LEWIS KATZ SCHOOL OF MEDICINE AT TEMPLE UNIVERSITY | TEMPLE UNIVERSITY HEALTH SYSTEM

Temple Health Magazine

SPRING 2016

MODERN DOCS:
OUR ESSENTIAL, INTENSE EXPECTATIONS

IDENTITY REDEFINED:
THINK YOU'RE ONLY HUMAN? THINK AGAIN.

Picture of Health

How Radiology's Super-Sharp Focus Advances Patient Care

TEMPLE HEALTH

Informed Innovation

At Temple Health, we continually recast our clinical, education, and research programs to give our patients and students every possible advantage. This is our contract with society: to put new solutions and technologies to best use.

Progress — especially in science and medicine, however — isn't progress when it's only about the shiny and new. Scientifically sound progress, socially relevant progress, requires the co-adaptation of the innovative with the tried-and-true, the amalgamation of tradition and innovation.

In academic medicine, we live in a nexus of forces. On one hand, we are propelled by the creative spark of our clinicians and researchers. On the other hand, we are grounded in allegiance to knowledge with demonstrated effectiveness (as evidence-based medicine attests). There's dynamic tension between innovation and tradition. We live and work in it every day. It isn't always a comfortable place to be. But without the interplay between these oft-opposing forces, medicine simply could not advance.

When academic medical centers like Temple Health accumulate knowledge and refine practices over successive generations, we do right by our patients and our students. It's through this considered process of informed innovation that Temple Health attains the harmonizing values and practices that define reputational world-class.

Larry R. Kaiser, MD, FACS

Senior Executive Vice President for Health Affairs, Temple University
Dean & Professor of Surgery, Lewis Katz School of Medicine
President & CEO, Temple University Health System

SURGERY: TUHS MARKETING; KAISER: DOMINIC EPISCOPO

Temple Health Magazine

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Glenn S. Gerhard, M.D.

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ON THE COVER: Imaging has transformed virtually every aspect of medicine. Photograph by Fredrik Broden. Brain: iStock

LEFT: JOSEPH V. LABOLITO; TOP RIGHT: EDDIE GUY; BOTTOM LEFT: MATT CLOUGH; BOTTOM RIGHT: TIM O'BRIEN

CURRENTS

Gone Global

It really is quite the geographic extravaganza. With alumni of the school practicing medicine all across the globe, and with alliances in education, patient care, and research as far afield as China and the Middle East, you'll find Temple's medical footprint on every continent on Earth (except, perhaps, Antarctica).

"A new venture with international flair has been added to the growing list of health-related partnerships we've developed in recent years," says Larry Kaiser, MD, FACS, Temple Health's CEO. "We've signed a memorandum of understanding with Universal Hospital in Abu Dhabi to explore the possibility of creating a cancer center in the United Arab Emirates."

Furthermore, Kaiser points out that "Temple Health is co-owner of PIM, Philadelphia International Medicine, an organization that caters to patients from around the world seeking American medicine's gold standard." PIM's members — Fox Chase Cancer Center, Temple University Hospital, and Thomas Jefferson University Hospital — give international patients access to top-tier physicians and specialty programs providing the advanced treatments patients require. PIM helps patients and families with visas, travel, accommodations, and other services — and generates over 5,400 patient encounters per year.

For more, visit www.philadelphiamedicine.com.

Photograph by CLINT BLOWERS

Caspase Clue

A new research study at the Lewis Katz School of Medicine at Temple University sheds new light on how hyperlipidemia, a buildup of fat in the blood, raises risk for heart attack or stroke by impairing the growth of new blood vessels.

A team of researchers led by Xiao-Feng Yang, MD, PhD, Professor of Pharmacology and Microbiology and Immunology, found that a molecule known as caspase-1 plays a central role in blocking the growth of blood vessels. When the researchers employed a technique to inhibit the action of caspase-1, vascular cell growth was enhanced and new blood vessel formation (angiogenesis) was restored.

"This means it may be possible for scientists to develop a therapy to prevent caspase's activity, thus enabling new blood vessels to grow, restoring blood supply to oxygen-starved tissues," says Yang. "This important insight could lead to the development of an early intervention strategy for metabolic cardiovascular diseases and inflammation," Yang notes.

The study was published in the *Journal of Biological Chemistry*.

BETWEEN 2012 AND 2015, TEMPLE PERFORMED OVER

700

TRANSPLANT SURGERIES.

MATT CLOUGH

Cancer Insights

BRCA GENE-RELATED CANCERS

Cancer cells with mutations in BRCA1 or BRCA2 genes are key targets for cancer therapeutics, yet few agents can selectively eliminate cells *deficient* in BRCA. That could change. Scientists at the Lewis Katz School of Medicine screened more than 18,000 compounds and discovered a small molecule (6-OH-dopa) that selectively kills BRCA-deficient cancer cells by blocking their "backup" DNA repair pathway. "The effect is like knocking out two legs of a table," says Richard Pomerantz, PhD, Assistant Professor of Medical Genetics and Molecular Biochemistry. The discovery of 6-OH-dopa could mean good news for more than just breast and ovarian cancer, those most widely associated with BRCA mutations. Cancers of the lung, prostate, and pancreas exhibit BRCA deficiencies. Leukemia does, too.

The findings were published in *Chemistry & Biology*. Department of Defense and NIH funds supported the research.

UROTHELIAL CANCER

Researchers are closer to finding a new treatment for urothelial cancer, which most commonly affects the bladder but can also involve the ureters and urethra. A recent study found that the immunotherapy agent pembrolizumab — a drug currently FDA-approved for metastatic melanoma — was effective against tumors in patients with recurrent or metastatic PD-L1–positive urothelial cancer. "Immunotherapy works by releasing the body's immune system to attack cancer cells," says Elizabeth Plimack, MD, MS, Director of Genitourinary Clinical Research and Associate Professor of Medical Oncology. "In contrast, chemotherapy, the standard treatment for urothelial cancer, works by killing cancer cells yet can also kill healthy cells, which leads to adverse effects." In a Phase III trial underway, the drug will continue to be evaluated for safety and efficacy in comparison to chemotherapy. The research, based at Fox Chase Cancer Center, is a collaboration with investigators at other cancer centers and the drug's manufacturer, Merck Inc., Approximately 4.5 percent of all new cancer cases each year are urothelial.

PANCREATIC CANCER

Pancreatic cancers tend to invade nearby veins and arteries, making surgery to remove the cancer difficult, if not impossible. But now researchers at Fox Chase Cancer Center have identified a way to safely pull the tumor away from vessels, to help make surgery possible. Lora Wang, MD, and colleagues found that giving extra boosts of radiation therapy to the tumor areas entwined with major vessels improved the rate of surgical resection. "Our practice is to give patients with borderline resectable or unresectable cancer chemotherapy and/or radiation therapy first to help shrink the tumor so surgery can proceed," said Wang. The study was published in *Practical Radiation Oncology*.

Lewis Katz School of Medicine Dedicated

In October 2015, during two days of festivities, Temple University celebrated the dedication of the Lewis Katz School of Medicine. Hundreds gathered to honor, the beloved late businessman, benefactor, trustee, and alumnus for whom the school is named. In their remarks, University officials and guest speakers — including Pennsylvania Physician General Dr. Rachel Levine and U.S. Senators Bob Casey, Jr., and Cory Booker — revealed the deep connection between Lewis Katz's personal mission and the medical school's: abiding love and respect for humanity, demonstrated by service and generosity thereto.

While the naming ceremonies had their share of pathos — a video featuring Katz's speech at Temple University's 2014 graduation brought many to tears — a sense of uplift pervaded. After all, Lewis Katz was a man who joyously gave much to the institution he loved. "Temple was everything to him," said Katz's son, Drew, who with his sister Melissa Katz Silver unveiled a portrait of their father that now hangs in the Medical Education and Research Building.

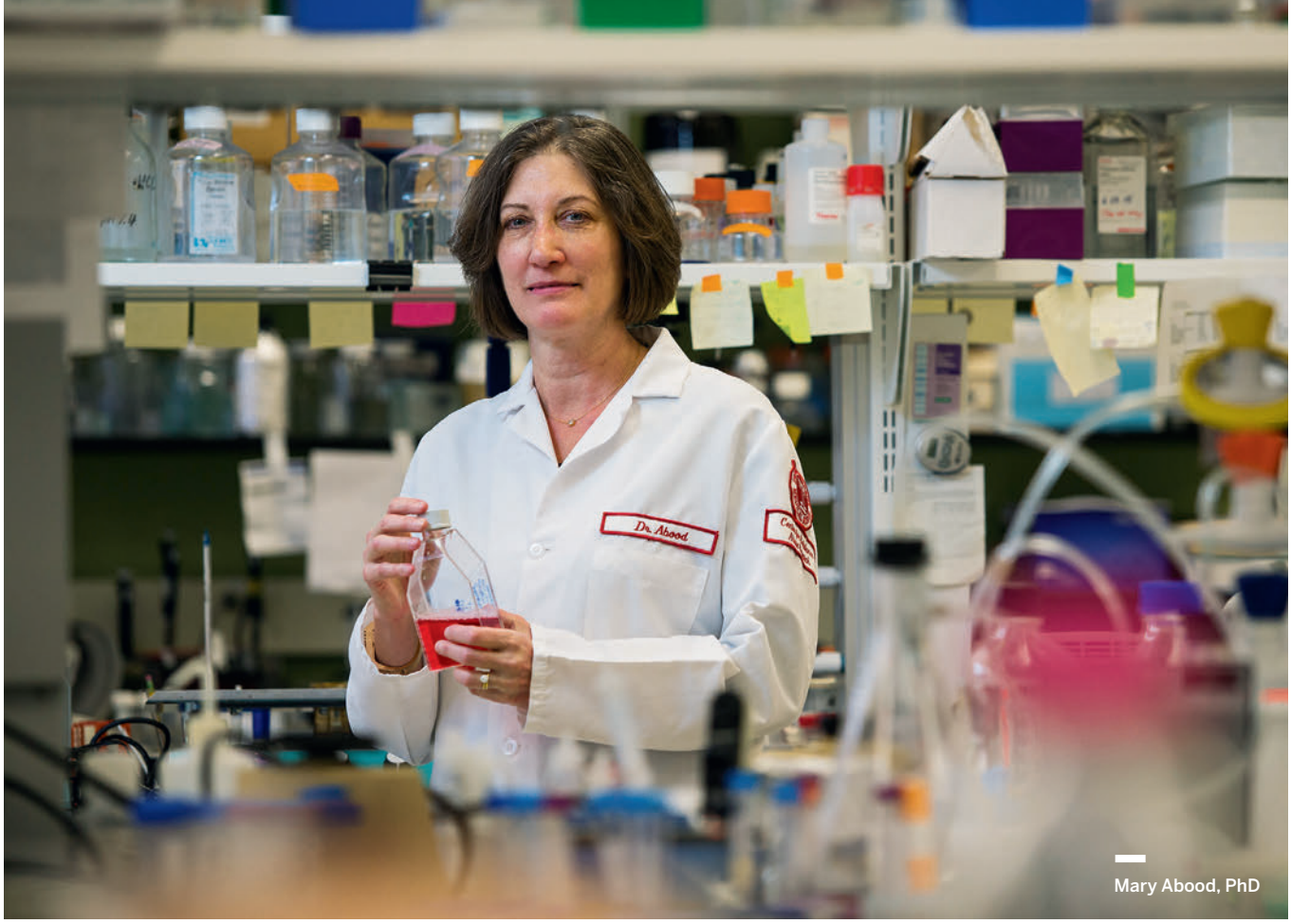
Visit the Lewis Katz School of Medicine's new website at www.medicine.temple.edu/katz for more.

Baby, We're a Rising Star

Only three hospitals in the United States earned the University HealthSystem Consortium's 2015 Rising Star Award — a national distinction presented to academic medical centers that have made significant improvements in safety, clinical effectiveness, and equity of care — and Temple University Hospital (TUH) was one of them, with an overall national ranking of 17. Also, for the third year running, the Joint Commission named TUH one of the nation's Top Performers on Key Quality Measures for sustained excellence. And for the second year in a row, the TUH Episcopal Division won the Press Ganey Guardian of Excellence Award, scoring in the top 5 percent of all inpatient behaviorial health hospitals in the nation.

Yet more awards for quality have been presented to TUH, such as the American Heart Association's Gold Quality Achievement Award for treating patients who suffer in-hospital cardiac arrests. Moreover, TUH and Fox Chase Cancer Center earned Blue Distinction (Blue Cross Blue Shield) *and* Optum™ Centers of Excellence status for bone marrow transplants. Also, the organization's community cancer program won an American Cancer Society Citation Award for excellence in cancer control and outreach — and celebrated Fox Chase's induction into the Caris Centers of Excellence Precision Medicine Network™, which develops standards of care and best practices in molecular profiling in oncology.

JOSEPH V. LABOLITO



Mary Abood, PhD

JOSEPH V. LABOLITO

Kudos to You

Mary Abood, PhD, Professor, Center for Substance Abuse Research, recently received the Mechoulam Award of the International Cannabinoid Research Society. The prestigious honor goes to scientists worldwide who have made significant contributions to the field of cannabinoid and endocannabinoid research.

Tahseen Al-Saleem, MD, Professor of Pathology, earned the Lifetime Achievement Award of the Iraqi Medical Sciences Association for his contributions to excellence in medical sciences.

Steven Carson, RN, BSN, MHA, Vice President for Clinical Integration and Chief of Operations for the Temple Center for Population Health, has been appointed to Pennsylvania's Patient-Centered Medical Home Advisory Council.

Nestor Esnaola, MD, MPH, MBA, FACS, Professor of Surgery and Associate Director of Cancer Health Disparities and Community Engagement, earned the American Cancer Society's 2015 Cancer Control Award for his efforts in increasing clinical trials literacy via the "Be the Breakthrough" program and related achievements in the field of cancer control.

Jeffrey Henderer, MD, the Bedrossian Professor and Chair of Ophthalmology, is a trustee of the American Academy of Ophthalmology and also serves the Academy as Secretary for Knowledge Base Development.

Enrique Hernandez, MD, FACOG, FACS, the Abraham Roth Professor and Chair of Obstetrics/Gynecology and Reproductive Sciences, serves on the Board of Directors of the American Cancer Society.

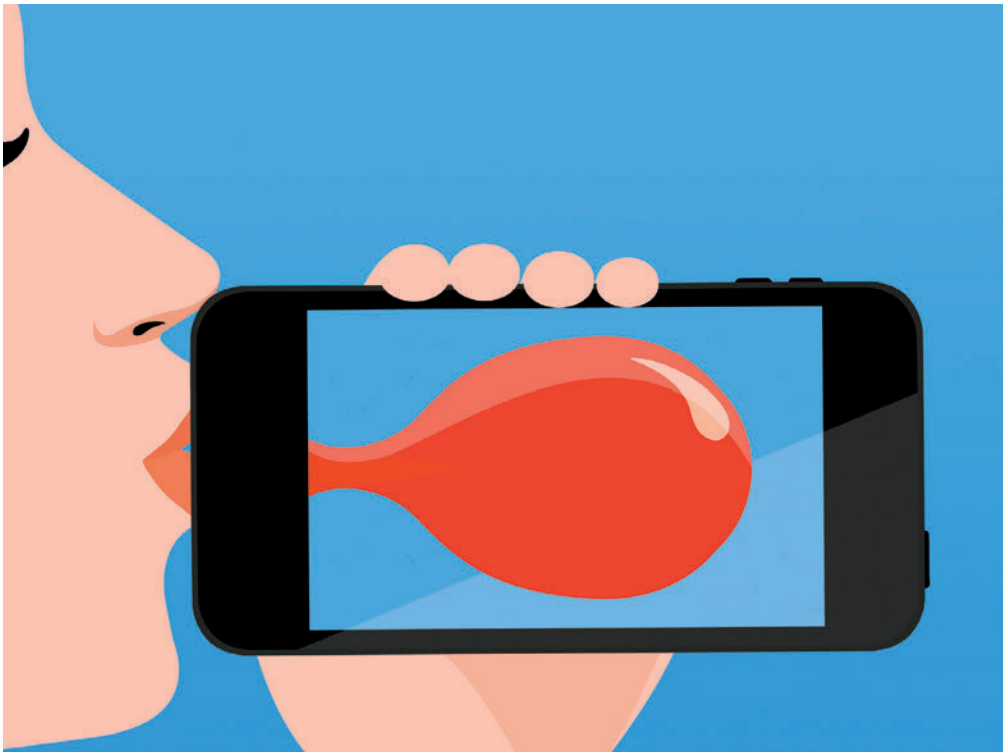
Steven Houser, PhD, FAHA, is President of the American Heart Association, the nation's oldest and largest organization dedicated to fighting heart disease and stroke. Houser is Senior Associate Dean for Research, the Vera Goodfriend Endowed Chair of Cardiovascular Research, and Director of the Cardiovascular Research Center at Temple's Lewis Katz School of Medicine.

Larry Kaiser, MD, FACS, President/CEO of Temple University Health System, Dean of the School of Medicine, and Senior Executive Vice President for Health Affairs at Temple University, was named one of 2015's top "Physician Leaders of Hospitals and Health Systems," by *Becker's Hospital Review*. Kaiser is one of only 100 physician leaders of hospitals and health systems in the country so recognized. *Becker's* also named Kaiser a 2015 "Nonprofit Hospital and Health System CEO to Know."

Leah Kiesow, MBA, CTR, Director of Fox Chase Cancer Center's cancer registry, has been named President of the National Cancer Registrars Association.

Charlie Ma, PhD, FAAPM, FACMP, FIOP, FASTRO, Vice Chair of the Department of Radiation Oncology at Fox Chase Cancer Center, has been elected to the North American Chinese Medical Physicists Association Hall of Fame.

Joseph Testa, PhD, the Carol and Kenneth Weg Chair of Human Genetics at Fox Chase Cancer Center, has been appointed Senior Editor of *Cancer Research*, a journal of the American Association for Cancer Research, the most frequently cited oncology journal in the world.



Breathe Easier

DIGITAL HEALTH APP FOR COPD:
A recent study funded by the Pennsylvania Department of Health showed positive results for patients who used the Temple Lung Center's digital health app for Chronic Obstructive Pulmonary Disease (COPD) symptom reporting. Because patients who use the app receive medical intervention more quickly than those who don't, they have fewer and less severe COPD flare-ups, along with improvements in daily symptom control, lung function, and activity status. "Daily COPD telemonitoring is an attractive approach to facilitate early intervention," says Gerard Criner, MD '79, FACP, FACCP, Chair of the Department of Thoracic Medicine and Surgery.

PULMONARY FIBROSIS NETWORK:
Temple University Hospital has been selected for membership in the Pulmonary Fibrosis Foundation's Care Center Network — reserved for organizations with expertise in treating patients with fibrotic lung disease. In addition to giving patients and their caregivers access to a wealth of resources, network membership enables Temple to collaborate with 39 other sites across the country to advance care for patients with the condition.

Faster Help for Depression

Temple University Hospital is one of five sites in the U.S. participating in a Phase II, NIH-funded trial testing a compound that could speed therapy for severe, treatment-resistant depression. Antidepressants often take weeks to work — or do not work at all. "When you're depressed, it's not easy to wait," says Mary Morrison, MD, MS, Vice Chair for Research Development for Psychiatry, noting that heightened suicide risk underscores the need for faster-acting treatment.

Implantable Heart Help

Three new FDA-approved heart devices, all implanted in minimally-invasive procedures, are available at Temple University Hospital:

For heart failure:
The CardioMEMS Heart Failure System® is a miniature, wireless sensor that monitors blood pressure in the pulmonary artery — and transmits the readings in real time to the patient's clinician so that treatment can be adjusted quickly. In clinical testing, the device reduced heart failure hospital admissions by up to 37 percent.

For risk of sudden cardiac arrest:
Patients with implantable cardioverter defibrillators (ICDs), which jumpstart the heart when abnormal rapid rhythm is dectected, generally cannot undergo MRI scanning, because scanners can make ICDs malfunction. Now, however, there's a new ICD that won't interfere with MRI scanning: the Medtronic Evera MRI™ SureScan® ICD System.

For atrial fibrillation:
In patients with atrial fibrillation (Afib, an irregular heartbeat), blood can collect and form clots in an area of the heart called the left atrial appendage (LAA). If the clots break free, they can cause a stroke. The WATCHMAN™ Left Atrial Appendage Closure device prevents that from happening and obviates the need for patients to take anticoagulant medications.

ANNA PARINI

Top Picks for Top Posts

Clifford Belden, MD, MS, has been appointed Chair of the Department of Radiology at Temple University Hospital, Professor of Radiology at the Lewis Katz School of Medicine, and Radiologist-in-Chief for Temple University Health System. Before coming to Temple, Belden was Chair of the Department of Radiology, Chief Clinical Officer, and Senior Associate Dean for Clinical Affairs at the Geisel School of Medicine of Dartmouth College and the Dartmouth-Hitchcock Health System in New Hampshire. He specializes in neuroradiology, epilepsy, brain tumor imaging, and head and neck cancer imaging.

Verdi DiSesa, MD, MBA, has been named President and CEO of Temple University Hospital. In this role, he will continue to improve the hospital's operating performance and optimize its clinical effectiveness and efficiency. Since his arrival at Temple in 2011, DiSesa has played an integral role in strengthening the Health System's clinical and financial operations — garnering increased satisfaction of both patients and referring physicians. Concurrent with his new role, DiSesa will maintain his duties as Chief Operating Officer of Temple University Health System and Senior Vice Dean for Clinical Affairs at the Lewis Katz School of Medicine.

Amy Goldberg, MD, FACS, has been appointed Chair of the Department of Surgery at the Lewis Katz School of Medicine, Surgeon-in-Chief for Temple University Health System, and Medical Director of Perioperative Services at Temple University Hospital. Since joining the faculty in 1993, Goldberg has held numerous leadership positions — including that of Chief of Trauma & Surgical Critical Care. A frontrunner in patient care, quality, and surgical education, Goldberg has earned numerous awards for teaching and clinical excellence. She is also a well-known violence-prevention champion — and was recently invited to the White House to help launch the Obama Administration's "Stop the Bleed" initiative.

Verdi DiSesa, MD, MBA

Eric J. Kropf, MD, FAAOS, has been named Chair of the Department of Orthopedic Surgery and Sports Medicine at Temple University Hospital. A faculty member since 2009, Kropf has served as Director of Resident Education and as Director of Sports Medicine. A Pennsylvania Delegate for the American Orthopedic Society for Sports Medicine, Kropf is a recognized leader in the field of hip arthroscopy, sports-related hip injuries, and joint preservation. He serves as a team physician for Temple University Athletics and is an orthopedic consultant for the Philadelphia Flyers hockey team.

John Krouse, MD, PhD, MBA, has been named Senior Associate Dean for Clinical Affairs at the Lewis Katz School of Medicine as well as President of Temple University Physicians. In these roles, he will oversee the clinical activities of the university physician practice plan with an eye toward increased clinical and service excellence. A faculty member since 2009, Krouse is Chair of the Department of Otolaryngology-Head and Neck Surgery and founding Director of the Temple Head and Neck Institute. He is Editor-in-Chief of *Otolaryngology-Head and Neck Surgery*.

Grace X. Ma, PhD, has joined the School of Medicine as Associate Dean for Health Disparities and Director of the Center for Asian Health. Ma will promote research focused on underserved communities in concert with the School's Office of Health Equity, Diversity and Inclusion; the Temple Institute for Transformative Medicine; and the Temple Center for Population Health. Ma is the Founding Director of the Center for Asian Health, the Laura Carnell Professor of Public Health, and a member of Fox Chase Cancer Center's Population Science Division.

TUHS MARKETING


R

By GISELLE ZAYON
Photography by FREDRIK BRODEN

PICTURE OF HEALTH

Radiology's Sharp Focus: Patient Care

The Hubble telescope and the electron microscope prove that the quest to *see* is the quest to *understand*.

"When Wilhelm Conrad Roentgen invented the X-ray in 1895, he revolutionized medicine. We could *see* into the body. Before that, the only way to see was through exploratory surgery," says Clifford Belden, MD, Professor of Radiology and Temple University Health System's Radiologist-in-Chief.

Advanced technologies such as CT, MR, and PET, all developed during the last 45 years, illuminate our inner-workings in both static images and in "movies" of anatomy as it functions. "Imaging can detect disease in very early stages — often long before noticeable symptoms appear," Belden says.

At first, radiology was strictly about diagnosing. Now it's evolved into treating and guiding therapy, too. It encompasses the ability to see *and* to intervene (hence the term interventional radiology). "We use imaging to view a patient's anatomy and to guide tools to the precise location within the body to provide treatment — for example, to place a new valve in the heart or to retrieve a clot inside a blood vessel in the brain," Belden explains.

According to Michael Weaver, MD, Chair of Neurosurgery, imaging plays a starring role in procedure rooms at advanced hospitals. The field is called intraoperative imaging. "Imaging during surgery has distinct benefits. While we operate, we refer to super-sharp, oversized images projected on big monitors

BRAIN: ISTOCK

in the procedure room that show us the patient's anatomical detail. This helps the surgeon navigate anatomy with even greater precision, refining the spatial positioning of instruments, even discerning the difference between normal tissue and diseased," Weaver says. "We are even able to rotate the image, look at the anatomy from any angle — which is a clearly helpful tactic."

The field of radiation oncology has also depended on imaging. Today's new image-guided radiation therapy techniques have further refined patient treatments — and outcomes — in impressive ways. Modalities such as intensity-modulated radiation therapy, proton beam therapy, stereotactic radiosurgery, and stereotactic body radiotherapy all utilize imaging in conjunction with computer-controlled X-ray accelerators, enabling precise areas of malignancy to be targeted with radiation while sparing adjacent tissues.

What a long way we've come from Roentgen's humble X-ray. Every year, biomedical engineers make established technologies better. They develop new modes of imaging, too. "But most important," Belden says, "is that radiologic procedures are undoubtedly safer and more comfortable for the patient than ever before." Thanks to the engineering prowess and patient-centered sensibilities of companies like General Electric, the CT scan that took a half-hour 20 years ago now can be performed in seconds. Engineers are turning the MRI scanner that knocked and banged like an iron foundry into something that purrs and hums.

HISTORIC AGREEMENT

In the United States, the average hospital MRI scanner is about 11 years old. With technology improving so swiftly, older machines simply can't compete with their new-generation cousins in terms of patient comfort, ease of use, speed, and clarity. That's why hospitals the world over always clamor for the newest and the best.

However, given the expense of radiology equipment — one machine can cost millions — the standard industry practice is to replace costly MRI and CT scanners one machine at a time. The typical competitive bidding process can take months, or even longer. "But Temple University Health System is looking at this challenge in an entirely new way. In fact, we have created a plan so unique that it has never been done before," Belden says.

On August 25, 2015, Temple University Health System and GE Healthcare announced a first-of-its-kind collaboration: a seven-year strategic alliance agreement that features two unified components. First, it makes GE the primary provider of radiology equipment for all of Temple's clinical facilities system-wide. "GE will replace Temple's equipment with state-of-the-art technology on a predetermined schedule. We created a detailed inventory and assessment of Temple's existing equipment — and plotted it against what we project we'll need to care for our patients going forward. It all comes together as a detailed, long-term plan for replacing our technology," Belden explains.

Second, the agreement calls for GE personnel to work onsite at Temple throughout the life of the agreement to help Temple develop radiology process-improvement. "GE will help us develop best practices for radiology workflow," Belden says. "With its wealth of experience and expertise in Six Sigma and Lean management principles, GE brings great depth to our radiology enterprise. They will work side by side with Temple personnel to analyze and optimize the many processes related to ordering, scheduling, and implementing tests and disseminating their results," Belden says.

"Employing radiology with good 'process intelligence' makes medical diagnoses and treatments a more efficient, less costly endeavor," says Susan Freeman, MD, MS, Temple University Health System's Chief Medical Officer.

HEART: GETTY IMAGES

At first radiology was strictly about diagnosing. Now it's evolved into treating and guiding therapy, too. It encompasses the ability to see and to intervene (hence the term interventional radiology).

Freeman is Chair of the Executive Governance Committee for the GE agreement at Temple University Health System. "Efficiency means better service and better products at a lower cost — in other words, *value,*" she explains.

To this end, the agreement projects $39 million in operational savings for Temple over the life of the contract. Both organizations, in fact, will be rewarded for meeting performance goals that demonstrate higher-quality imaging at a lower cost. As Freeman notes, cost-savings will help defray equipment purchases down the road — ensuring the rapid introduction of new technology. If Temple's radiology-related costs ultimately go down, the savings can be passed along to insurers and patients, she says.

"Higher-quality medical care at lower cost — real value — is the driving aim of the Patient Protection and Affordable Care Act, which took effect in March 2010. To navigate health care reform, medical centers must find innovative ways to approach cost management while enhancing the quality of care," Freeman explains.

These goals are challenging for all health care providers — and especially so for Temple. Because in addition to its immersion in the cost-intensive business of advancing clinical care, medical education, and research, Temple also provides health care to one of the nation's most indigent communities. In fact, the system's flagship hospital provides more free and under-reimbursed care than any other single provider in Pennsylvania.

"Such are the factors that make Temple's agreement with GE a strategic priority," says Larry Kaiser, MD, FACS, the health system's CEO and medical school dean. "The pioneering approach we are taking with GE — aligning financial incentives to work collaboratively in pursuit of higher quality and greater efficiency at lower cost — represents a new frontier in value-based health care contracting."

Jeffrey Immelt, Chair and CEO of GE, agrees. "Like many health systems throughout the country, Temple faces considerable clinical, operational, and financial demands. GE Healthcare understands these market challenges, and we are dedicated to helping customers deliver the best outcomes in today's environment," he says.

Both leaders predict that agreements like this will become a preferred business model over the next few years, with vendor and purchaser both putting "skin in the game," working side by side to achieve shared goals.

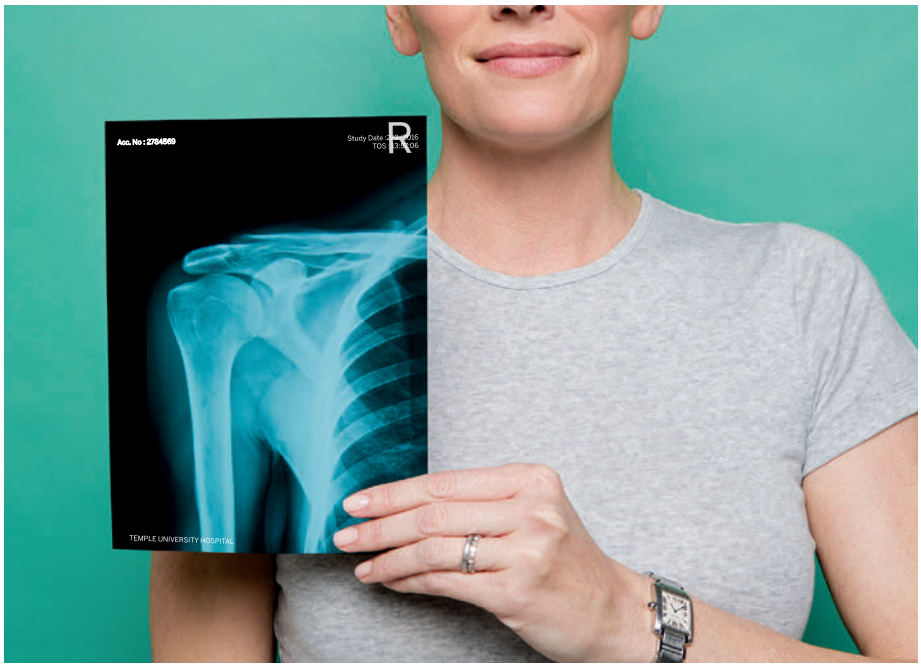
PICTURE PERFECT

The techniques of radiology come into sharper focus, with more clinical import, every year. GE Healthcare is a leader in enhancing established modalities and in bringing new modalities on line.

Several imaging modalities are based on tomography. A tomogram, Belden explains, is an image of a single plane or slice through the anatomy. Positron Emission Tomography (PET) scanning depicts blood flow, glucose metabolism, and other biologic functions as they are occurring. PET can even detect metabolic changes associated with cancer before tumors form. Computed Tomography (CT) is a mainstay technology that works by passing X-rays through the body from several angles, then consolidating them with sophisticated computer software to create an image. CT images of the heart and its arteries can be "snapped" in just one heartbeat. Another tomographic technique is called SPECT, Single Photon Emission Computed Tomography. SPECT uses gamma camera data from many projections to create 3-D images that can be reconstructed in different planes. Like PET, SPECT detects regions of biologic activity associated with disease.

Another technology with exceptional capabilities is Magnetic Resonance Imaging (MRI). "With GE's new MRI technology, we can provide brain examinations and whole-body imaging — quickly and quietly — in just a few simple steps," Belden says.

A number of different tests are performed with MRI technology. Diffusion tensor imaging (DTI), for example, is great at depicting



SHOULDER: DREAMSTIME

white-matter neuronal structure and brain connectivity — therefore useful for diagnosing and treating neurological disorders such as stroke. A technique called intravoxel incoherent motion diffusion is useful for detecting and monitoring cancer. Other diffusion studies include diffusion weighted imaging and diffusion spectrum imaging. All diffusion tests are based on the movement (diffusion) of hydrogen atoms (water) to reveal abnormalities, Belden explains.

Another test based on the MRI platform is magnetic resonance elastography (MRE). This modality provides information on the texture and hardness (elastic properties) of organs and tissues deep in the body — factors that are important indicators of health. "A diseased liver, for example, is stiffer than a healthy one. It's like being able to 'palpate' an organ or area of tissue with a virtual hand," Belden explains.

Magnetic particle imaging (MPI) is another test performed on the MRI machine. It involves injecting superparamagnetic iron oxide nanoparticles into the blood stream — which results in images of extraordinary detail.

Medical ultrasonography is another essential imaging technology with multiple applications. And like MRI, the modality is radiation-free. Ultrasound employs high-frequency sound waves that are reflected by tissue in varying degrees to produce images — even in three dimensions. While most commonly associated with imaging a fetus, ultrasound also fulfills an important role in imaging abdominal organs like the liver and gallbladder. It's excellent for imaging muscles, tendons, and blood vessels, too. Real-time moving images help guide biopsies and other procedures. When applied to the heart, ultrasound is called echocardiography — a hugely important tool in cardiology.

"Newer-generation machines manufactured by GE are able to operate on multiple platforms — and much is gained by combining techniques," Belden says. Utilizing PET with CT, or MRI in conjunction with CT, reveals metabolic information and anatomic detail at the same time — and provides imaging of greater sensitivity and specificity than any single technique could alone — thus generating a deeper and broader view of a patient's condition than ever before. According to Belden, we'll see more combinations of different imaging techniques in the future.

To see is to understand, to understand to see. In the laboratory, ever-improving visualization techniques enable the human eye to see what's never before been seen. A platform called stochastic optical reconstruction microscopy (STORM) reveals pathogens at 4 angstroms (four ten-millionths of a millimeter — nearly at the atomic level). Future developments in visualization portend yet more techniques that will elucidate metabolism and physiology at the cellular and molecular levels. It's deep space travel indeed.

ROCKING RADIOLOGY

When Belden was recruited from Dartmouth College in September of 2015 to lead Temple's radiology team, the GE agreement definitely attracted him. "It was an opportunity to get in on the ground floor of something that's never been done before," he says. Temple's mission was a draw for him, too. But what really clinched it is Temple's history and expertise in radiology.

In 1937, Temple's W. Edward Chamberlain, MD (1905 - 1976), rocked the radiology world when he invented the image amplifier, a device that converted the X-ray beam into light that can be seen — making dull, subtle images several thousand times brighter. "Thanks to Chamberlain, gone are the days when images could be viewed only in the darkroom," Belden says. "Most important of all, his invention made the X-ray safer, enabling the radiation to which the patient is exposed to be reduced to a hundredth of what it had been." Chamberlain also invented the first stereoscopic (3D) X-ray.

ULTRASOUND: TEMPLE UNIVERSITY HOSPITAL

Another Temple great is Akbar Bonakdarpour, MD, one of the "fathers" of musculoskeletal radiology. Through intense research and systematic analysis over many years, he helped to establish a whole new discipline based on the radiologic diagnosis of conditions affecting the skeleton, muscles, ligaments, tendons, and cartilage. Bonakdarpour is a past president of the International Skeletal Society. Every year it gives an annual award in his honor.

In addition to creating catheterization techniques to visualize internal structures, Temple's Herbert Stauffer, MD (1914-1970), designed the television stereoscopic fluoroscope and a biplane high-speed cineangiographic device to study blood flow — transformative work.

National safety and technical standards regarding the use of radioactive material in medical diagnosis and therapy owe much

Clifford Belden, MD

JOSEPH V. LABOLITO

The CT scan that took a half-hour 20 years ago now can be performed in seconds. Engineers are turning the MRI scanner that knocked and banged like an iron foundry into something that purrs and hums.

to Leon S. Malmud, MD, who for a decade chaired the Nuclear Regulatory Commission's National Advisory Committee on the Medical Use of Isotopes. This committee establishes national safety and technical standards for the use of radioactive materials in medical diagnosis. The NRC recently awarded Malmud a gold medal for his work. A past president of both the American College of Radiology and the Society for Nuclear Medicine, Malmud has been honored for his contributions.

Another longtime faculty member honored nationally for making radiology safer is Marvin Ziskin, MD. As a consultant to the FDA's Radiological Devices Panel, Ziskin developed methods to quantify exposure metrics and dosimetry. Ziskin is also a pioneer in diagnostic ultrasound. In 2012, the World Federation of Ultrasound in Medicine and Biology awarded him its highest honor. Ziskin is perhaps the world's foremost expert in bioelectromagnetics, too, Belden says.

"We have other faculty who are nationally recognized in radiology," Belden says, mentioning N. David Charkes, MD, who won the 2014 de Hevesy Nuclear Pioneer Award of the Society of Nuclear Medicine and Molecular Imaging, and Alan H. Maurer, MD, who recently served as President of the Society of Nuclear Medicine. "Innovation and leadership in radiology have been trademark at Temple for 80 years — and continue today," Belden says.

INNOVATION AND LEADERSHIP

The GE-Temple agreement is inventive, new, and exciting. It's also based on a well-founded relationship going back a long way. Temple has purchased GE technology for as long as anyone can remember. And in the 1980s, the construction of Temple University Hospital's Rock Pavilion depended on GE's ability to make good on a promise, Malmud says.

At the time, the Radiology Department was located in an old building that had to be torn down in order to complete construction on a new one, the Rock Pavilion. The old department, however, could not be demolished until the new department (in Rock) was fully functional, ready to go. "Healthcare is a 24/7 commodity. We could not interrupt patient care. Moreover, demolition or construction delays would have meant enormous cost overruns," Malmud says.

GE was competing with other major manufacturers for the multimillion-dollar contract, Malmud recalls. As chair of the department at the time, the decision was ultimately his. Confident that GE would perform in the reliable and expeditious manner they always had, he awarded GE the job. The results? "Exceptional. On time, on point, and within budget," Malmud says.

Exceptional products and services continue to put Temple in the lead in imaging services in the Philadelphia region today.

"By working collaboratively with GE across Temple University Health System to enhance the value of our services, we will deliver high quality at reduced cost, meet challenges in a changing economic climate, and ensure our radiology enterprise supports the changing demands of our patients, physicians, and payers," Belden says. "That's the goal. To be best in class, quality, and value. To focus on consistently delivering an outstanding experience to every patient, every time."

To make an appointment with a Temple physician, call 1-800-TEMPLEMED.

Role Call

Doctoring, Redefined

"In days gone by, physicians were the unquestioned authorities," recalls Audrey Uknis, MD, a 1987 Temple University Lewis Katz School of Medicine alumna and Senior Associate Dean for Admissions at the school.

Her colleague Larry Kaplan, MD, was also a student and resident at the school in the 1980s. He, too, remembers that time. "Had a nurse suggested ideas about a patient, my reaction would have been 'Why are *you* approaching *me*?'" he says.

This worldview was even more manifest in the 1950s, when Kaplan's father, Alvin Kaplan, MD '55, was in medical school. "The other professions were merely there to help physicians," Alvin says.

"But today, patients are the captains of the ship — and physicians are part of the crew steering them to optimum health," the younger Kaplan says.

Since 2006, as Associate Dean of Interprofessional Education, Larry Kaplan has been bringing medical students together with Temple students in nursing, pharmacy, dentistry, podiatry, social work, and other disciplines to learn how to work together. "Each profession brings differing strengths to patient care," he says. "Watch and you'll see."

With this, Kaplan takes us to the William Maul Measey Institute for Clinical Simulation and Patient Safety, a training facility at the Lewis Katz School of Medicine. He flips a light switch outside a patient exam simulation room, illuminating three students and a patient behind a one-way mirror. They cannot see or hear us, but we can observe them.

By BRUCE E. BEANS *and* GISELLE ZAYON
Photograph by CLINT BLOWERS


LEWIS KATZ SCHOOL OF MEDICINE
TEMPLE UNIVERSITY
Patient Advocate
Quality Specialist
Clinical Innovator
Care Planner
Value Promoter
Ethics Expert
Access Advocate
Team Leader
Technology Adopter
Diversity Promoter
Barrier Identifier
Cultural Champion
Peer Educator
Care Architect

Inside, Mrs. D, a middle-aged patient with Parkinson's disease, is telling Rachel Kominsky, a medical student, that her vision is blurry. She feels unsteady on her feet. Kominsky suspects Mrs. D's Parkinson's is worsening — until she and Tenielle Watkins, a pharmacy student, and a student in the nursing program review the list of medications Mrs. D is on. Instantly they spot the problem: Mrs. D has been taking a homeopathic remedy for depression that can cause an adverse interaction when combined with Parkinson's medications. Therefore, the students advise Mrs. D to stop taking the homeopathic drug, and arrange for her to see a psychiatrist who could prescribe an antidepressant that won't cause untoward interactions. They also fine-tune her Parkinson's medications to create a better overall regime.

Mrs. D is actually an actress trained to portray a patient. But the students are real, the scenario realistic, and the encounter an example of how students at Lewis Katz School of Medicine are trained: together.

"Professionals practice as a team. Therefore, they need to be educated that way," says Kaplan.

Teamwork benefits patients. Studies show that when teams of physicians and other health care professionals make hospital rounds together, lengths-of-stay and the likelihood of complications decrease. "Patients benefit when professionals with specialized knowledge and skills come together," Kaplan says.

Arc of the Story

The rise of the physician to American health care king was swift and steep. In fact, in 1901, the founding year of the Lewis Katz School of Medicine, people were as likely to seek medical help from a druggist, midwife, folk healer, nurse, or neighbor as they were a physician. It was not automatically assumed that a physician would provide superior care.

"That's because American medical training was a poorly regulated affair in those days," says Gerald Sterling, PhD, Senior Associate Dean for Education. "The content, quality, and methods of education varied considerably from school to school, as did requirements for admission and graduation."

At the turn of the 20th century, Sterling explains, many of the 155 U.S. and Canadian medical schools were small, for-profit trade schools. Hardly any were affiliated with a college or university. And only 10 percent required that applicants complete two or more years of college before applying.

Then came the 1910 release of the Carnegie Foundation's landmark Flexner Report, the first assessment of medical education nationwide. Flexner shook things up, to say the least. Some schools closed. Others merged. By 1935, only 66 MD-granting schools remained. Today there are 141 accredited medical schools in the United States and 17 in Canada.

Flexner had plenty of not-so-flattering things to say about Temple University's medical school. Its evening curriculum, for example, did not impress the reviewers as a worthy innovation. "But 'the midnight medical school' did have its advantages," says Sterling. "It was part of a university, for one thing. It also had a solid curriculum — designed by experienced educators who were physicians. And it was a five-year program. Many schools granted MD degrees in just two years back then."

A big criticism leveled at most schools by Flexner concerned the dearth of practical experience for students. "Students were subjected to interminable lectures," the report said. "If fortunate enough to gain entrance to a hospital, they observed more than participated."

Here, too, students at Temple (now the Lewis Katz School of Medicine) were fortunate. They apprenticed with faculty who saw patients at the Samaritan Hospital (Temple University Hospital), founded in 1892.

"We have always distinguished ourselves by producing outstanding clinicians," says Uknis. "It is still our strong suit. Our physicians know how to develop strong doctor-patient bonds. They understand the value of quick, practical thinking regarding patient care. Year after year, residency program directors around the country tell us that, compared to students from other top schools, our students start off differently. Graduates of the Lewis Katz School of Medicine are more comfortable working with patients, better prepared."

As Sterling adds, "The difference is that students here serve on the health care team. They *do* things."

At the Lewis Katz School of Medicine, students learn the physician's art and science in a course called "Doctoring," a longitudinal and fundamentally important course that runs through two full years of medical school. The Doctoring course employs tactics to integrate basic science concepts with actual clinical situations, introducing students to the ways that seasoned professionals think and behave.

With their professors observing behind one-way mirrors and later debriefing them, students learn safely with standardized patients like Mrs. D, and with SimMan®, a highly sophisticated patient "robot" in the school's clinical simulation center. Students participate in clinical reasoning conferences that hone their diagnostic skills. They're given lab test results, symptom lists, and health histories — and must "figure out cases" by deciphering the clues. Students also interview hospitalized patients to better understand what it is like to be ill and on the receiving end of care.

Community service learning is fundamental to professional development, too. During her first two years, Rachel Kominsky volunteered with faculty members on a specially equipped medical van that serves the community's most vulnerable patients, part of Prevention Point Philadelphia's Streetside Health Project.

Students also shadow faculty physician mentors. After rounding with Jeffrey Liu, MD, Assistant Professor of Otolaryngology-Head and Neck Surgery, Kominsky became enthralled with otolaryngology. "It played a huge role in determining the specialty I want to pursue," she says.

As Sterling puts it, "Professors were once 'the sage on the stage.' Now they're more likely to be 'the guide on the side.'"

Students also learn from students at more advanced stages and from students in other health care professions. In fact, to further the aims of team-based, inter-professional medicine, the Lewis Katz School of Medicine has launched a brand-new program for physician assistants (PAs), a 26-month course leading to the Master of Science degree. In much of it, physician assistant students and medical students train side-by-side, and with students in other health professions.

"This will effectively 'bake' collaborative teamwork into the roles they learn," Kaplan says.

Larry Kaplan, MD

JOSEPH V. LABOLITO

All Hands on Deck

The emphasis on teamwork, according to Kaplan, is a clear recognition that there are major issues regarding access to care. "Statistics prove we need more health care for many populations. Interprofessional collaboration better enables us to meet rising demand," he says. According to the Bureau of Labor Statistics, by 2020 the need for PAs will increase 38 percent.

Teamwork has another potent motivator: the biomedical science information explosion. The rate of increase is approaching warp speed. Experts predict that by 2020, medical knowledge will double every 73 *days*. "This means that four doublings of knowledge will occur while the Class of 2020 is in medical school," Sterling says.

If ever a situation called for more heads and hands, this is it. Students must possess a vast amount of medical knowledge to pass the medical licensing exams. And to make the order even taller, medical school graduates must demonstrate 58 realms of competency in seven different domains. Many of these competencies hurtle beyond scientific facts and formulae. For example, students must demonstrate their ability to incorporate cost-awareness and risk-benefit analysis in patient care.

"There is no question that we have great expectations of our physicians today," says Larry Kaiser, MD, FACS, Dean of the Lewis Katz School of Medicine and President/CEO of the Temple University Health System. "Medicine goes far beyond biology. Today's students learn medicine within the wider context of health and of patient care. We teach medical students to judiciously use their knowledge, skills, and sociopolitical awareness to benefit their patients. This is the physician's contract with society," Kaiser says.

The contract with society doesn't stop at clinic walls. It requires collaboration with community and government agencies, advocacy groups, insurers, elected officials — and of course with patients and families.

According to Kathleen Reeves, MD, Senior Associate Dean for Health Equity, Diversity and Inclusion, physicians must grasp the market forces of medicine, the societal exigencies that make health status and access to care different for different people. It is not a level playing field. "Contemporary health care is a complicated affair. Its multiple and evolving aims require the ongoing scrutiny and adjustment of our curricula," Sterling says. To this end, the school calls its educational strategic plan "Improving Health Through Innovation in Medical Education."

In addition to educating 840 medical students, the Lewis Katz medical school also trains 535 residents and fellows in 34 residency and fellowship programs. Specialization requires that physicians complete an additional three to nine years of postgraduate work and then pass board-certification examinations. These, too, encompass rigorous, broad-based competency measures, medical and contextual.

Competencies are pursued by *all* members of the health care team, at every level. Temple University Health System follows Culturally and Linguistically Appropriate Services (CLAS) standards, among other guidelines promoting cultural competence set forth by The Joint Commission and the U.S. Department of Health and Human Services.

"More than ever before, medical education concerns itself with preparing physicians to address the socioeconomic determinants of health," Kaiser says. "Recognizing the impact these things have on health, it is our moral and professional imperative to do so."

Hannah Ravreby, MD '10, Assistant Professor of Clinical Medicine, is a Katz school alumna, who like many others, came back to serve on her alma mater's faculty. "When physicians care for a patient, it is our responsibility to treat the whole patient — not just their illness," she says.

Her husband, Daniel Mueller, MD '10, is now an infectious diseases fellow at Temple. "I stayed and Hannah came back because we get so much satisfaction caring for patients from the North Philadelphia community. But we know we can't do it alone. Patients get the best treatment when the whole health care team is involved and working together," Mueller says.

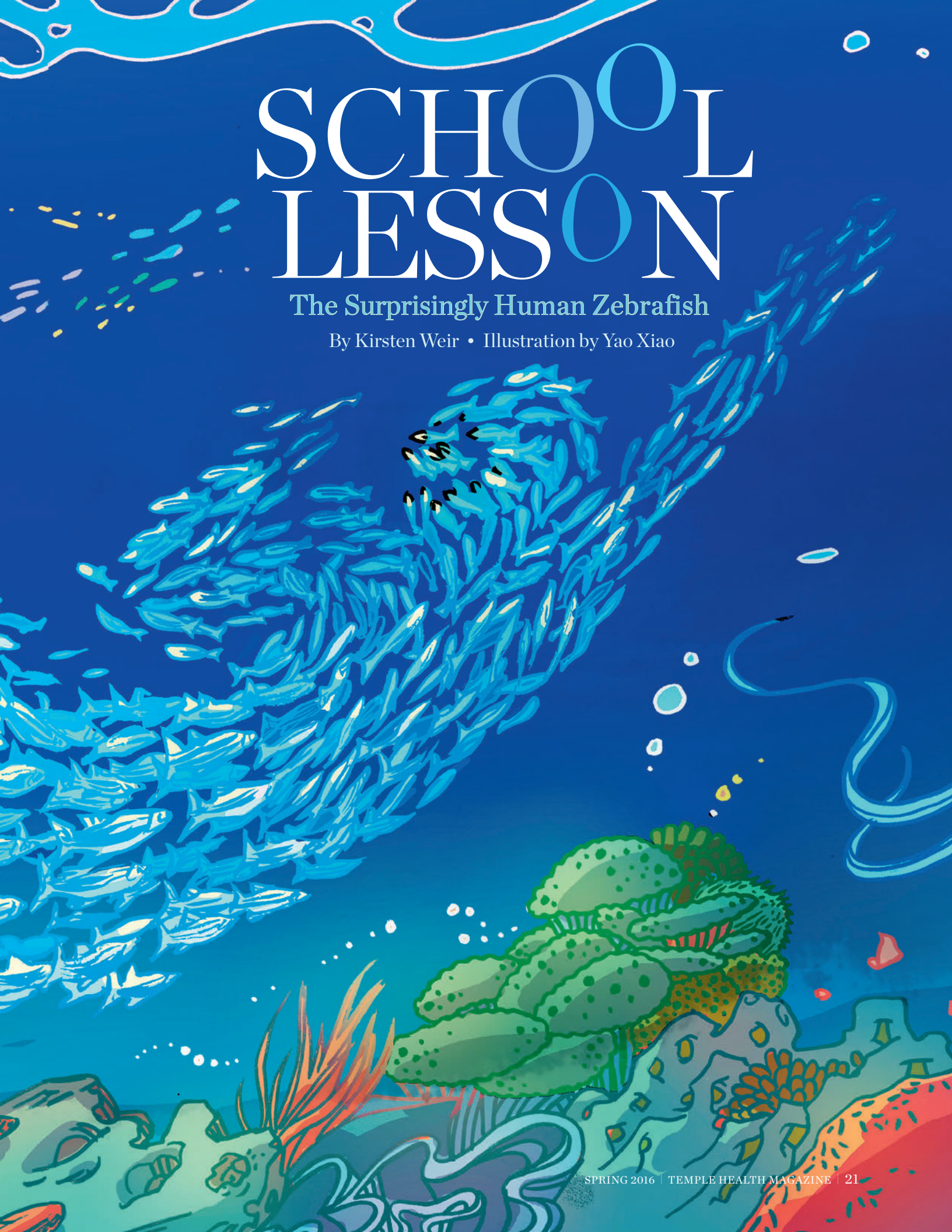
Once upon a time, children dreamed about becoming a doctor. Now they dream about becoming a doctor with a social conscience, a doctor with paradigm-shifting roles to play.

For more about the Lewis Katz School of Medicine, visit https://medicine.temple.edu/

SCHOOL LESSON

The Surprisingly Human Zebrafish

By Kirsten Weir • Illustration by Yao Xiao



When recruits come to work in the new zebrafish lab at the Lewis Katz School of Medicine, Glenn Gerhard, MD, welcomes them with a few words of warning: "When you work with fish, you get wet." But it's a small price to pay. As laboratory animals go, zebrafish have a lot going for them.

"Unlike mice, zebrafish don't bite. They're happy to see you when you come to feed them. In fact, they're always smiling," says Gerhard, Chair of the Department of Medical Genetics and Molecular Biochemistry. True, he admits — that's just how their mouths are shaped. But an amiable countenance is just a bonus on their impressive list of attributes.

The species is also the world's first genetically engineered pet; a variety known as GloFish™ is designed to fluoresce in neon hues. Up on the International Space Station, the fish are being used in research to understand how muscles atrophy in zero gravity. Back on Earth, zebrafish *(Danio rerio)* have become virtually indispensible in studies of developmental biology, disease modeling, cancer genetics, and more.

Though native to tropical streams of the Himalayas, the freshwater species is hardy enough to be sold in Walmart for home aquariums. In recent decades, zebrafish have also gained popularity in research labs around the world. At the Lewis Katz School of Medicine, Gerhard recently put the finishing touches on a new facility capable of housing 5,000 adult fish. He's studied these energetic inch-and-a-half-long swimmers for more than two decades, and knows they pack a serious scientific punch.

"Zebrafish have earned their spot in the lab because they combine many of the best traits of other model organisms," Gerhard says. Fruit flies and roundworms are popular in research because they produce plentiful offspring at relatively little cost, but they're invertebrates, only distantly related to humans. As fellow mammals, we have much more in common with mice and rats. But rodents are more expensive to rear, and their development is hidden away inside the mother's womb.

Enter the zebrafish. "About 70 percent of human genes have clear analogues in the fish," says Gerhard, the Joseph and Rebecca Goodfriend Endowed Chair in Genetics.

The zebrafish's reproductive capabilities are a marvel. Each female can lay up to several hundred eggs per clutch, and the embryos develop rapidly. "You take a fertilized single-celled embryo, and 24 hours later you have a little fish," Gerhard says.

Rapid and plentiful reproduction is a benefit for laboratory studies. A real boon is that the embryos develop outside the mother's body, where they're easy to access and large enough for researchers to manipulate. Better still, the embryos are transparent. "We can see the organs develop, the blood cells flowing through, even watch physical abnormalities take shape in real time," Gerhard notes.

Drawn by this useful combination of characteristics, scientists started using zebrafish in the 1980s to study the processes underlying vertebrate development. Researchers found they could add chemical compounds to the fish's water to induce mutations. By studying the mutated genes in the abnormal fish that resulted, scientists identified a range of genes that are critical to normal vertebrate development. "The zebrafish is still a mainstay of developmental biology," Gerhard says. "But over the last few decades, the fish have proven their mettle in many other ways."

Much of Gerhard's research focuses on identifying the genetic variants that underlie human diseases. And zebrafish, he's found, are a great means to that end. "If you look at genes that cause disease in humans, 84 percent have zebrafish analogues," he says.

Gerhard uses zebrafish to create disease models to better understand genetic contributors to conditions such as obesity, cancer, fatty liver disease, and heart failure. And that's just for starters. In his lab and others, the fish have been enlisted in studies of a wide range of age-related human diseases, including diabetes, osteoporosis, hearing loss, macular degeneration, Parkinson's disease, and Alzheimer's disease. As Gerhard points out, these diseases are complex. So complex, that so many different genetic mutations have emerged as suspects that it would be nearly impossible to study them all in humans — or even in mice.

"If you want to quickly, easily, and cheaply figure out which mutations have the biggest impacts, zebrafish can be very useful," Gerhard says.

Unlike humans, zebrafish have a fascinating ability to regenerate damaged body parts, from hearts to tails. Therefore, they've proven ideal for Darius Balciunas, PhD, Assistant Professor of Biology, who maintains a zebrafish laboratory of his own. He is particularly interested in understanding the genetic mechanisms that enable the fish to regrow pieces of a damaged heart.

Twenty percent of the fish's ventricle can be removed, and after one month it regrows, the heart is as good as new. "By elucidating the mechanisms that underlie regeneration," Balciunas says, "scientists might one day be able to develop methods to help repair or regrow human heart tissue."

Regeneration, in large part, replays the processes of embryonic development, Balciunas says. But that presents a catch-22: fish with genetic mutations that impair the regeneration process are hard to come by, since most of those mutations would have prevented them from developing into adult fish in the first place.

To get around that, Balciunas and colleagues developed a biotech tool called a gene trap, which enables them to switch off genes at will. "We can inactivate genes in adult fish to determine if that gene is necessary for regeneration," he says.

These energetic inch-and-a-half-long swimmers pack a serious scientific punch. "If you look at genes that cause disease in humans, 84% have zebrafish analogues," Gerhard says.

Glenn Gerhard, MD

JOSEPH V. LABOLITO

As a result of this work, he has zeroed in on at least one gene that appears to be critical to the regeneration process — all thanks to a stripey, slippery little fish.

The fish is also gaining fans in the world of cancer research, says Jennifer Rhodes, PhD, Assistant Professor at Fox Chase Cancer Center and director of the Center's zebrafish facility, which houses some 15,000 fish. Researchers there are using the fish to study processes such as immune cell development, the immune system's response to cancer, and the mechanisms that cause tumors to form and grow.

In her own research, Rhodes uses the fish to study the development of blood cells and blood-cell cancers. Though zebrafish and humans last shared a common ancestor some 340 million years ago, we share the same spectrum of blood cell types. "For the most part, the developmental processes and the actions of genes are well-conserved between species," she says.

As with regeneration, many of the basic processes of embryonic development are also key to keeping the blood system in check. "If something goes wrong in that process, it can contribute to leukemias, lymphomas, myelomas, and other blood cell diseases," Rhodes says. Blood cancers account for almost 10 percent of cancer deaths, and leukemia causes more deaths than any other cancer among people under age 20.

Rhodes and her colleagues perform random mutagenesis screens, using Balciunas's gene trap vector to silence genes without any preconceived notions of the gene's function. Then they look to see which, if any, influence blood-cell development.

The fish are also extremely useful for digging deeper into genes already on the suspect list. By silencing a zebrafish gene of interest — or, conversely, cranking up a gene's activity — Rhodes can determine more about each gene's role in blood-cell development. In fact, using zebrafish, Rhodes has identified a new gene family that seems to be important to blood-cell development. Next she'll explore exactly how those genes function in normal and abnormal cell development. "Zebrafish are expanding our knowledge of blood-cell biology," she says.

And the little fish might be poised for even greater use — in studies related to cancer and beyond — thanks to new technologies such as a gene-editing technique called CRISPR, which enables DNA sequences to be altered more cheaply and more precisely than ever before. Balciunas says the technique enables scientists to quickly and easily create custom strains of fish in their own labs.

Zebrafish are also proving a top choice for small-molecule screening, an important first step in the drug discovery process. Potential drug candidates are typically applied to human cell cultures to gauge their effects before they are tested in organisms such as rodents. In many cases, zebrafish could take the place of cell cultures, Balciunas says, enabling medications to be affordably tested in a living system instead of a petri dish.

"Zebrafish are almost like a cell culture model themselves, but they're a little organism," says Gerhard. "They have a beating heart, a brain, muscles, behavior. You can do alcohol studies, appetite studies, anxiety studies. Whatever you do in mice, you can probably do with these unsung heroes of the science lab."

Rhodes started studying zebrafish in 2000, and says the species has gained a lot of proponents in the years since. "Fifteen years ago, a few hundred people attended the annual meeting of zebrafish researchers; now there are thousands," she says.

Serendipity brought the fish to Gerhard's attention in the early 1990s. One day, during his fellowship at the University of Pennsylvania, he substituted for his faculty mentor, who was out sick, to meet one-on-one with a scientist invited to present a seminar about zebrafish. "It was one of the most amazing hours I've ever spent," he recalls. "I was spellbound."

Soon after, Gerhard secured his first faculty job, at Penn State. As luck would have it, a zebrafish lab was located across the hall, where colleagues were studying developmental biology. They needed lots of embryos. As soon as the fish's embryo production began to decrease, however, the biologists had no use for them. But Gerhard, who is interested in diseases of aging, happily took the fish off their hands. "In 2002, we published the first paper describing basic aging characteristics of zebrafish, and launched that area for the field," he recalls.

In 2014, Gerhard was recruited to Temple to launch a new Department of Medical Genetics and Molecular Biochemistry, "one of just a handful in the nation to combine clinical medicine, research, and education for future generations of scientists," Gerhard notes. The department is being engineered toward translational research, one of Temple's priorities, transforming basic science discoveries into better patient care.

Zebrafish, it seems, have been engineered to similar ends, by nature and by science.

"Jump in," Gerhard says. "The water's great."

Kirsten Weir has written for *Discover, New Scientist,* and *Popular Science.*

Mirror Medicine

Pain Relief from a Pane of Glass

By Meredith Mann

If, one year ago, you had mentioned mirror therapy to Arnold Carlton, he probably would have thought you mad. But by the end of 2015, the Philadelphia resident was a believer in this innovative therapy, offered by Temple University Hospital's Physical Medicine and Rehabilitation Department.

"I was impressed," says Carlton, who received mirror therapy to ease pain following the amputation of his lower left leg. "I feel good now."

THE PHANTOM MENACE

Carlton's reaction — serious skepticism, followed by wholehearted acceptance — is typical for patients encountering mirror therapy for the first time. After all, the treatment (developed at the University of California-San Diego by neurologist V.S. Ramachandran, MD, PhD) has only been in use since the late 1990s. Mirror therapy is a physical process, but its surprising results stem from changes in the brain.

When a patient loses a limb, whether through trauma or planned amputation, he or she may still "feel" that missing body part — in a painful way. Scientists don't fully understand why this lingering "phantom limb pain" happens. It may be related to crossed wires in the body's nervous system. Suddenly and inexplicably, the spinal cord and brain stop receiving signals from the nerves of the amputated area — so they confusedly react to this absence by sending out signals of pain, as if the limb still exists.

"Phantom limb pain has existed since time immemorial, and often written off as people being crazy or making it up," explains Eric Altschuler, MD, PhD, Associate Professor of Physical Medicine and Rehabilitation at Temple. But the pain is very real. "Phantom pain has entered the realm of regular medicine, and is no longer considered psychosomatic, or 'all in the patient's head,'" says Altschuler, who worked with Ramachandran when he was a medical student, and joined him in publishing the first paper on the use of mirror therapy for patients with hemiparesis following stroke. Today, with funding from the Foundation for Physical Medicine & Rehabilitation, Altschuler is researching whether the treatment can help combat veterans recover from pain due to nerve or orthopedic damage.

AN OPTICAL ILLUSION

The key to mirror therapy lies in the brain's visual cortex. "Basically, vision overrides or supercedes other sensory perception," notes Altschuler. The patient moves the still-functioning limb in front of a mirror, and the reflection stands in for the phantom limb. This visualization overrules other sensory perceptions and tricks the nervous system into calling off the pain. The approach seems to work best with motor pain — such as spasms — as opposed to burning-type pain, according to Altschuler. Mirror therapy has been used not only for amputation but also in cases of stroke and complex regional pain syndrome, a condition in which a damaged limb experiences chronic pain.

The process works like this: The patient is positioned in a way that enables him to see the mirror clearly, but not see his amputated limb. He is then asked to focus on the mirror the entire time and to move "both" legs or arms at the same time. Usually the patient is instructed to perform simple range-of-motion exercises. Therapy sessions may last for 15 to 30 minutes daily. After discharge, the patient can continue to perform the exercises at home. "Often, after a few weeks, the phantom pains are basically gone," Altschuler says.

"IT REALLY DOES WORK"

The therapy has done a world of good for Carlton, a former security guard and concierge, whose poor circulation and diabetic neuropathy started claiming the toes of his left foot. In the fall of 2015, he was left with no option but to have his leg amputated below the knee. Soon his phantom limb hurt. "It was a throbbing, sharp, constant pain," he says.

When Altschuler suggested mirror therapy as a solution, Carlton was dismissive: "I said, 'Yeah right, that stuff isn't going to work.'" Yet, once persuaded to try, Carlton was amazed at the results. "They put a mirror between my legs and said to move both legs at the same time. It looked like I had two legs," he recalls. "I realized, 'Oh yeah, it really does work.' It relieves the pain." He didn't need much convincing after the first session. In fact, Carlton continued doing mirror therapy at home. "It relaxes you and makes you feel good. I would recommend anybody with phantom limb pain to do it," he says.

Illustration by Tim O'Brien

Microbial Musings

Insights About Infection and Immunity

It turns out that bacteria, viruses, fungi, and protozoa are just as essential to human health as food, water, and air. Our bodies house some 100 trillion organisms representing 10,000 different species. With microbial cells outnumbering human cells 10 to 1 (and 100 microbial genes for every human one), we begin to see ourselves for the ecosystem we really are.

Each of us coexists with a unique microbial community. At birth, we get a starter set. When we pass through the birth canal, we pick up the microbes that inhabit our skin, mouth, gut, and lungs all our lives long. Babies delivered by cesarean section, thus uninoculated, begin life at a deficit — and remain more susceptible to asthma, eczema, and other conditions. In addition, mother's colostrum and milk contain oligosaccharides that help essential microbes colonize the infant.

By GISELLE ZAYON
Illustration by EDDIE GUY

According to Doina Ganea, PhD, Chair of the Department of Microbiology at Temple University's Lewis Katz School of Medicine, our microbial tenants are nonpathogenic. They do not cause disease. "To the contrary, they are indispensable to us, performing a range of cellular 'housekeeping' and metabolic functions that humans, strictly speaking, lack," she says.

For example, the bacteria in our gastrointestinal tracts do much of "our" digestion, extracting nutrients from food, breaking down fiber and complex carbs and fats, even helping to detoxify carcinogens we ingest. Specific bacteria help to synthesize vitamins, metabolize drugs, and inhibit pathogen growth. They also play a lead role in our immune system.

Each individual's microbiome is cultivated by — and idealized to — his diet, lifestyle, and environment. Consider the traveler who gets sick after drinking water in a foreign country, while the natives who drink it daily feel just fine — having not just developed immunity, but also having developed the proper consortium of microbes to resist the pathogens, Ganea explains.

The state of human health *depends* on microbes. We live and work together. We co-evolved together, too. In some cases, to the point of merging. Mitochondria, the tiny organelles inside our cells that create adenosine triphosphate (ATP), the chemical energy that maintains life, are a good example.

"Mitochondria evolved from cyanobacteria that came to live inside our forebears' cells about two billion years ago," says Muniswamy Madesh, PhD, Professor of Biochemistry. "Incorporating cyanobacteria gave us a considerable evolutionary advantage — because it took on the job of respiration in host cells that once relied on glycolysis and fermentation," he notes.

We have other human parts that weren't always strictly human. The cells that form the outer layer of the placenta may have originated from a virus. Even the way that the human genome works, the "technology" that turns genes on and off in human embryonic stem cells, may well have its origins in ancient viral infections.

COEXISTING, COOPERATING, CONFLICTING

According to Bettina Buttaro, PhD, Associate Professor of Immunology and Microbiology, we learn more about the microbiome every day. "This exploding body of knowledge will transform all branches of medicine and science," she says.

Buttaro teaches future physicians and scientists just how central the microbiome is to normal human physiology. Bacterial function and human function are intertwined. Twenty years ago, we knew little about this, but students today learn about the human-microbe alliance, about the benefits our commensal microbes exchange with us.

Throughout our bodies, microbes of different species create distinct environments. "Thousands to millions of bacteria, for example, inhabit every square centimeter of our mucosal surfaces and skin, with discrete communities occupying specific niches serving specialized functions," Buttaro says.

When learning about pathology and disease, students see the dark side of the microbiome, too.

Yet in microbial terms, good and bad are a matter of degree, proportion, and context. "Our health depends not just on what 'germs' we have," Buttaro says, "but in what relative proportions of species — combined with a host of other factors." *Host* is the apt term here. Because host behaviors and conditions can turn a microbe from innocuous to infectious. Healthy individuals are exposed to opportunistic pathogens all the time. Normally our microbially-mediated immune systems hold them in check. But a significant change — taking an antibiotic, for example — can let them seize control.

Thomas Fekete, MD, Chief of the Section of Infectious Diseases at Temple University Hospital (TUH), reminds us that, in the proper degree, exposure to even classically "bad" microbes is a good thing. "When Europeans came to the 'new world,' they were already infected by viruses such as smallpox and measles, yet the population had already developed partial immunity, so new infections only involved a fraction of the whole. The unexposed Native Americans, on the other hand," he says, "were decimated by these old-world infections." They'd never been exposed before, thus never had the chance to develop immunity.

The state of human health *depends* on microbes. We live and work together. We co-evolved together, too. In some cases, to the point of merging.

Exposure is the primary mechanism of immunity. Even the much-feared Ebola virus is harmless to the fruit bats that carry it.

Infection and immunity are a yin-yang world. The very word "germ" represents a stark dichotomy. A germ is an organism that can cause disease. Yet a germ is also something capable of building new tissue (egg and sperm are germ cells). Gardeners germinate seeds. One word, polar opposite connotations.

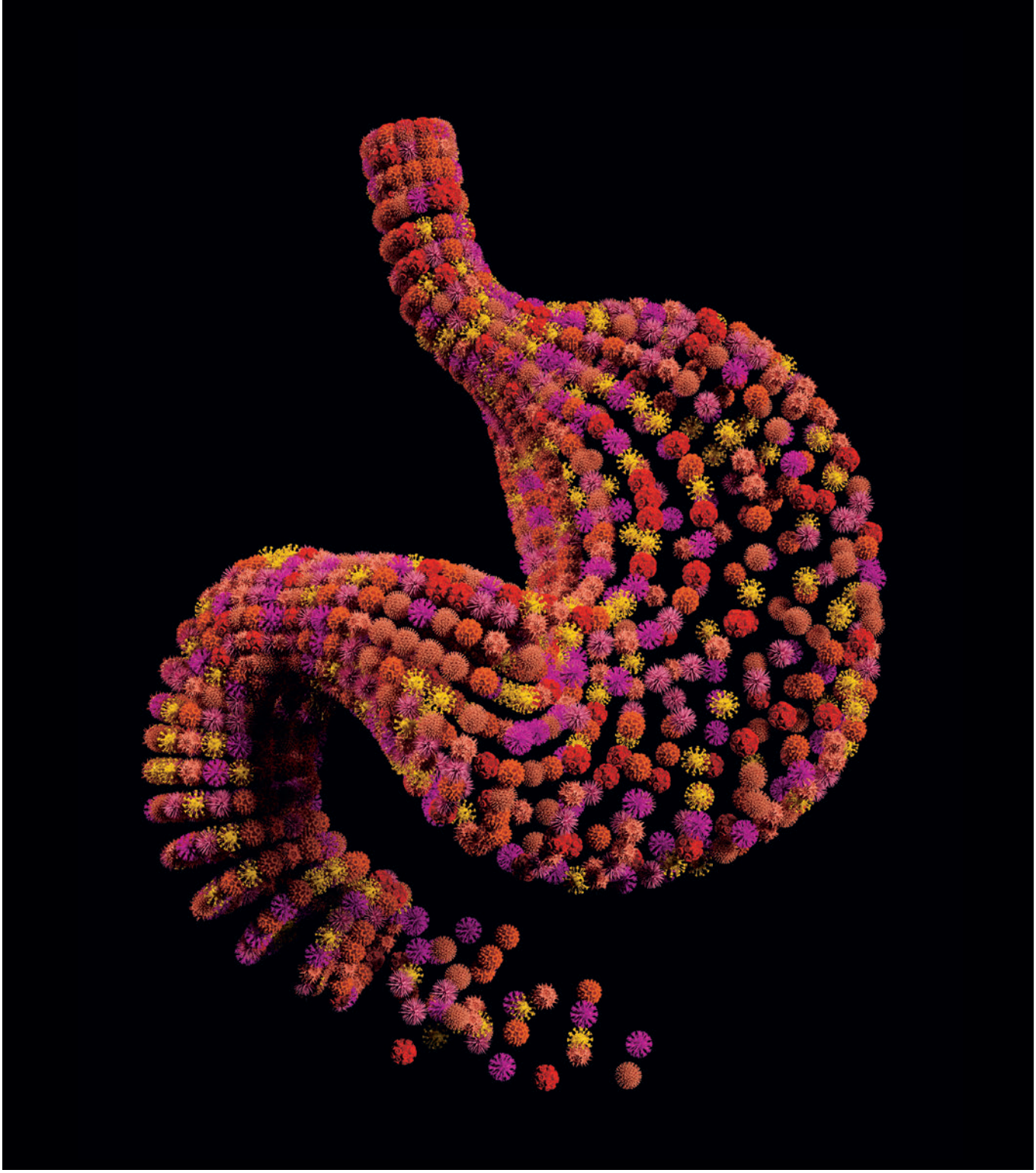
In microbial terms, it's even possible to be too clean. Overcleaning a wound, for example, will kill off the bacteria that help it heal. Triclosan, the active ingredient in most hand sanitizers, eradicates commensal microbes as well pathogens, possibly making us more susceptible to certain infections.

OVERKILL

The first antibacterial wonder drugs — sulfonamides, penicillin, and streptomycin — were developed in the 1930s and 1940s. Additional formulations followed. Patients were eager to take them, physicians keen to prescribe.

A million pounds of antibiotics are prescribed in the U.S. annually. Their overuse and misuse have created drug-resistant superbugs that kill about 23,000 Americans yearly. One, the notorius *Clostridium difficile*, was even named for its difficulty.

"Actually it was recognized early on that bacteria can evolve strategies to survive the agents devised to kill them — Sir



Alexander Fleming so noted in the *New York Times* in 1945 — but it seems we had to learn the hard way," Fekete says. The hard way that the drugs were too-often prescribed for viral pathogens (which antibiotics can't cure). The hard way what happens when unfettered access to antibiotics, as exists in other countries, results in the wrong drug being prescribed at the wrong dose — promoting development of highly resistant strains.

Some pathogens are pan-resistant, that is, resistant to all available antibiotics. The World Health Organization calls antibiotic resistance "a problem so serious that it threatens the achievement of modern medicine."

Moreover, we're battling a escalating problem with a scanty armamentarium. Many drugs simply don't work anymore. We've also seen a dramatic drop in the development of new antibiotics in recent years.

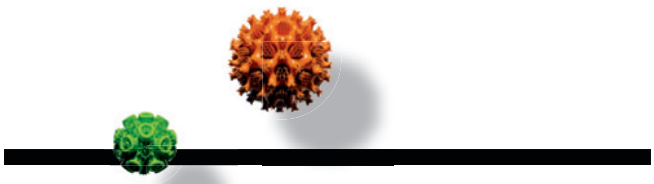
And even under ideal circumstances, antibiotics do collateral damage. They shift the balance of species present in the microbiome. Even short-term disruption can have long-term impact.

Fekete chairs TUH's Pharmacy and Therapeutics Committee — physicians, pharmacists, clinical microbiologists, and infection control specialists who monitor the use of antibiotics in the inpatient setting. "Antibiotic stewardship is essential to patient safety and public health. We must contain the emergence of antibiotic-resistant strains," he says.

The objective of antibiotic stewardship is to ensure that antibiotics are used only when needed — and that the most

appropriate one is selected for the patient's condition — and administered at the optimum interval, duration, and dose. A "drug-bug" database, updated in real time as patients' microbiology test results come in, informs the surveillance. The data show how well each antibiotic is working for each patient — giving clinicians early opportunity to adjust course.

"Temple has stewarded antibiotics since 1988, and we were among the first to do so. We have always been forward-thinking about infection control," Fekete says, noting that in 1958, Temple's Howard Steel, MD, was awarded the American Medical Association's Billings Gold Medal for mounting an infection control education campaign that helped bring hospitals all over the world into step with impeccable aseptic surgical techniques to prevent hospital-acquired infections.



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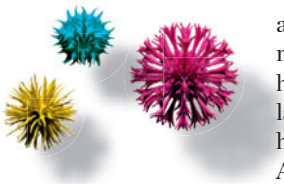


Peter Axelrod, MD, Professor of Medicine and Microbiology and Immunology, has chaired TUH's Infection Control Committee for 30 years — and presides over Fox Chase Cancer Center's as well. "Our facilities follow a comprehensive, systematic approach to hygiene and infection control. It is an ongoing vigil, integrated into everything we do," he notes, with protocols covering everything from health care waste handling to patient-room disinfection to intensive, ongoing training for personnel at all levels.

"Not all health systems devote the resources to infection control that we do," adds Patricia Heys, Director of Infection Control at TUH, noting that six full-time professionals are dedicated exclusively to infection control at TUH alone.

One special resource Temple enlists, when circumstances merit, is a robot that bathes an entire room in a spectrum of ultraviolet that kills organisms lurking on tray tables, bedrails, call buttons, grab bars, and other niches. When used in combination with manual disinfection, it kills more than 90 percent of bacteria. All told, infection rates throughout the Health System continue to remain at or below the national average.

MICROBIOME BY TRANSPLANT

In 1917, a German physician isolated a microbe called *Escherichia coli nissle* in the feces of a soldier who survived a potentially lethal *Shigella* infection. *E. coli nissle* is a probiotic. Probiotics contain live microorganisms that seed the growth of flora with beneficial properties.

At Temple, Adam C. Ehrlich, MD, MPH, Assistant Professor of Medicine, restores the growth of beneficial microbiota in very ill patients through a novel therapeutic approach. "These are patients with recurrent *Clostridium difficile* infections that have not responded to standard therapy," Ehrlich explains.

Ehrlich transplants healthy microbiota into the colons of patients whose own microbiomes are compromised, using a procedure called fecal microbiota transplantation (FMT). The microbiota used in FMT are remarkably effective, killing the *C. difficile* bacteria in just days. "In the coming post-antibiotic age, harnessing microbiota to combat infections represents an important new treatment avenue," Ehrlich says.

The fecal samples that Ehrlich uses are prepared by a Boston-based nonprofit stool bank. They come packaged and shipped frozen, diluted with saline. Since a healthy microbiome cannot yet be grown in a lab, humans supply the donations — which are rigorously screened and full of friendly microbes.

"The objective of FMT is to reintroduce bacteria that will jump-start the colonization of healthy bacteria to naturally overwhelm the *C. diff*," Ehrlich explains. He performs the procedure via colonoscopy, placing the microbial sample in the proximal region of the patient's colon.

The results have been spectacular, Ehrlich says. Moreover, the positive shift in the recipient's intestinal microbiota is lasting, not temporary — which is a beautiful thing, because the gut is an immune system mainstay.

While things like lymph glands, white blood cells, antibodies, and T-cells might first come to mind when we think about immunity, they're actually secondary players in immune response. The human-microbiome alliance is the first line of defense — and the largest community is housed in the gut. The gastrointestinal tract has more immune cells than the rest of the body put together. And it's no accident, says Toby Eisenstein, PhD, Professor of Microbiology and Immunology, that the gastrointestinal tract, skin, and lungs — the tissues that house most of our microbiota — are also the portals by which most pathogens enter.

"Healthy microbiota reinforce our 'barrier immunity,'" she explains. "Barrier sites are complex networks of microbes and host tissues that form a structural and biochemical immunological arsenal."

In the gut, microbiota ally with epithelial cells (which line the GI tract) to form a mucosal barrier against pathogens. In addition, commensal microbes stimulate our epithelial cells to produce antimicrobial peptides (AMPs), which are crucial in regulating the relationship between our microbes and our innate immune cells. Eisenstein says AMPs might one day be used therapeutically, potentially replacing antibiotics.

"AMPs co-evolved within the microbiome. They represent an ancient defense mechanism found in virtually every multicellular organism," says Eisenstein, who has taught a graduate course on AMPs for many years.

"In the gut, there's strong interaction between microbiota, food-derived antigens, and potential pathogens," Eisenstein

Adam C. Ehrlich, MD, MPH

explains. When these responses are not well-regulated, the composition of gut microbiota can become altered, or dysbiotic. This can destabilize epithelial defenses — and problems can ensue. In ulcerative colitis, for example, the antimicrobial mucus layer is thinner or partially absent.

Ulcerative colitis is an autoimmune condition. In westernized countries, autoimmune disorders and chronic inflammatory conditions have risen dramatically in recent decades. And many scientists believe that a compromised microbiome could be to blame.

DIVERSITY RULES

According to Stefania Gallucci, MD, Associate Chair of Microbiology and Immunology, modern life has not been kind to the microbiome. "It's been compromised by big changes in diet, by antibiotics, even by the elimination of intestinal helminthes, parasitic worms, from our GI tracts." We evolved in close association with helminthes. They were standard issue in our microbiome. But now the role they played in mediating immunity is gone.

"We are seeing the chronic disappearance of potentially essential components of the human microbiome," Gallucci says. Diminished diversity means less resilience, less capacity to keep immune responses well-tuned.

All autoimmune diseases and chronic inflammatory conditions share common ground in a microbiome in a dysbiotic state. Dysbiosis in the respiratory tract may contribute to asthma and other inflammatory disorders of the airway. "Dysbiosis in the intestine is associated with chronic inflammatory conditions collectively known as inflammatory bowel disease (IBD). In IBD, there is low microbial diversity," says Ehrlich, a gastroenterologist and IBD expert. In IBD there is also an abnormal response to commensal microbiota. Activated T-cells and antibodies aren't aimed at specific pathogens, but at regular gut organisms instead.

In addition to promoting inflammatory and autoimmune disorders at *barrier* sites like the intestine, dysbiotic microbiota are implicated in obesity, metabolic syndrome, Type II diabetes, Lupus, and other conditions that affect us *systemically*.

As highlighted last summer in the journal *Immunity*, Gallucci and Çagla Tükel, PhD, Assistant Professor of Microbiology and Immunology, identified a microbiome-related trigger that appears to underlie the autoiommune disease Systemic Lupus Erythematosus (SLE). They investigated biofilms, bacterial communities in the gut, and found that when microbes within it crossed the intestinal barrier, it triggered immune responses leading to SLE in genetically-susceptible mice.

"The beneficial bacteria in our guts can cause problems when they get into places they shouldn't," Tükel says. Translocation of friendly microbes, via leaks in the digestive tract, might underlie other autoimmune diseases. The team is now working with Roberto Caricchio, MD, Director of Temple's Lupus Clinic, to study biofilms in SLE patients.

In another study, published in *Biofilms and Microbiomes*, Tükel found that a naturally occurring protein in biofilms called curli significantly reduced the severity of IBD in laboratory studies — heralding potential for a new drug that could bring relief to the 1.3 million Americans affected.

Cancer, too, is influenced by the microbiome. For example, approximately 35 percent of Americans have *Helicobacter pylori* in their stomachs. This bacterium can burrow into the stomach lining, causing chronic inflammation. While most *H. pylori* carriers are asymptomatic, about 20 percent develop ulcers, and another five percent stomach cancer.

According to Sergei Grivennikov, PhD, Assistant Professor of Cancer Prevention and Control at Fox Chase Cancer Center, dysbiosis may influence whether the immune system contributes to cancer, or protects against it.

"Microbes are critical regulators of the host immune system and, ultimately, of inflammation," he says. Chronic inflammation has long been suspected to play a major role in the pathogenesis of cancer. Inflammation causes cells to divide at a faster rate than normal, increasing the likelihood of mutation. Inflammatory responses are culprits in tumor development, too. "Someday we may be able to harness the ability of commensal microbiota to impede the development of tumors," Grivennikov says. This approach could have profound clinical implications.

The idea that organisms do not live in isolation, but as part of a bustling microscopic community, was proposed by Pierre-Joseph van Beneden (1809-1894). What we have learned since van Beneden's time all but redefines what constitutes "human." Really, we are a meta-organism, composed of human and non-human cells. We can change our microbiome — and it can change us — to keep us well or make us sick. Deciphering the complex negotiations going on between tenant and host will yield new opportunities to develop novel strategies in the name of better meta-health. Exciting possibilities await us in this ancient new clinical frontier.

To make an appointment with an infectious diseases specialist or gastroenterologist, call 1-800 TEMPLEMED.

TUHS MARKETING

Stephen Permut, MD, JD

CHAIR OF THE BOARD, AMERICAN MEDICAL ASSOCIATION
CHAIR, DEPARTMENT OF FAMILY AND COMMUNITY MEDICINE, LEWIS KATZ SCHOOL OF MEDICINE

Q & A

You are Chair of the Board of Trustees of the American Medical Association (AMA), the largest professional association of physicians in the United States. What is the nature of this responsibility?

The AMA Board is responsible for setting the AMA's priorities, for financial resource allocation, and for big-picture policy interpretation and implementation. Therefore, my fundamental responsibility as Board Chair is to ensure that the AMA remains focused on its mission — which is to promote the art and science of medicine and the betterment of public health.

Q: *We're profiling you as a change agent. Are you trying to change the AMA?*
A: The AMA is *itself* an agent of change, making a real-world impact in the most relevant issues facing medicine today. These include Medicare physician payment reform, increasing access to care, combating prescription drug abuse, and other initiatives aimed at improving health care delivery and health status.

Improving the nation's health requires the cooperation of many organizations. First and foremost, it requires physician leadership. The AMA is the national voice of the medical profession in the U.S. and its biggest advocate in Washington, DC. No other physician-related organization has the AMA's political clout. The AMA advocates on behalf of all physicians and represents them with a unifying voice. The bottom line is this: when physicians benefit from what the AMA does, patients do as well.

Q: *What are the AMA's priorities?*
A: The AMA has three interrelated goals. One is to accelerate innovation in medical education, developing methods and models to ensure that new physicians can meet patients' needs, today and tomorrow. Another aim of the AMA is to enable physicians to thrive, to help them navigate our nation's complex and evolving health care system with initiatives that enhance practice efficiency, promote professional satisfaction, and improve the delivery of care. The third priority of the AMA is a direct focus on strategies and programs to improve national health outcomes, with a special emphasis on diabetes and heart disease, two leading, interrelated causes of morbidity and mortality.

Q: *You are a Fellow of the American College of Legal Medicine, with degrees in law and medicine. Much of your service and leadership targets health care legislation, medical liability, and other regulatory matters. Aren't law and medicine a bit like oil and water?*
A: It is essential to bridge the gap between the medical and legal professions, to rectify misperceptions and stigmas, and work from common ground. At the end of the day, law and medicine have the best interest of patients and the public in mind. The two professions actually work well together in a number of areas. For instance, the AMA Foundation and the National Health Lawyers Association recently co-developed a handbook to assist organizations starting free clinics. Unfortunately, however, we tend to hear only about cases that highlight polarized positions in law and medicine, particularly in the medical liability arena.

Q: *Your track record of volunteerism includes executive-level service and direct service to patients. For instance, you presided over the Medical Society of Delaware as president and also received the Governor's Volunteerism Award for working with indigent patients as a physician volunteer. What motivates you?*
A: Issues in health care are not abstractions. They affect people. I'm not one to sit on the sidelines. I believe in teaming up with like-minded people to get things done. For instance, a lot of great people helped me develop a Health Care Reform Plan for the State of Delaware when I was president of the state medical society. As a lone wolf, I never could have managed it. But when people work together, good things happen. That is what the AMA — and Temple Health — are all about: people working together to make a difference in the world.

Photograph by JOSEPH V. LABOLITO

Stephen Permut, MD, JD

Mastering Mitochondria

Muniswamy Madesh, PhD, is a towering presence in mitochondrial research. He has discovered things about mitochondria that have eluded scientists for decades. "Most people don't realize that mitochondrial dysfunction contributes to neurological disorders, diabetes, heart disease, stroke, and other diseases," says the Lewis Katz School of Medicine biochemist.

Mitochondria are organelles inside our cells. They play a number of roles but are best known as cellular power plants — biological engines that convert nutrients into energy, adenosine triphosphate (ATP). "To produce ATP, just the right number of calcium ions must flow into the mitochondria. Too much calcium can damage, even kill, cells. Too little will halt energy production, sometimes to the point of the cell's demise," explains Madesh.

Many mitochondrial functions involve calcium control. Therefore, Madesh has been elucidating the process in exacting detail. "Every new piece of knowledge related to calcium regulation could be a new clue toward a possible treatment," he says. For example, a discovery that Madesh and colleagues made in 2013 could transform treatment for sepsis, a bacterial infection that kills a quarter of the 400,000 Americans it affects every year. Sepsis incites a wild over-reaction of the body's immune response, prompting attack on its own tissues and organs. Many sepsis patients die when their lungs swell and fill with fluid.

Scientists knew that proteins called STIM1 within endothelial cells (the cells lining blood vessels) were involved in sepsis, but they did not understand exactly how — until Madesh discovered the role that STIM1 proteins play in sensing oxidative stress and the amount of calcium inside a cell. These roles were previously unknown.

"When STIM1 proteins detect sepsis toxins, they drive more calcium into the cell," he explains. "Fluctuating calcium levels then activate endothelial cells, which have sticky surface molecules. White blood cells attach to them, then migrate from the blood into lung tissue, driving inflammatory molecules into the bloodstream — inciting the swelling and fluid buildup that can cause death."

Madesh figured this out by *blocking* the activity of STIM1 to see what effect it might have. He was the first to try it, and it paid off. It halted the cascade of events that leads to severe lung damage — opening the door to a new treatment strategy.

Madesh discovered something else about calcium regulation that eluded scientists for 55 years. It pertains to the MCU, the mitochondrial calcium uniporter. Although this tiny one-way valve was discovered in 1961, its mechanisms of control baffled scientists until 2012, when Madesh and colleagues determined the role of two proteins in the inner mitochondrial membrane. The first protein, MICU1, was discovered years ago, yet Madesh's team was the first to demonstrate that it establishes a calcium "set point." Like a guard on duty, it blocks excessive calcium from coming in. Madesh also identified a previously unknown protein (he named it MCUR1, mitochondrial Ca^{2+} Uniporter Regulator 1) that regulates the opening of the pore, letting just enough calcium in. These discoveries were published in *Cell* and *Nature Cell Biology*. "Although the study of the MCU complex is still in its infancy, it is tempting to speculate that any aberration of normal function, loss or gain, leads to detrimental clinical outcomes," says Madesh.

Last year, Madesh and his colleagues discovered something related to mitochondria that marks a major advance in the understanding of necrosis, premature cell death. The breakthrough relates to the mitochondria's permeability transition pore and a newly discovered role for a protein complex embedded in its surface, SPG7. "In states of disease and injury — particularly those involving hypoxia (oxygen deficiency), calcium overload, and oxidative stress — SPG7 can cause the pore to abruptly open, and that's not good," says Madesh. The opening disrupts the normal flow of electrons and protons across the mitochondrial membranes. This causes a catastrophic drop in energy production, resulting in cellular death. "With this knowledge in hand, we can now look for ways to prevent the pore from opening — hopefully averting cell death. This approach could be a real boon for treating heart attack and stroke," Madesh says.

The SPG7 breakthrough was published in *Molecular Cell*. Madesh's research has also been published in *Diabetes* and *Circulation Research*. The National Institutes of Health, the American Heart Association, and other funders support his work. "I'm just warming up," says the bioenergetics expert, "so stay tuned."

Photograph by GENE SMIRNOV

Muniswamy Madesh, PhD

SPIN CYCLE

How MRI Works

Computed Tomography (CT) scanning is effective for imaging bone and soft tissue, but if you *really* want to differentiate among soft-tissue structures and evaluate their function, Magnetic Resonance Imaging (MRI) is the way to go. "With its unsurpassed contrast resolution, MRI is used to diagnose a variety of disorders from head to foot," says Chandra Dass, MBBS, DMRD, Associate Professor of Clinical Radiology and Director of Body and Cardiovascular MRI at Temple University Hospital.

An ingenious process, MRI creates images by harnessing the magnetic properties of the hydrogen nuclei (protons) abundant in the human body. These protons spin, creating tiny magnetic fields around them. "Think of the body as made of billions of tiny magnets that are oriented randomly," says Dass. "When exposed to a strong magnetic field created by the MRI machine, these tiny magnets polarize, in other words, line up with the strong magnetic field." A select group of these protons are the ones targeted in MR imaging, Dass explains.

"The next part of the MRI process entails choosing the specific body part we want to image," Dass says. This is done by activating special gradient coils in the MRI machine that are adjacent to the target anatomy.

"Now comes the most exciting part," Dass says. "We activate a radio frequency (RF) coil in the machine that emits radio waves which 'flip' the protons. These protons absorb the RF energy. When the RF pulse is switched off, the protons release the energy, emitting signals that we call MRI signals. These signals are picked up by a receiver coil in the machine — and then processed by a powerful computer that translates them into images in different shades of grey." Two-dimensional (slice-type) images can be created as well as three-dimensional ones.

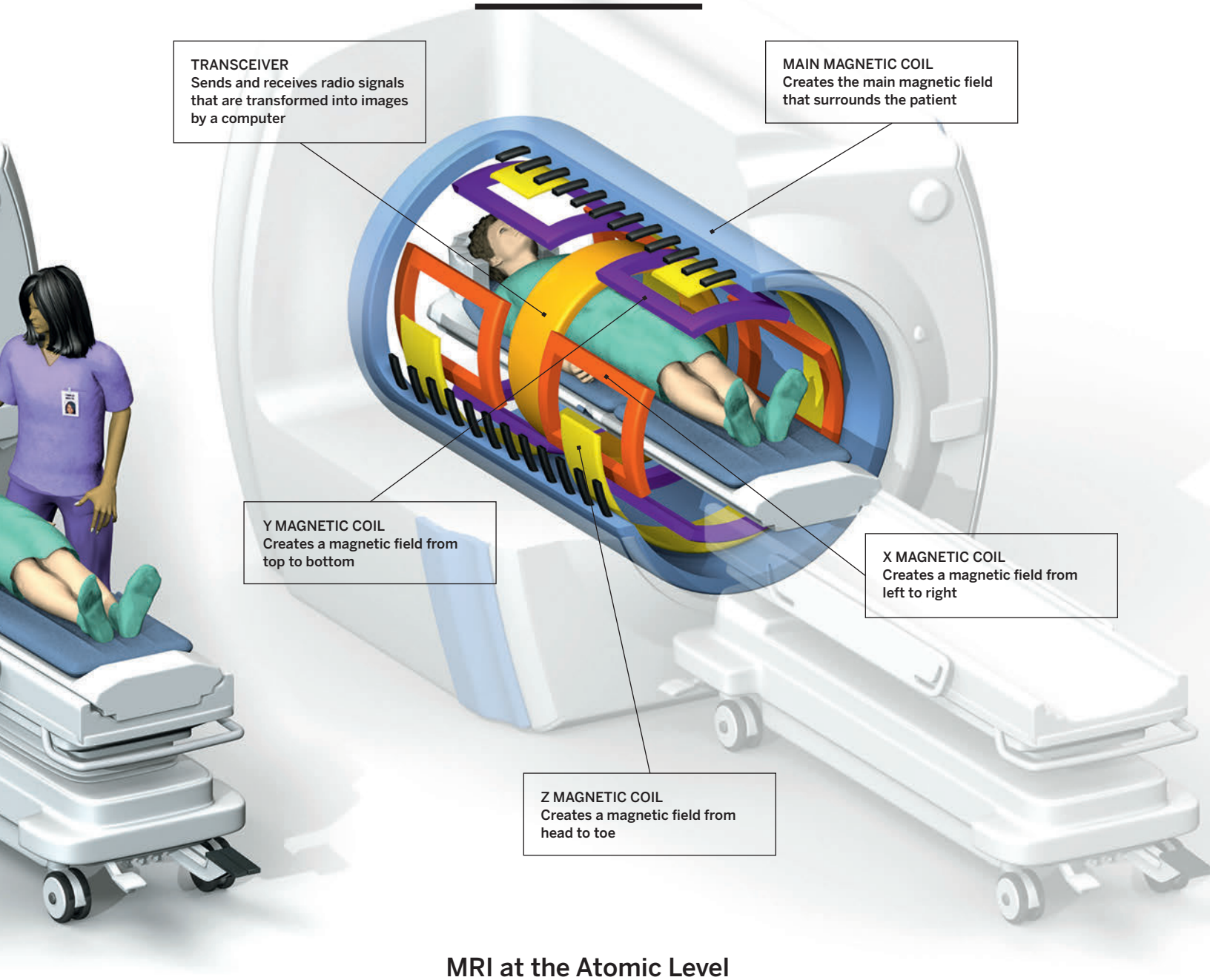
The unique power of MRI comes from its ability to depict different types of tissue. By altering the timing of the RF pulses by fractions of a second, we can illuminate the contrast between different types of tissues, Dass notes. In computed tomography, the contrast is limited. Each type of tissue has a fixed appearance. In MRI, however, running different "pulse sequences" in the machine will enable fine contrast between tissues to appear.

Some pulse sequences are used to study anatomy and to identify pathology, others for assessing tissue capillary blood flow or to diagnose acute stoke and tumors. Special MRI-based tests such as cardiac MRI and MR angiography (MRA) have revolutionized cardiovascular imaging, Dass explains. Functional MRI (fMRI) techniques such as Diffusion Tensor Imaging (DTI) are used both in clinical care and in research for mapping neuronal activity. A technique called MR spectroscopy (MRS) probes into the chemical composition of normal and abnormal tissue. All MRI tests are radiation-free.

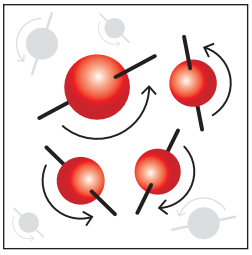
"New MRI scanners, such as those Temple University Health System is acquiring from GE, are quiet, fast, and produce images of superb quality," Dass says. "Since its debut in the 1970s, MRI technology has come a long way."

Illustration by NICOLAS RAPP

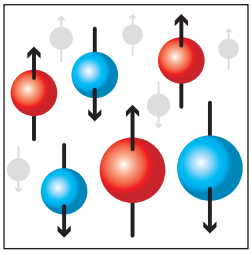
MRI SCANNERS: The Inner Workings



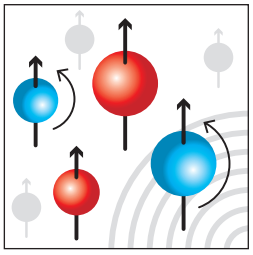
MRI at the Atomic Level



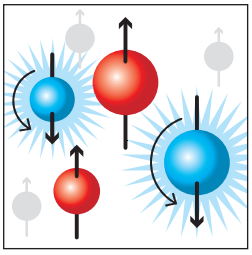
1. Billions of hydrogen atoms in our bodies continuously spin in random directions.



2. In the strong magnetic field of the MRI scanner, the atoms line up.



3. Radio frequency (RF) pulses are directed at the body part being imaged, causing certain protons to spin, or resonate, as they absorb the RF energy.



4. When the radio wave pulse is turned off, these protons release energy, emitting a signal.

5. The computer translates the signals into an image. Different tissues have different signals that are represented by different gradations of gray.

TIMELINE

WE GOT GAME

Scoring Points in Sports Medicine

Early in the 20th century, before "sports medicine" existed, Temple University began putting it on the map. Temple is the birthplace of Physical Medicine and Rehabilitation, an essential component of the field. It also developed a host of orthopedic surgery innovations. And the nation's first hospital-based sports medicine department opened at Temple University Hospital in 1974.

Temple's sports medicine advances include diagnostic indicators for cervical-spine injury ("Steel's Rule of Thirds" and the "Torg-Pavlov Ratio") and one used widely for the knee (the Lachman Test). As a result of Temple research, the NFL banned "spearing" in football (tackling with the crown of the helmet) and redesigned the cleat-type athletic shoe — saving untold thousands from injury. Temple orthopedic surgeon Joseph Torg, MD '61, the "godfather" of Philadelphia sports medicine, credits his colleague Ray Moyer, MD, with refining the techniques surgeons used in the 1980s on such athletes as Seattle Seahawk Curt Warner, Philadelphia Eagle Wes Hopkins, and Washington Bullet Bernard King.

Today, Temple Sports Medicine provides comprehensive, tertiary-level care to athletes of all levels. "We treat the whole picture of the athlete, never just an injury in isolation," says sports medicine director Eric Kropf, MD, Chair of Orthopedic Surgery.

With six offices in the Delaware Valley, the full-service program features treatment for acute and chronic musculoskeletal injuries, sports performance counseling, customized rehabilitation and exercise, injury prevention education — and advanced treatment for concussion and athletic neurotrauma.

▶ **1928**

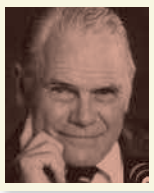
Frank Krusen, MD (1898–1973) opens the nation's first physical therapy unit at Temple. His techniques impress Temple Owls coach "Pop" Warner, namesake of the youth football league. Krusen's specialty, PM&R, is codified in 1947.

▶ **1944**

John Royal Moore, MD (1899–1988) pioneers bone fracture treatment techniques soon used nationally. Moore treats professional Philadelphia athletes for 30 years. In 1960 he becomes President of the American Orthopaedic Association.

▶ **1956**

John Lachman, MD '43 (1929–2007) develops a simple, accurate test still used worldwide to identify anterior cruciate ligament tears: the Lachman Test, which was formalized in the orthopedic lexicon by his protégé Joseph Torg, MD '61.



▶ **1958**

Howard Steel, MD, devises Steel's "Rule of Thirds" to describe the anatomical positioning of normal cervical spine.

▶ **1959**

Stanley Lorber, MD (1917–2014) joins the Philadelphia Warriors (76ers), becoming the first team doctor in the NBA, a position he held for 25 years through two NBA championships.

▶ **1971**

Ray Moyer, MD, and Joe Torg create the "National Head & Neck Injury Registry." As a result, the NCAA and NFL ban "spear tackling" in 1975. Torg and Moyer link knee injuries with the seven-cleat athletic shoe — prompting redesign.

▶ **1974**

Joseph Torg, MD, establishes the nation's first university-based sports medicine program at Temple University Hospital.

▶ **2000**

Torg and **Ted Quedenfeld (1935–2001)**, Temple's longtime lead athletic trainer (the first of the modern trainers and inventor of the "wounded owl" logo) are made namesakes of the Philadelphia Sports Medicine Congress's annual top honors.

▶ **2007**

Temple alumnus **John Bergfeld, MD '64**, former Medical Director of the Cleveland Clinic Sports Medicine Program (longtime team physician for the Cleveland Browns and Cleveland Cavaliers), wins an NFL Lifetime Achievement Award.

▶ **2015**

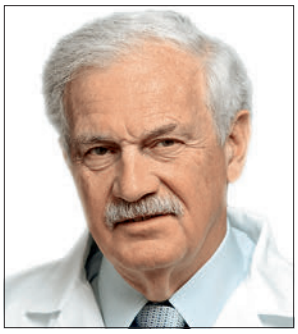
Temple's Sports Medicine Director, **Eric Kropf, MD**, is named Chair of Orthopedic Surgery. Kropf is team physician for Temple Athletics, St. Joseph's Prep, and consultant for the Philadelphia Flyers.

ARCHIVAL PHOTOS: TEMPLE UNIVERSITY LIBRARIES SPECIAL COLLECTIONS; ITEMS IN COLOR: JOSEPH V. LABOLITO

ALUMNI NEWS

Temple's 13,000+ medical school graduates are advancing health and social welfare across the globe.

1960s



Gerald M. Lemole, MD '62, Huntingdon Valley, PA, recently co-authored *After Cancer Care, The Definitive Self-Care Guide to Getting and Staying Well for Patients* (Rodale Press, Inc., 2015). With a foreword by Mehmet C. Oz, MD, the book offers comprehensive, concrete recommendations for living optimally after cancer treatment. Lemole served as Founding Medical Director of Christiana Care's Preventive Medicine and Rehabilitation Institute and its Center for Integrative Health. He is also the System's W. L. Samuel Carpenter III Distinguished Chair of Cardiovascular Surgery.

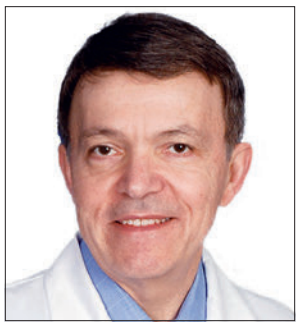
Richard F. Lockey, MD '65, Tampa, FL, received the 2015 Gold Medal Award of the World Allergy Organization (WAO) in recognition of his exceptional service to the international alliance of 95 regional and national asthma, allergy and immunology societies. A Distinguished University Health Professor at the University of South Florida College of Medicine, Lockey serves as the Joy McCann Culverhouse Chair in Allergy & Immunology; Director of the Division of Allergy & Immunology; and Professor of Medicine, Pediatrics, and Public Health. He is a past president of both the WAO and the American Academy of Allergy, Asthma, and Immunology.

Palmer Evans, MD '67, Tucson, AZ, Chair of the Board of Arizona Connected Care and Executive-in-Residence for the Center for Management Innovations in Health Care at the University of Arizona's Eller College of Management, has been honored with the inaugural Lifetime Achievement Award in Health Care, the highest honor presented by Tucson Local Media's Influential Health and Medical Leaders program, honoring "innovative and critical work done by members of the health care industry." Evans, a faculty member of the Arizona Healthcare Leadership Academy, has held many leadership roles during his career, including that of Senior Vice President and Chief Medical Officer at Tucson Medical Center.

1970s

Stephen Ajl, MD '75, Brooklyn, NY, has been appointed to the New York City Child Fatality Review Advisory Team by New York City Mayor Bill de Blasio. The team reviews data on child fatalities to identify trends and risk factors for injury-related deaths among children in New York City — to help expand the City's child-safety efforts. Ajl is Director of Pediatric Ambulatory Care at the Brooklyn Hospital Center and serves as medical director of two child advocacy centers in the city.

M. Douglas Baker, MD '78, Baltimore, MD, is Director of Pediatric Emergency Medicine and Vice President of Community Outreach at the Johns Hopkins Children's Center, and also serves as Professor of Pediatrics and Director of Emergency Medicine. In 2014 he received the Jim Seidel Distinguished Service Award of the American Academy of Pediatrics Section on Emergency Medicine for his distinguished contributions to the field.



William DeLong, Jr., MD '78, Haddonfield, NJ, is the Charles and Anna Kasych Chair of Orthopaedic Surgery and Chief of Orthopaedics at St. Luke's University Health Network in Bethlehem, PA. An expert in orthopaedic biogenics and in the use of stem cells to accelerate bone growth and healing, DeLong serves on the faculty of the Lewis Katz School of Medicine at Temple University.

1980s

Adolph Lombardi, MD '81, New Albany, OH, is recipient of the 2015 American Association of Hip and Knee Surgeons (AAHKS) Humanitarian Award. Lombardi, President of Joint Implant Surgeons, Inc., in New Albany, Ohio, is Co-Founder And President of Operation Walk USA. Now in its sixth year, the program has provided treatment at no cost to some 600 patients to date, with services valued at more than $15.5 million. The AAHKS Humanitarian Award recognizes Lombardi's distinguished humanitarian service.

Fred Rachman, MD '82, Chicago IL, is CEO and Chief Medical Officer of the Alliance of Chicago Community Health Services, a network of 25 safety-net community

LEMOLE: COURTESY CHRISTIANA CARE; LOCKEY: COURTESY UNIV. SOUTH FLORIDA; BAKER: COURTESY JOHNS HOPKINS; DELONG: COURTESY ST. LUKE'S HEALTH SYS.; LOMBARDI: JOINT IMPLANT SURGEONS

health centers that serve more than 600,000 patients annually. A health information technology expert, Rachman also serves as Vice Chair for Ambulatory Information Systems for the Healthcare Information and Management Systems Society.

Victor Waters, MD '84, JD, Oxon Hill, MD, is Interim President and CEO of Nexus Health, the parent company of Fort Washington Medical Center, in Fort Washington, MD. Prior to this position, he served as VP for Medical Affairs at the University of Maryland Charles Regional Medical Center.

Ken Duckworth, MD '86, Roslindale, MA, is the Medical Director of the National Alliance on Mental Illness (NAMI) and Assistant Clinical Professor at Harvard University Medical School. He also serves as Associate Medical Director for Behavioral Health at Blue Cross and Blue Shield of Massachusetts. Prior to joining NAMI in 2003, he was Medical Director for the Department of Mental Health of Massachusetts.

Michael Gette, MD '87, Hershey PA, received the Pennsylvania Academy of Dermatology and Dermatologic Surgery's 2015 Dermatologist of the Year Award, recognizing his significant contributions as a leader. Gette is a Clinical Assistant Professor of Medicine at Pennsylvania State College of Medicine.

1990s

Lynn Holden, MD '91, New Rochelle, NY, Associate Professor of Clinical Emergency Medicine at Albert Einstein College of Medicine, is Founding Executive Director of Mentoring in Medicine, a nonprofit organization that connects disadvantaged students in New York, Philadelphia, Detroit, Washington, D.C., New Orleans, and Atlanta to potential careers in medicine. She is also a founding member, with Aletha Maybank, MD '00 (see below), of the Artemis Medical Society, a national organization that draws black women into medicine.

Robert Harrington, Jr., MD '93, Atlanta, GA, is President of the Society of Hospital Medicine, the professional society representing more than 14,000 practicing hospitalists in the U.S. Harrington is Chief Medical Officer at Reliant Post-Acute Care Solutions, a health care company that designs post-acute networks to manage Medicare patients upon discharge.

Natalie Hartenbaum, MD '99, MPH, Ambler, PA, is recipient of the 2015 Meritorious Service Award of the American College of Occupational and Environmental Medicine (ACOEM), the nation's largest medical society dedicated to promoting employee health. The honor recognizes Hartenbaum's role as founder of ACOEM's training program for commercial driver medical examiners and her service as past president, board member, and editor. Hartenbaum is President and Chief Medical Officer of OccuMedix, Inc. based in Dresher, PA.

2000s

Aletha Maybank, MD '00, Brooklyn, NY, is Assistant Commissioner for the New York City Health Department and a founding member, with Lynn Holden, MD '91 (see entry above), of the Artemis Medical Society, a national organization devoted to drawing black women into medicine. To this end, Maybank has appeared on the Disney Channel's *Doc McStuffins* show, TV's top-rated preschool series, in segments featuring the real-life stories of African American female physicians. Maybank also founded the blog On Call in the City (www.oncallinthecity.com) and authors Doctor's Orders, a column at EBONY.com.

Richard Shoemaker, MD '03, Philadelphia, PA, an emergency medicine physician at Delaware County Memorial Hospital, recently competed on the popular TV show *American Ninja Warrior*, in which participants strive to complete a difficult obstacle course that tests physical fitness and agility. Shoemaker competed against 100 finalists in the show's seventh season — and was eliminated in the final episode.

Animesh Petkar, MD '09, Los Angeles, CA, practices with Eye-Q Vision Care and specializes in the treatment of vitreoretinal diseases and the management of advanced diabetic retinopathy, diabetic macular edema, age-related macular degeneration, and retinal detachment.

Adaobi Nwaneshiudu, MD-PhD '10, Ardmore, PA, is Assistant Professor of Dermatology at the Lewis Katz School of Medicine at Temple University, with a clinical appointment as Director of Dermatopathology and Director of Ethnic Skin, Hair and Women's Dermatology.

NEWS TO SHARE?
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WATERS: COURTESY NEXUS HEALTH; HOLDEN: COURTESY MENTORING IN MEDICINE; HARTENBAUM: COURTESY ACOEM; MAYBANK: COURTESY COLUMBIA UNIV.; PETKAR: COURTESY EYE-Q VISION CARE; NWANESHIUDU: TUHS MARKETING

Lectureship Legacy

One Family's Impact on Education

Every year for the past 55 consecutive years, Temple's Department of Obstetrics, Gynecology and Reproductive Sciences has hosted the Annual Isador Forman Post Graduate Course, a daylong symposium of obstetrics/gynecology resident presentations, capped by a keynote lecture from a visiting scholar. And, every year for the past 55 years, members of the Forman-Diamond family have not only attended the program, but have also made additional gifts to the lectureship fund — distinguishing themselves among the medical school's most steadfast, long-standing supporters.

An integral part of ob/gyn education at the Lewis Katz School of Medicine, the Annual Isador Forman Post Graduate Course brings leading experts to campus to discuss the latest trends and advancements.

"Even were it not for the family's incredible streak of continuous philanthropy, the Forman legacy at Temple would remain secure," says Enrique Hernandez, MD, the Abraham Roth Professor and Chair of the Department of Obstetrics, Gynecology and Reproductive Sciences.

The Forman-Temple connection began in 1922, when young "Iz" came to Temple to earn his medical degree. Iz was a high-achiever, well-liked, known for his sharp intellect and thirst for problem-solving. In 1926, he graduated first in his class. Soon he began courting a young woman named Rose. As the story goes, they spent a good part of their courtship riding through Philadelphia in Iz's car while he made house calls. In 1932 they married, and soon had two children, Miriam and Paul, both delivered at Temple.

As the Forman family grew, so did Isador and Rose's reputations. Isador established himself as one of the top fertility specialists in the region. Patients came from around the country to see him. Between 1930 and 1960, he consulted with unknown numbers of families, delivered many hundreds of babies, and taught generations of students and residents.

Rose made her own mark. She volunteered for the Temple University Hospital Auxiliary, serving as treasurer in the 1940s. For a time she worked as her husband's receptionist. In 1960, Rose became the Director of Volunteers at the now-defunct Philadelphia General Hospital. In 1965, she was appointed Executive Director of Planned Parenthood of Southeastern Pennsylvania. "The two likely had a greater impact on fertility and women's health in Philadelphia in the mid-20th century than anybody else," Hernandez says.

Miriam Forman Diamond says that Temple was an important part of her childhood as well as her brother Paul's. Every Sunday morning, to give their mother some respite, they would go to Temple University Hospital with their father. While he made his rounds, Miriam and Paul kept company with the telephone operators.

In 1960, Iz passed away unexpectedly, at the age of 57. It was wrenching for the family and for Temple, too. Family, friends, colleagues, and students gathered to mourn his passing — keen to create something lasting in Iz's honor. Leading the charge, Dr. Norman Kendall, a Temple Hospital pediatrician, asked that contributions be made to a lecture fund in Iz's name. "The fund should be used to further the teaching to which he was so devoted," said Kendall at the time. Miriam believes it was a fitting tribute. "Nothing gave my father more pleasure and satisfaction," she says.

(L-R): Enrique Hernandez, MD, Chair of Obstetrics/Gynecology and Reproductive Sciences, with Samuel Diamond, JD; Miriam Forman Diamond; and Paul Forman, PhD. Isador and Rose Forman are depicted in the background.

Rose attended the first Forman lecture in 1960 and every lecture thereafter until her death in 1988. In honor of Rose's commitment to the Course, the lecture given by the visiting professor was then renamed The Rose and Isador Forman Lecture. Every year, in remembrance of their parents, Paul Forman, Miriam Forman Diamond, and her husband, Samuel, attend the Lecture. Rose and Iz Forman's granddaughter, Deborah Diamond, now attends as well.

"What a great example of the impact that one family can have on medical education," Hernandez says. "We are so grateful."

DANIEL BURKE

Points of Pride Celebrated at Signature Events

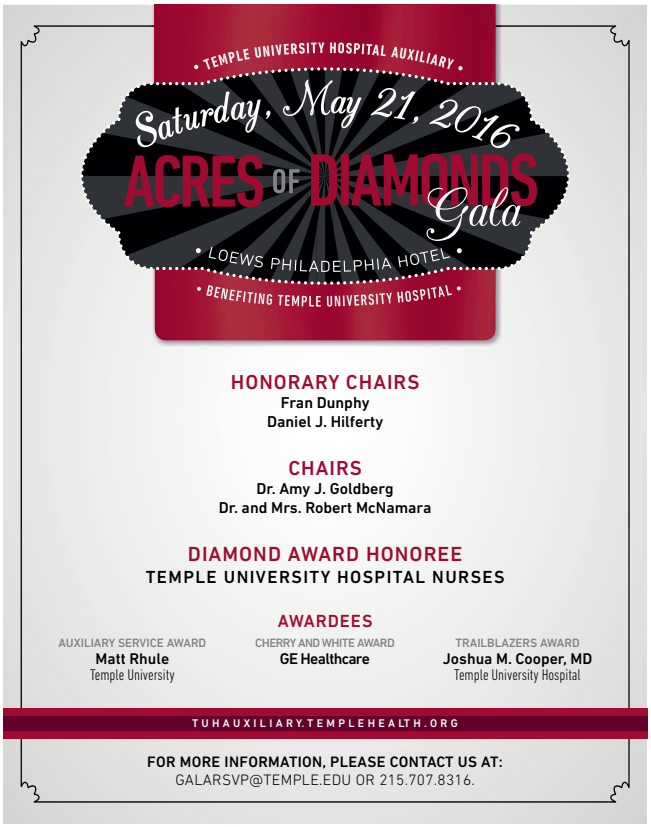
This spring, Temple Health held its two premier annual fundraising events benefiting its health system. On April 9, Fox Chase Cancer Center held its **In Vino Vita** benefit and wine auction. And on May 21, Temple University Hospital held its **Acres of Diamonds Gala**.

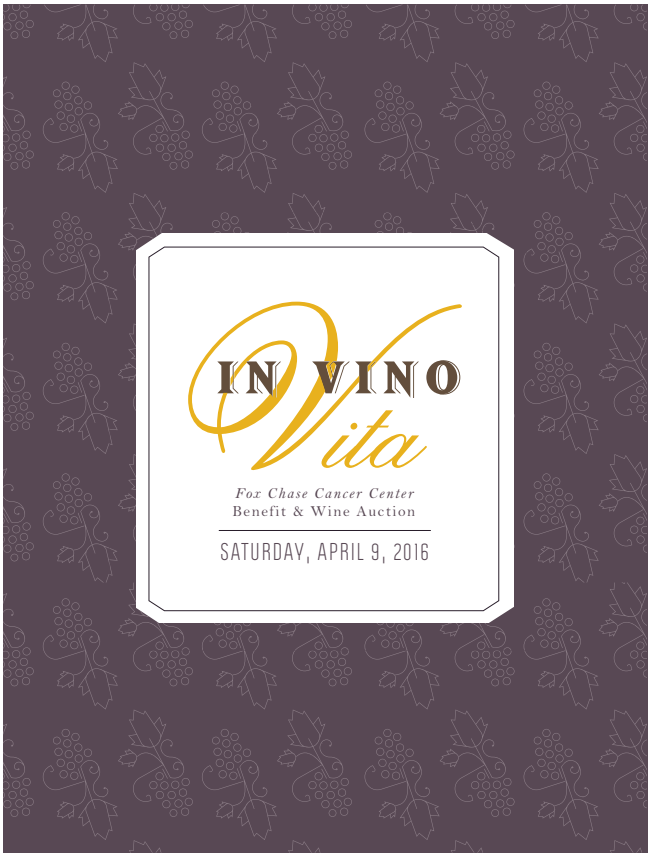
These popular events present an opportunity for hundreds of Temple Health supporters to gather, to honor some of Temple Health's great friends and physician and staff leaders, and to raise hundreds of thousands of dollars to support the academic medical center's mission. Now in its 63rd year, the Acres of Diamonds Gala, sponsored by the Temple University Hospital Auxiliary, is one of Philadelphia's longest-standing social fundraising events.

In addition to raising funds, the Acres of Diamond Gala presents an opportunity to recognize some of the Health System's greatest friends and leaders, with four marquee awards presented:

- The 2016 Diamond Award, which recognizes exceptional social responsibility, went to **Temple University Hospital**'s Nursing Department, led by Chief Nursing Officer, Elizabeth Craig, RN, DNP.
- The Auxiliary Service Award, which honors a member of the Temple family who has demonstrated tireless dedication to those in need, went to **Matt Rhule**, Temple University's Head Football Coach.
- The Cherry and White Award, which honors a partner whose long-standing generosity and commitment have contributed greatly to the hospital's mission, went to **GE Healthcare**. (For more about GE Healthcare and Temple, see the story on page 10.)
- The Trailblazer Award, which recognizes a visionary leader whose perseverance and pioneering spirit improve health care for the community, went to **Joshua Cooper, MD**, Director of Cardiac Electrophysiology.
- During the event, a special appeal recognized and supported the **Temple Transport Team**.

Proceeds of the Gala support the Hospital's clinical programs and patient-care needs. Proceeds from In Vino Vito support research and patient care at Fox Chase.





"CENTRAL TO MEDICAL EDUCATION IS THE EXPANSION OF SOCIAL CONSCIENCE."
— LARRY KAISER, MD, FACS (DEAN & CEO)

TEMPLE UNIVERSITY HOSPITAL IS AN INDISPENSABLE PROVIDER OF HEALTH CARE IN THE LARGEST CITY IN AMERICA WITHOUT A PUBLIC HOSPITAL.

"Research is not something done to people. It is done with people."
— GRACE MA, PHD (ASSOCIATE DEAN & DIRECTOR, CENTER FOR ASIAN HEALTH)

"Advancing medicine is a partnership between patients and physicians."
— NESTOR ESNAOLA, MD, MPH, MBA, FACS (SURGICAL ONCOLOGIST)

Approximately 20% of students at the Lewis Katz School of Medicine represent ethnic groups under-represented in the medical profession.

The Lewis Katz School of Medicine ranks

9TH

in the country for graduating African American physicians.

700

students at the Lewis Katz School of Medicine belong to at least

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of

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— VERDI DISESA, MD, MBA (VICE DEAN & PRESIDENT, TUH)

"Clinical research is where bold science and breakthrough medicine converge to improve patient outcomes, to improve health — of individuals, of entire nations."
— RICHARD FISHER, MD (PRESIDENT/CEO, FOX CHASE CANCER CENTER)

Revelatory Ribbons

These confetti-like figures represent structures created inside our cells when protein kinases kickstart one another, launching a variety of cellular functions. The process is called autophosphorylation. These images, which depict it, were created with a novel structural bioinformatics method developed by Qifang Xu, PhD, and Roland Dunbrack, PhD, at Fox Chase Cancer Center. Xu and Dunbrack used the method on a sample of proteins — and identified 15 different complexes, including five never-before described. The journal *Science Signaling* reported the news as its cover story (December 2015). "Identifying small molecules that disrupt these complexes could lead to new kinds of cancer therapy," Dunbrack says.

QIFANG XU, PHD, AND ROLAND DUNBRACK, PHD

Temple Health
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