen Shaddox   Photographs by Harold Shapiro



# Lucian Capozzo spent a lot of his time

in intensive care cracking jokes, and he's still at it as he sits in the kitchen of his Wallingford home in February. "I need one more hospital stay to get down to 160," he said—a jibe at his struggle to lose weight. Between the jokes a story emerged about his massive heart attack last year and the surgery and rehabilitation that followed. He finally grew serious when he talked about his children—Frankie, 13, and Marissa Rose, 9—whose pictures decorate the refrigerator, the walls, and every shelf of the family's home. When doctors told him he'd need a heart transplant, his thoughts flew to them. "Am I going to see them graduate high school?"







Today Capozzo, 48, is back at work, and in his spare time shoots baskets with the kids. He's planning family trips to Disney World and the Jersey shore and looking forward to more distant milestones, like sending his children off to proms and dancing at their weddings.

Capozzo was in heart failure in early 2013 when he was referred to Pramod Bonde, M.D., assistant professor of surgery, for a left ventricular assist device (LVAD) as a bridge to transplantation. The device keeps the heart pumping until a donor heart becomes available—if the patient is fortunate. More than 10,000 Americans have died since 1995 while waiting for a donor heart.

Instead of an LVAD, Bonde proposed to repair Capozzo's heart through surgical ventricular restoration (SVR), an operation first performed by Vincent Dor, M.D., in France in the 1980s. Though Bonde regularly performs LVAD procedures and heart transplants, he said that it is important to match the procedure to the patient's particular need—even if that means doing a relatively uncommon operation.

Bonde is one of only a handful of surgeons in New England who perform SVR, and he might seem an unlikely proponent of the surgery. It relies more on surgical skill than technological support, yet much of Bonde's work focuses on technology. He is director of mechanical circulatory support in the Department of Surgery at Yale and a frequent collaborator with engineers. His research group has close to a dozen medical, engineering, and undergraduate students and research assistants working on problems that must be overcome before an innovative artificial heart can be made viable for humans. Bonde's team is also working on designs for an artificial lung, a portable device for producing circulation and oxygenation support outside the hospital, and a mechanical CPR device. They are developing a wireless LVAD instrumentation for minimally invasive cardiac surgery, as well as simulators for teaching surgical techniques. One of the most advanced projects is for a tiny, implantable pump that would switch on only when needed, as a pacemaker does, allowing some patients to be weaned from the device. But Bonde is also a surgeon who, with new techniques and tools at his disposal, likes to think outside the box.

"We believe a creative and imaginative environment is essential to innovation," says a message to

visitors to the lab's website. "This has been the cornerstone of our approach to solving complex problems in cardiac surgery."

If his work creating new devices suggests that Bonde is interested primarily in technological solutions, that's only half of the story. The SVR procedure requires a fair bit of artfulness on the surgeon's part. Despite extensive imaging, surgeons cannot really see the damage to the heart until they are looking inside the patient's chest. Knowing where damaged muscle ends and healthy muscle begins is a matter of experience and judgment. "That really is the challenge of the procedure," explained Bonde.

Adapting the procedure to individual patients is critical to its success. Bonde has seen men and women of various ages benefit from it even though their heart attacks left different kinds of damage. Among his patients was a woman with heart failure whose medical team was discussing withdrawing life support. After an SVR and a bypass operation in November 2013, the woman was able to enjoy the winter holidays with her family—and go out shopping for presents.

Although SVR is now more broadly used to address scarring that contributes to heart failure, the procedure was originally conceived as a strategy to repair ventricular aneurysms like Capozzo's. His aneurysm—a thinning of the heart wall that makes it vulnerable to rupture—had forced his left ventricle from its natural elongated shape into a life-threatening spherical form. To fix it, Bonde would have to cut away damaged muscle and use a mesh patch to reshape the ventricle. Bonde usually performs this operation in conjunction with CABG, a bypass operation.

This procedure spares patients the many lifestyle adjustments that an LVAD dictates, like bathing restrictions and the need to cart the device and a backup power source everywhere. SVR can also postpone—or make unnecessary—a heart transplant or implantation of an LVAD. Capozzo never had to wait for a donor, worry about immune system rejection, or take immunosuppressive drugs. "This can be a permanent fix for those patients who have been so sick and have lost all hope," said Bonde.

#### INDIGESTION OR HEART ATTACK?

Capozzo had not paid much attention to the symptoms that first surfaced during a dinner he had hosted for his



One of Pramod Bonde's recent inventions is a replacement for the left ventricular assist device, which he holds in his hands and must be implanted in the patient's chest. Medical student Brian Letzen, who works in Bonde's lab, holds the smaller device.



wife's family in November 2012. "I blamed it on the extra sausage and peppers." Capozzo found it impossible to sleep lying down that night. "I felt like I ate fast and the food got stuck somewhere," he said. Because he never felt pressure on his chest, it didn't occur to him that he'd had what his doctors later concluded was a massive heart attack.

He spent the following weeks treating with antacids what he still wrote off as indigestion. After a night shift at his job as an IT professional, he sat down to a snack of tuna and potato chips. Again, he had the feeling that he just couldn't lie down, and again he blamed it on what he had eaten—he may have had his second heart attack.

His sister Louise saw her brother looking sicker by the day. In mid-December she took him to the Yale-New Haven Shoreline Medical Center in Guilford, where an electrocardiogram revealed that his left ventricle was barely pumping. "I've never seen so many doctors run toward a patient in my life," said Capozzo.

"How did you get here?" a physician asked.

His sister had driven him, he answered. How had Capozzo gotten from the car to the emergency room? the doctor asked.

"I walked in," he said.

"You *walked* in!"

Discussing the case in his office months later, Bonde pulled up an MRI of Capozzo's heart before surgery. The heart was misshapen and filling most of the chest cavity. Capozzo had arrived at the Shoreline Medical Center with an ejection fraction—a measurement of the amount of blood the heart pumps with each ventricular contraction—of 8 percent. The normal rate is between 50 and 60 percent.

The immediate plan was for a heart transplant, until Capozzo was referred to Bonde. "I was pretty upbeat about the transplant," Capozzo remembers. But he was relieved to hear of another option and immediately agreed to SVR. He had the surgery in April 2013.

The procedure should be far more common than it is, according to John Conte, M.D., a professor of surgery and director of mechanical circuitry support at Johns Hopkins, where Bonde learned the procedure. "There are many, many reasons why you don't want to do an LVAD or transplant. They are expensive therapies. They are therapies that are fraught with complications; and they are therapies that, despite their best intentions, have limited lifespans," Conte said.

But SVR had gotten bad press from a trial initiated in 2002 that reported that the procedure, often done in conjunction with coronary bypass, conferred no advantage over bypass alone. Conte and Bonde say that the Surgical Treatment for Ischemic Heart Failure (STICH) trial was flawed. Conte points out that low enrollment prompted the National Institutes of Health to extend the search for volunteers to countries that did not determine whether patients were good candidates for SVR and did not perform the operation according to study guidelines. Editorials in medical journals criticized the trial, and studies conducted before and after STICH showed a benefit over bypass alone. Yet the well-publicized study made physicians hesitate to make referrals for SVR—a chilling effect that Conte says has moderated in recent years. SVR is more common in Europe, where surgeons have more experience with the procedure and have achieved good outcomes.

#### **MATCHING PATIENT AND TREATMENT**

Since his surgery, Capozzo has had a chance to reflect on the behaviors that contributed to his heart disease. "I did this to myself," he said. "I smoked, ate bad, never exercised."

That's changing. Now he hits the elliptical trainer three or four times a week. He misses his high-salt diet, especially his favorite guilty pleasure, pickle juice. But for the most part, he's passing up potato chips and heading for the big bowl of fruit he keeps on the kitchen island. He would like to reach out to other patients who are candidates for SVR and talk with them about his experience.

Not every patient referred for transplant is a good candidate for SVR, Bonde stressed. Those most suited for SVR, Bonde said, are patients who need a bypass or valve operation, have scar tissue from a previous heart attack, and have a resulting low ejection fraction. Conte agreed. "It is a great therapy for a small number of patients," he said. "And it should be done by people who have expertise in that therapy, like Dr. Bonde; people who also have at their disposal the opportunity to do heart transplants and LVAD. It allows you to match the right operation with the right patient." */yale medicine*

*Colleen Shaddox is a freelance writer in Hamden, Conn.*

In the Winchester Chest Clinic, medical student Ruth Wang'ondu uses her iPad to check a patient's chart and recent lab tests. "She finds things out in a quarter of the time it takes me," says Robert Baltimore, the clinic's director.



## How a pocket-size tablet is changing medical education

Students and faculty embrace the unexpected benefits of iPads in the classroom and the clinic.

By Jill Max



# On a rainy day in February,

Ruth Wang'ondu arrives at the Winchester Chest Clinic. The clinic is packed with patients making up appointments missed due to a rash of recent snowstorms, and Wang'ondu, who's in the M.D./Ph.D. program, is armed with the arsenal of references and notes that every medical student requires during clinical rotations. Last year, these materials would have filled her pockets, weighing down her petite frame and forcing her to rifle through a multitude of pages to check a dosage or learn more about a lab value. This year, all these materials, as well as additional texts, videos, and access to Epic, Yale's electronic medical record system (EMR), are contained in her iPad mini, a 5x8-inch device that fits neatly in the pocket of her white coat or the back pocket of her scrubs.



Since the School of Medicine began issuing iPads to medical students in 2010, the devices have changed the dynamic in the classroom. The iPad allows students to sync to the most recent versions of curriculum material.

In the fall of 2011, Yale made headlines by switching from paper copies of course materials to providing every medical student with an iPad. Two of the key incentives were to go green by saving paper and to ensure that students had a HIPAA-compliant mechanism for protecting patient information. The change was transformative—students now have constant access to the entire medical curriculum, electronic textbooks, instructional videos, and Web content, as well as the opportunity to develop and download applications that render their educational experience highly interactive. In the clinical years, however, students weren't using their full-size iPads as much as expected, which led the School of Medicine last fall to offer iPad minis to third-year students at a subsidized rate. Out of 100 students, 99 accepted the offer. The mini provides unfettered access to updated course content, Internet resources, and patient records in a light, thin, and small device. The mini and its big brother enrich the medical school experience in ways that are both obvious and unexpected. They are changing the way students learn.

### 24/7 ACCESS TO MEDICAL RECORDS

Wang'ondu's first patient at the chest clinic is a 4-year-old girl with latent tuberculosis (TB). She has seen the girl before during her year-long elective at the

TB and HIV clinics. Before she enters the exam room, Wang'ondu uses her tablet to compare today's blood pressure reading with a previous one from November. She uses the encrypted device in other settings as well.

During the HIV clinic, a supervisor often asks her to look up patients' lab results—a task more easily accomplished with the mini than at the clinical workstation, which is in another room and in high demand. If Wang'ondu wants to prepare for the cases she'll be seeing in the clinic, she can log in to Epic the night before.

She uses a wide variety of apps to help her learn, including Lab Values Pro, which explains lab values; Heart Sounds to hear what cardiac conditions sound like; and a video atlas as an ultrasound reference and to view laparoscopic images. In the HIV clinic, for example, she frequently uses Epocrates, a mobile and online clinical and drug reference resource, to show patients photos of pills when they're not sure which ones they've discontinued or may be causing side effects.

### INVENTING NEW APPS

Students have embraced the iPads in their curriculum so much that some are devising new applications for them. Last year, Paul Guillod, a second-year student, created Quizzler to help study for boards. Amy Yuan, a first-year student, turned a neurobiology lab manual into a digital book that Michael Schwartz, Ph.D.,



associate professor of neurobiology and associate dean for curriculum, now distributes to all of his students. A self-proclaimed “closet geek” who spearheaded the iPad initiative, Schwartz praised the tablet’s versatility, interactive capability, and multimedia features. “It’s not the iPad per se; it’s the technology that the iPad allows in our pedagogy that’s important,” said Schwartz.

Unlike many medical schools, where students download one file at a time from their learning management system (LMS), Yale enables students to sync electronically to the latest version of curriculum material. “Students tell us that if we expect them to use these materials and take notes on them, they have to be able to access what they’re actually seeing during the lecture. If a faculty member changes a slide the night before, the outdated version isn’t good enough,” said Schwartz. “When faculty come into the lecture hall with modified presentations that have not been uploaded to the LMS, within two or three minutes that lecture material is converted at the podium, uploaded to the server, and students are notified, so they have immediate access to the most up-to-date material.”

In some instances, the iPad is changing the medical school’s approach to teaching. Some instructors use Quizzler and other Web-based applications for interactive small-group discussions and quizzes. The instructor can control what students see on their iPads and ask them questions. The responses are delivered to the instructor as well as to other students. This process enables everyone to see the correct answer and encourages discussion. The app tracks the students’ correct and incorrect answers on their iPads, so that group members know where to concentrate their efforts. “In many of our small-group settings, it has dramatically changed the interactive nature of the discussions,” said Schwartz.

The iPads, Schwartz has found, are also a terrific delivery mechanism for instructional videos that he encourages faculty to produce. In contrast to podcasts of full lectures, these short videos help students prepare for class more efficiently. Schwartz has set up a studio in the library for making and annotating the videos. “It expands a little bit what we’re capable of delivering to students in terms of curricular materials,” he said.

### THE IPAD IN THE CLINIC

Back in the clinic, Wang’ondy checks the 4-year-old’s record and confirms that she’s taking the prescribed medication. When she learns that the girl’s surgeon has postponed a tonsillectomy due to the TB diagnosis, she enters the surgeon’s name in her tablet, so that she can follow up later. After examining the girl, she excuses herself to present her findings to Robert Baltimore, M.D., professor of pediatrics (infectious disease) and of epidemiology (microbial diseases). She answers his questions, sometimes consulting her tablet. “She finds things out in a quarter of the time it takes me,” said Baltimore.

Wang’ondy and Baltimore move on to their next patient, a 5-year-old girl. Before entering the exam room, Wang’ondy orders a chest X-ray for Baltimore to sign, then looks up the girl’s chart on her device. It shows that the girl had a positive PPD skin test for latent TB, but a blood test gave a contradictory result—negative. Wang’ondy also discovers that the girl had received Bacillus Calmette-Guérin (BCG) immunization, which is given in some countries to prevent TB. The BCG may explain the positive PPD.

After she and Baltimore finish with the 5-year-old, Wang’ondy returns to the clinical work stations. The room is normally crowded with attendings, fellows, residents, and nurses who need access to the computers. Before she had her mini, Wang’ondy would wait her turn, but now she can consult and update patient records before, during, and after patient visits. During a lull in activity, she sits down at a work station to write her notes in the charts of both patients, referring to notes she had taken on her mini.

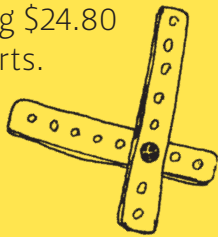
She finishes typing in her notes on Epic and then heads back to her surgery rotation. She is out the door quickly; using her mini, she accesses the surgery schedule and locates the case she is following. She didn’t have to decide before leaving home that morning which notes and texts she might need or want to review during the day. “You have all the information you could possibly need in that tiny electronic device,” she said. “I think it’s the best thing that’s ever happened.” */yale medicine*

*Jill Max is a freelance writer in Trumbull, Conn.*



# 36

Number of years between when Yale medical school graduate A.C. Gilbert first marketed the Erector Set and when an early heart pump was developed at Yale in 1949 using \$24.80 in Erector Set parts.



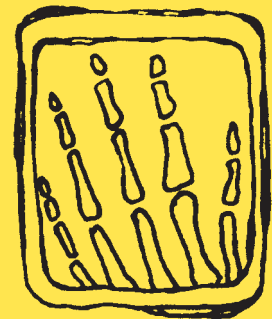
# 19

Number of students majoring in biomedical engineering in 1999, the first year of the program.



# 1896

Year of the first X-ray image taken at Yale.

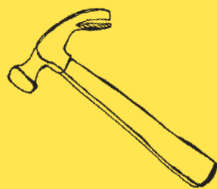


# 1958

Year of the invention of continuous electronic fetal monitoring at Yale.

# 58

Number of Yale-affiliated biotech startups.



# 59

Number of students currently majoring in biomedical engineering.

# 99

Percentage of Yale third-year med students who use an iPad on rounds.





## Winning fame and fortune at play

How alumnus A.C. Gilbert made the Erector Set his brand and inspired generations of young people, including seven Nobel laureates.

By Ashley P. Taylor

Alfred Carlton Gilbert, M.D. 1909, won an Olympic gold medal for pole vaulting in 1908; graduated from the School of Medicine a year later; founded a company in New Haven to produce magic tricks that same year; and in 1913, introduced the product for which he is best known: the Erector Set.

Throughout his whimsical and wildly successful career, Gilbert had a Mary Poppins-like way of combining work and play. As a youngster in Oregon, he got his friends to help him bring in firewood by saying that they couldn't play in his barn, which he had rigged up as an athletic club, until the chore was done. "I have never worked at anything to make money unless it was fun, too," he wrote in his autobiography, *The Man Who Lives in Paradise*. Success through play became his brand.

Gilbert knew the importance of persistence as well as prizes to successful entrepreneurship. In addition to his athletic pursuits, Gilbert

had trapped squirrels, caught wildcats, and sold magazine subscriptions in exchange for rewards, including the magic set that sparked his career. Athletic ambitions brought Gilbert to Yale for medical school; he hoped to become a college athletic director. But in addition to studying, Gilbert started giving magic shows to finance his Yale education. Just before graduating, he co-founded the Mysto Manufacturing Company to produce and sell magic sets. Then, inspired by the towers built to hold up the wires on the newly electrified railroads, Gilbert created his famous construction toy—a set of miniature steel girders, wheels, a real working motor, and accompanying parts—in time for the 1913 holiday season. He also renamed the enterprise, still headquartered in New

Haven, after himself: the A.C. Gilbert Company.

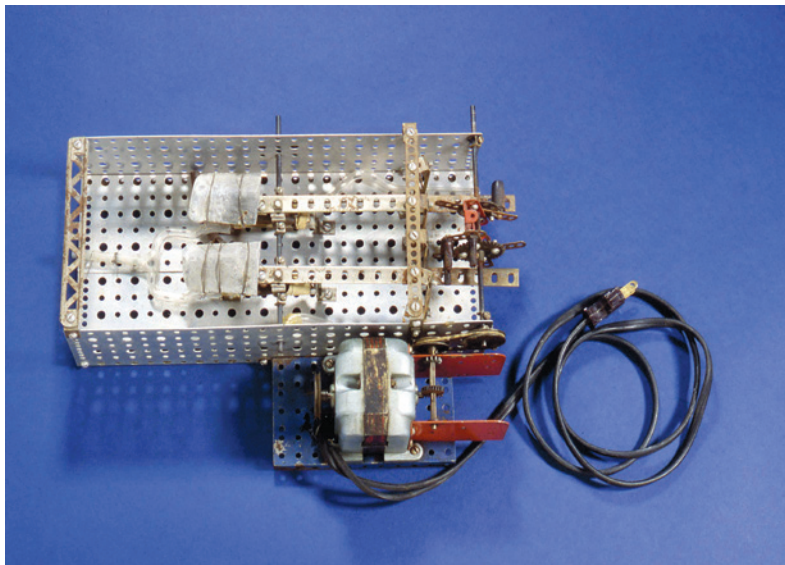
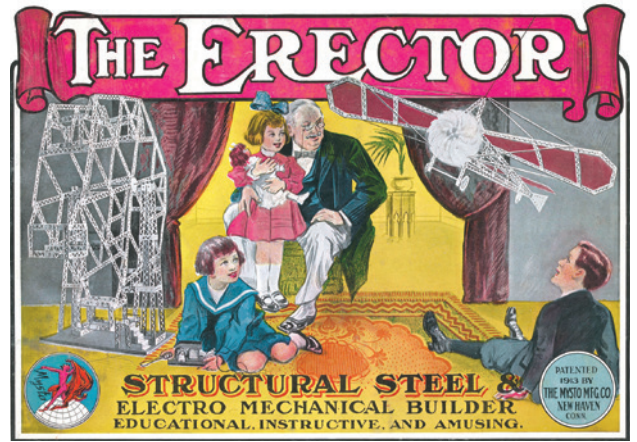
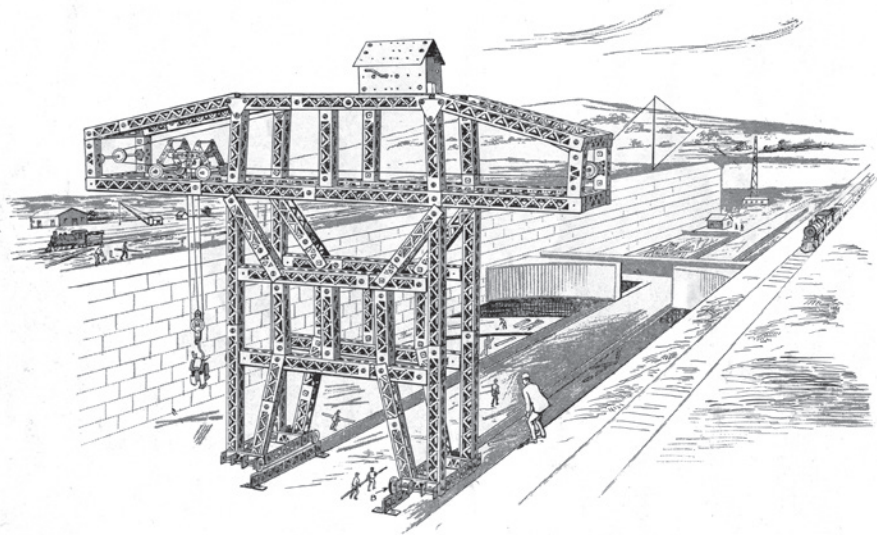
What distinguished the Erector Set from similar products, as Gilbert's biographer Bruce Watson wrote, was that Gilbert made himself a brand. He affixed his photo, signature, and message to Erector ads and publications. Boys wrote him letters. His message? "Win Fame While at Play," as one ad said. "He uses his story," said Bill Brown, director of the Eli Whitney Museum and Workshop in Hamden, Conn., "to promise that if you play with [Erector Sets], you'll grow up to become a tycoon like him."

Gilbert also sold the idea that his products were educational—and they were, indeed, inspiring many scientists and engineers. Last fall, the Eli Whitney Museum featured an exhibit about Gilbert and the Erector Set, including the Erector memories of seven Nobel prizewinners. In a nearby notebook, museum visitors could record their reminiscences

of Gilbert's "toy." "My first exposure to my friend's Erector Set inspired me to become a mechanical engineer," one visitor wrote. More directly, Erector Set parts were used in notable inventions—including the first heart pump, powered by an Erector Set motor and invented by the late William H. Sewell Jr., M.D. '50, then a Yale medical student; and his professor, the late William W.L. Glenn, M.D.

Despite his charismatic public face, Gilbert was somewhat retiring in person. "A.C. was clearly the man in charge, but quiet," said grandson Jeff Marsted, who remembers "sledding, baseball, golf, apple picking, etc.," at his grandparents' home in North Haven. "We all knew it, not by his personality but what he represented."

Gilbert left a legacy both scientific and physical. At the Eli Whitney Museum exhibit, visitors worked together on a model of Manhattan's Woolworth Building, a landmark skyscraper completed in 1913—the same year the first Erector Sets were marketed. The exhibit model was 22 feet tall and required 3,800 girders. The organizers had no trouble at all gathering donated pieces for the exhibit, Brown said. "I don't think anyone throws away an Erector Set."



**OPPOSITE PAGE**  
Meccano, the main competition to A.C. Gilbert's Erector Set, also produced sets for model airplanes. In 1929 Gilbert bought the company that produced Meccano in the United States.

**CLOCKWISE FROM TOP LEFT**  
An illustration from 1913 shows the possibilities of an Erector Set, here a gantry and crane.  
  
The Erector Set appeared on the market in 1913 at a toy fair in New York City. By 1935, Gilbert had sold more than 30 million sets.

Gilbert, who won a gold medal in the 1908 Olympics for pole vaulting, came to the School of Medicine to study sports medicine.

In 1949 Yale medical student William Sewell and heart surgeon William Glenn developed a heart pump, powered by a motor from an Erector Set, and supplemented with laboratory supplies and dime store items. The device cost \$24.80.





## More than easing the suffering of patients

WHEN HELENA HANSEN, M.D. '05, PH.D. '05, decided to go to medical school, she wanted to learn more than just how to relieve the suffering of individual patients. Just as health care professionals use biotechnology to treat patients, they should also understand and act upon the institutional, social, and cultural influences on people's health. "I wanted to combine medical training with community-based research," Hansen said, adding that "it was important to understand how social forces influence health."

Now an assistant professor of anthropology and psychiatry at New York University Langone Medical Center, she continues to study those intersections of social forces and medicine, with a goal of providing accessible care to all. She studies community-based health movements and the ethnic marketing of pharmaceuticals. She recently completed a one-hour documentary video that examines the historical and contemporary political-economic forces shaping the treatment of opiate addiction in the United States.

Hansen traces her interest in social inequalities to 1992, when she graduated from Harvard and took a job as program officer at the National AIDS Fund's

New Jersey office. "It was the early '90s, people were dying like flies, but it was an exciting time in AIDS policy," she said. "We were helping to design studies, inventing community collaborations."

She went on to the M.D./Ph.D. program at Yale and completed her doctoral studies in anthropology rather than the basic sciences most students choose. That was the start of a wide-ranging career that, in her first year of the program, brought Hansen to Havana with a delegation of medical students who visited the clinical research facilities of the Instituto de Medicina Tropical Pedro Kouri. For her doctoral thesis, Hansen did fieldwork in Puerto Rico on Pentecostal ministries founded and run by people recovering from narcotics addiction. The ministries operate a network of faith-based detox units and residential

rehabilitation centers that comprise the majority of the drug treatment programs in Puerto Rico. They are modeled on similar ministries in the inner cities of the United States.

During her residency at the New York University Langone Medical Center/Bellevue Hospital, Hansen continued to study social causes of health disparities. Part of her work included a political-economic and ethnographic study of buprenorphine, a synthetic opioid approved by the FDA in 2002 to treat opioid addiction. Opioid maintenance treatment, she realized, fell into two tiers—office-based buprenorphine therapy largely available to affluent abusers of prescription opioids, and DEA-regulated methadone



Even as a medical student, Helena Hansen was drawn to research that shows how social forces affect health and health care.



ONLINE EXCLUSIVES

Why government, academia, and industry need to work together.

Art of Caring: med students chronicle the unsung heroes of YSM.

Photos and video of 98 smiling faces on Match Day.

Full stories and event photo galleries, as well as other online-only content, can be found on our homepage at [medicine.yale.edu](http://medicine.yale.edu)

For Alumni Notes and In Memoriam, visit [medicine.yale.edu/alumni/alumni\\_news](http://medicine.yale.edu/alumni/alumni_news)

clinics for low-income heroin injectors. The result, according to Hansen, was a further stigmatization of drug addiction, and a shift in emphasis away from psychiatric services as a component of recovery to cursory 15-minute medication checks. With funding from NIDA, she is comparing primary care-based addiction treatment with psychiatry-based substance abuse programs to determine their impact on the stigma that patients experience, as well as how the programs affect patients' social networks and access to resources.

Her interest in video began with the realization that journal articles do not draw a broad audience. She had been participating in a video therapy group started by an art therapist

Hansen has observed that interest in the social forces that shape health inequalities is growing among clinicians. With her colleague Jonathan Metzl, M.D., Ph.D., she organized a series of conferences and a special issue of the journal *Public Library of Science Medicine* on the topic of what she and Metzl term "structural competency." The term indicates the need for physicians and other health practitioners to work at the level of institutions, policies, and community collaborations to reduce health inequalities. At their first conference on structural competency in 2012, they expected to fill a room with capacity for 70 people—more than 200 showed up, a blend of medical school faculty and students, state and city health policy makers and administrators, community health advocates, and social scientists. "We need to think and act collectively

## An alumna's journey through social movements and forces that affect health.

and two patients with production and editing experience. Members narrated and produced fictional stories, commentaries, or documentaries about their lives. When she shows the videos, Hansen said, residents and premed students are better able to engage with the subject matter—the political and ethical quandaries of treating opiate addiction with opioid medications. In an academic setting, she learned, video "is a really good tool for communicating."

around health and health care," Hansen said. "Clinicians need to collaborate with others who have expertise in education, housing, and city planning. There are myriad ways to work across disciplines to create better health conditions."

—Jennifer Kaylin



### Hip names and modern life inspire a children's book

Matthew Goldenberg's book for children also pokes fun at their yuppie parents.

When Matthew Goldenberg, M.D. '03, became an uncle, his niece, Ava, came into a world that was vastly different from the one depicted in Goldenberg's own childhood storybooks. "Bobby has a new ball" no longer described this world.

"The vocabulary that a baby needs today was not going to be found in a traditional baby book," Goldenberg said.

Little Ava lived in Park Slope, Brooklyn, home to hip babies with cool names and urban gear. "There are a lot of yuppie baby things in the world now. And many of my friends were naming their babies Ava, Sophie, Jack. Nobody my age is named Ava or Jack," he said.

Modern babies needed a modern book, thought Goldenberg, a psychiatrist who joined the medical school faculty last fall. So he wrote *A is for Artisanal: An Alphabet Book for the Hip, Modern Baby*. The 26-page picture book, illustrated by physician-turned-cartoonist Benjamin Schwartz, M.D., is as entertaining for parents as it is for their children.

The first page reads, "Ava adores artisanal asiago." From Ava to Zoey, the book is a tongue-in-cheek portrayal of modern urban life, complete with farmer's markets, iPads, vegetarians, and yoga.

Goldenberg particularly enjoyed writing the page for the letter B, “Bjorn is brought to brunch in a Bob. Bob is brought to brunch in a Bjorn.”

“I had no idea what a Bob was until some friends who had recently had a baby mentioned it,” Goldenberg said of the three-wheeled all-terrain stroller that’s suitable for jogging. (A Björn is what older generations would call a Snugli.) “It seemed like every conversation I had with new parents after that involved Bobs. So that was my baby gift to my brother and sister-in-law.”

It’s as if Goldenberg shares an inside joke with parents while their children enjoy pictures and alliteration in lines like “Noah needs nightly news from NPR” and “Jack jocularly jabs like Jon Stewart.” Reviewers on Amazon.com get a good-natured laugh out of Goldenberg’s jabs. “BrooklynSFDad” wrote in his online review, “A hilarious skewering of urban parenting. Having brought my babies to brunch in both a Björn and a Bob, I can say with certainty that I am the target (and target demographic) of this hilarious book.”

Goldenberg agrees. “It’s a good way for us to chuckle at ourselves. It’s a comment on modern hipster society. I eat Greek yogurt. I go to a farmer’s market every Saturday. I like women’s soccer,” Goldenberg said, referring to images that appear in the book. “It’s meant to poke lighthearted, good fun at my generation.”

Goldenberg observed many parents and children as research for his book, but not being a parent himself allowed him the time to write the book and shop for publishers. “When I’d come home from work and Whole Foods and CrossFit,” he joked, poking fun at the hipster aspects of his own life, “I’d send it out to publishers and agents.” But he can’t say the book is completely separate from his day job.

“It allows me a creative side that I don’t always find in my day-to-day work, but as a psychiatrist, I am an observer and appreciator of human behavior. That certainly informed this book.”

*A is for Artisanal* is his first professional artistic endeavor, but what Goldenberg calls his “creative impulse” manifested years ago.

“I was a producer of the second-year show. It was one of the highlights of my medical school career,” he said. “The writing of this book comes from that same creative impulse.”

Goldenberg is an attending psychiatrist in the psychiatric emergency room at Yale-New Haven Hospital. He is also the interim medical director of a new psychiatric observation unit that became fully operational in November. The unit is for patients whose psychiatric symptoms may not require hospital admission but do require a longer stay than a typical ER visit.

Prior to earning his medical degree, Goldenberg was a history major in Yale College.



He returned to New Haven in September after 10 years away. He had spent four of those years on the faculty of the Uniformed Services University of the Health Sciences in Washington, D.C., and a year in London pursuing a master’s degree in global mental health. At the School of Medicine, he plans to develop programs in global mental health for students.

In his free time, he plans to write more books.

“I’ve always had a very diverse set of interests: history, politics, football, documentary films, geography. One of the fun things about writing is the opportunity to pursue some of that.”

—Sonya Collins

Matthew Goldenberg was inspired by his niece, Ava, and his nephew, Joseph, (in photo) to write a children’s book that also pokes fun at parents’ lifestyles.

## How Harlan Krumholz got big pharma to open its data

HARLAN KRUMHOLZ, M.D., HAS STREET CRED. In scientific circles, the Harold H. Hines Jr. Professor of Medicine (Cardiology) and professor of investigative medicine and of public health (health policy), is known as a gadfly who calls out pharmaceutical giants for—among other things—sitting on clinical trial data that might hurt their bottom line. So when Krumholz came up with a plan to collaborate with big pharma to release such data to other scientists, his colleagues told him it would never happen. “People said that industry would never share data. If they did share data, they would never share them with me because they’d think I’d be too tough on them,” Krumholz recalled.



watch an interview with  
Harlan Krumholz at  
[yalemedicine.yale.edu](http://yalemedicine.yale.edu)

But it did happen. Twice.

First, Medtronic allowed Krumholz to farm out their clinical data to two independent research groups. They came back with slightly different analyses, reinforcing Krumholz's view that opening up data can only benefit science, physicians, and patients. And early this year the Yale University Open Data Access (YODA) Project, which Krumholz directs, entered into

an agreement with Johnson & Johnson. Under the agreement the company relinquishes control of its clinical trial data to YODA, which sends the data to two independent research groups for analysis. The company will initially release pharmaceutical trial data, followed by data from clinical trials of medical devices and consumer products.

“I have not done this alone,” Krumholz said. His collaborators include Joseph Ross, M.D., M.H.S. '06, assistant professor of medicine; Cary Gross, M.D., professor of medicine; and the British physician and academic Richard Lehman, M.D. Leading

YODA's steering committee is bioethicist Ezekiel Emanuel, M.D., Ph.D. “The progress we have made is a tribute to the companies that have been willing to lead a new approach. We forged a vision of what could be accomplished together.”

Krumholz talked with *Yale Medicine* in February about the agreement with Johnson & Johnson and his career in outcomes research.

{ To nominate a subject for Q&A, contact

{ [Yale Medicine, 1 Church Street, Suite 300, New Haven, CT 06510](http://YaleMedicine,1ChurchStreet,Suite300,NewHaven,CT06510) or email [yymm@yale.edu](mailto:yymm@yale.edu)



### How did you get involved in health policy and outcomes research?

When I was a Yale undergrad, I had the opportunity to do an internship at the office of rural health service in North Carolina. They had set up a series of clinics run by nurse practitioners and connected to general practitioners at a distance. My job was to learn about those community clinics and do some surveys about what the challenges and obstacles were. Before that I had worked in basic science labs and thought that that might be a direction that I would take. This [internship] turned me more toward thinking about the public and society and patients, and how you could generate knowledge that would have a practical impact on people.

### What is outcomes research?

It's saying we want to know at the end of the day whether we've helped people. Have patients experienced a good outcome? Are they in a better place than they would otherwise be?

### What was the problem you wanted to solve with YODA?

It turned out in our research that half of clinical trials are not published within three years—and many of them are never published. If science is to be progressive and self-correcting, it is critical that

the data be available for multiple groups to look at—to draw their own conclusions, to put the results in public view, and to allow dialogue to take place.

### Why are studies not being published?

It is not entirely clear. We saw that studies that are sponsored and owned by industry are now published at a slightly higher rate than previously. We did an audit of NIH and saw again that half the studies at three years were not being published. This is part of our culture—people run to finish studies; then they move on to the next thing. They may lose interest. They may get results that didn't excite them. Maybe there is a profit motive and the results aren't what they were looking for.

### How did YODA begin?

We were trying to figure out how we could partner with industry and show a way forward. Prior to that, litigate and regulate were the two primary ways to get data to be more widely shared. There was a third path, which was to partner. It turned out Medtronic was having some problems with a product. I approached the chief science officer and started a huddle with their leadership. I said

you'd probably hire a consultant, hire someone to look at the data, do an internal review, circle the wagons, and try to defend yourselves. How about a different path? What we're going to do is share all the data assets related to these products; we're going to partner with an independent academic organization; and we're going to allow them to enlist two expert groups to do reviews.

### Why did Johnson & Johnson agree to participate in YODA?

At Johnson & Johnson there seemed to be sincere interest in this third path. They have a credo that is built on trust and serving the public. And they had had some issues with some of their products. They wanted to be leaders in setting the standard for the future.

### How will YODA benefit patients?

There should be a more complete picture of the balance of risks and benefits of the drugs and clinical strategies that lie in front of them. There should be more confidence in the scientific system—that it's not just one group that's maybe getting paid by another group that has a vested interest. It's a more trustworthy, more credible system that is producing information better, faster, and cheaper.



# Why we spend more but get less

American society values access to doctors and the latest medical technology over social determinants of health.

By Cathy Shufro

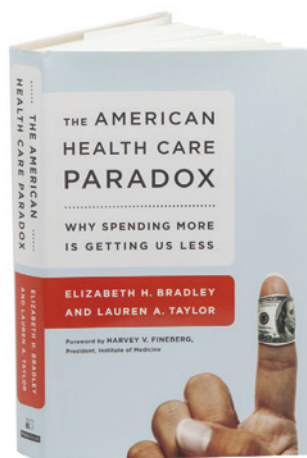
When New York Mayor Michael Bloomberg proposed to limit sales of jumbo sodas in 2012, dissent on the banks of the Hudson could be heard clear down on the Mississippi Delta. The Mississippi legislature responded in 2013 with the so-called anti-Bloomberg bill, which forbids towns and cities from making such rules governing food and drink as restrictions on soda size or requirements to list calorie counts on menus. That's in a state where one in three residents is obese—a circumstance that costs Mississippi an estimated \$4.2 billion extra in medical costs each year.

For Elizabeth H. Bradley, Ph.D. '96, professor of public health and director of the Yale Global Health Initiative, Americans' narrow view of health maintenance combined with a culture of individualism explains why

initiatives like Bloomberg's raise hackles. With co-author Lauren A. Taylor, M.P.H. '09, Bradley explores this hypothesis in a new book, *The American Health Care Paradox: Why Spending More is Getting Us Less*.

The paradox, of course, is that the United States spends far more on health care than do other developed countries; yet Americans have shorter life expectancies, lose more babies, suffer more often from diabetes and heart disease, are more likely to be obese, and so on.

Bradley and Taylor argue that one cause of the “spend more, get less” system is that Americans regard good health as synonymous with access to doctors. “Most of the evidence would say that medical care contributes 10 to 20 percent of health and well-being,” said Bradley in a recent interview, “but you would think that medical care determined 100 percent of our health.” This outlook, she said, “is very much aligned with having created a very big



medical complex that is quite profitable for many of us: It's 18 percent of our economy.”

The authors contend that doctors and patients alike seek medical care even for problems that could be solved through nonmedical means. In one case study, a physician pushes for surgery on a patient's shoulder that heals successfully through physical therapy. In another, parents insist on one test after another to diagnose their teenager's headaches, even after several doctors concur that the headaches arise from anxiety.

The United States has built its health care system on the assumption that people are largely responsible for their own welfare, said Bradley. As a counterpoint to American individualism, she and Taylor analyzed the attitudes of Scandinavians, who stay healthier while spending

less. The authors found that Scandinavians are more open to collective action and far more willing to invest in projects beyond new hospital wings. “In Scandinavia,” Bradley said, “you could see left and right a broader understanding of the social determinants of health”—factors like the quality of housing, the richness of social support, safe streets, and urban design that promotes exercise. The American viewpoint, on the other hand, essentially reduces health care to a transaction between two individuals: a doctor and a patient. “It would be hard for a population with that basic culture [that is, American] to recognize and invest in the parts of our health that are collectively determined,” said Bradley.

But she said that American physicians interviewed embraced the need for change. “Doctors we talked with said, ‘I am in the emergency room with a patient who has diabetes, and I can't even get to diabetes and wound care because the person has so many social issues. I'm not even able to do my job.’” If the American system addressed health more comprehensively, Bradley argued, doctors could be freed to do medicine, the profession they trained for, without feeling the need to be social service providers as well.

{ Send notices of new books to  
Yale Medicine, 1 Church Street, Suite 300, New Haven, CT 06510 or email [yymm@yale.edu](mailto:yymm@yale.edu)

## The greatest show ever?

SINCE 1949 Yale medical students have been lampooning their professors, deans, and classmates in an annual spoof that often revolves around goings-on at the School of Medicine. This year's production, *The Greatest Second-Year Show Ever?*, presented by the Class of 2016, took as its theme the impending implementation of a new medical curriculum. Students were panicking over the show's possible demise—the new curriculum left no time for such frivolity. (Any professor at the med school knows the folly of scheduling classes in the final days before opening night.) As did past shows, this year's installment targeted such familiar campus figures as Deputy Dean for Education Richard Belitsky, M.D.; Associate Dean for Student Affairs Nancy R. Angoff, M.P.H. '81, M.D. '90, HS '93; Professor Margaret Bia, M.D.; and Professor Auguste Fortin, M.D., M.P.H. Jessica Ye and Simon Kigwana were the show's producers.

—John Curtis



Visit [yalemedicine.yale.edu](http://yalemedicine.yale.edu) to see more pictures from this year's Second-Year Show.