

Temple Health

WINTER 2014

Magazine



Hope for Broken Hearts

Fast-Tracking Tomorrow's
Treatments

SELWYN ROGERS:
THE STATE-OF-THE-ART AND
THE UNDERSERVED

CANCER'S TRAILBLAZERS:
PATIENTS ON PHASE 1
CLINICAL TRIALS



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Temple Health Magazine

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Temple Health refers to the health, education, and research activities carried out by the affiliates of Temple University Health System and Temple University. Many Temple Health programs have been ranked among the best in the region and nation by U.S. News & World Report and other ratings and rankings agencies.

Tomorrow Belongs to Those Who Invent it Today.

The rapidly-changing landscape of healthcare requires bold steps and clear vision to transform obstacles into opportunities. Temple Health is seizing tomorrow's opportunities with a potent combination of expansion, quality, and innovation – today.

Investing strategically. Broadening our geographic footprint. Building centers of excellence. Attracting students – and renowned physicians and scientists – from all over the country.

We are fast-tracking Temple's special brand of education, healthcare, and research onto the national stage as we continue the long and proud traditions of some of the most widely-recognized names in Philadelphia medicine – Temple University School of Medicine, Temple University Hospital, Fox Chase Cancer Center, Jeanes Hospital, and Temple University Hospital's Episcopal and Northeastern campuses.

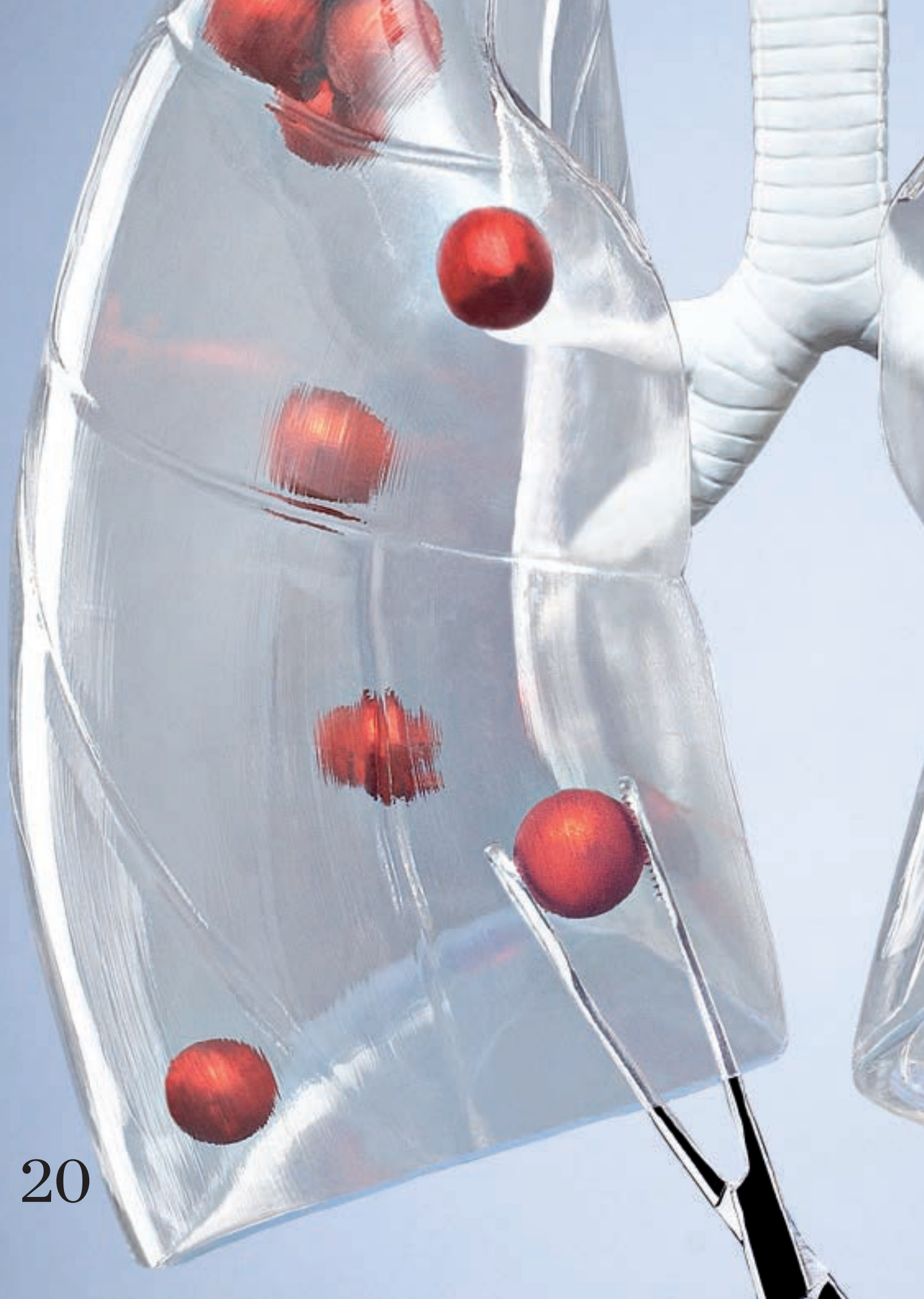
We are Temple Health – a name that means state-of-the-art care, superior medical education, pioneering translational research, and deep commitment to the most vulnerable. A name built on mentoring and discovery, passion and integrity, curing and caring. Great organizations working in unison to demonstrate the world-class power of an integrated clinical, research, and medical education enterprise at this transformative time in American healthcare.

As you will see on the pages of this new magazine, it's a new era for Temple Health, as we forge our future together.

Please let me know what you think. I look forward to hearing from you.

Larry R. Kaiser, MD, FACS
*Senior Executive Vice President for Health Sciences, Temple University
Dean, Temple University School of Medicine
President & CEO, Temple University Health System*

LOBBY: JOSEPH V. LABOLITO; KAISER: DOMINIC EPISCOPO



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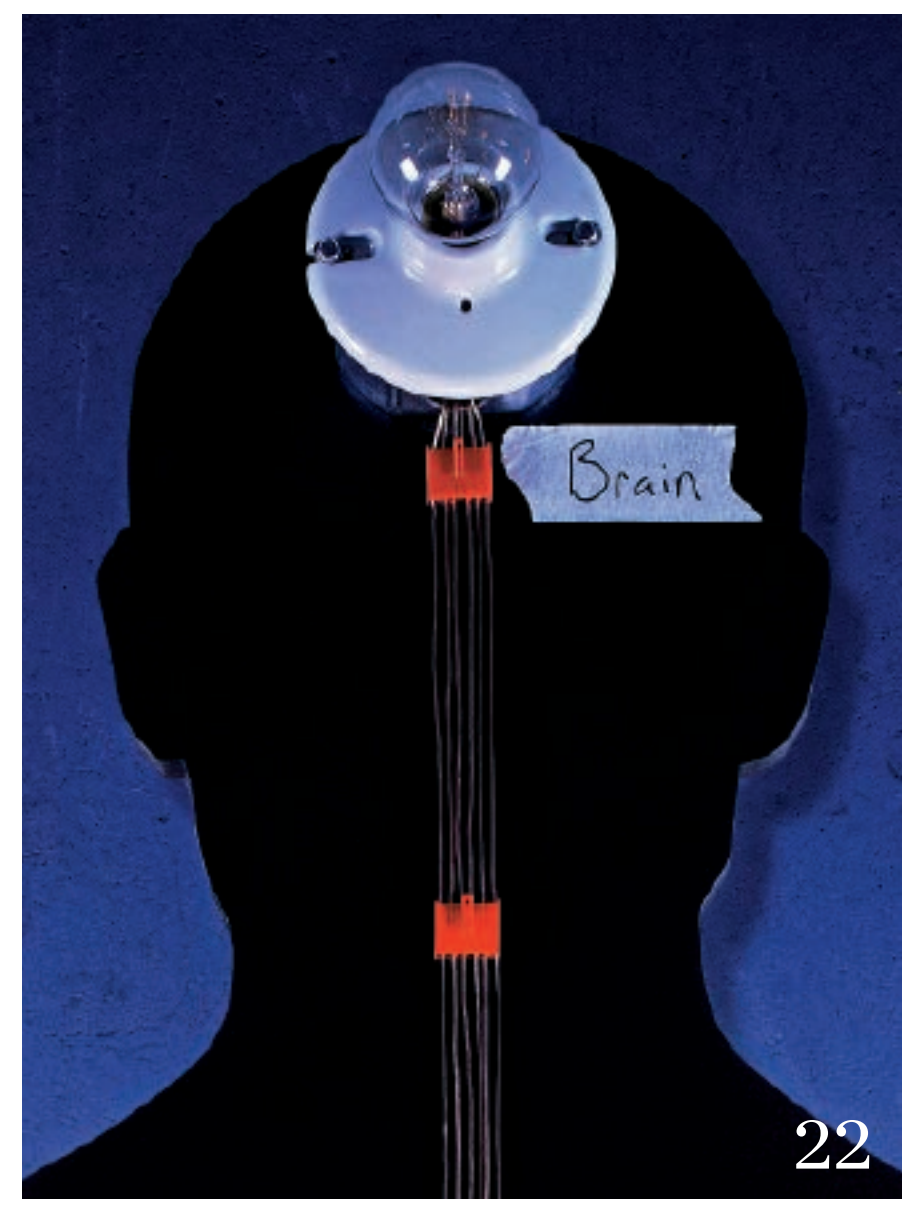
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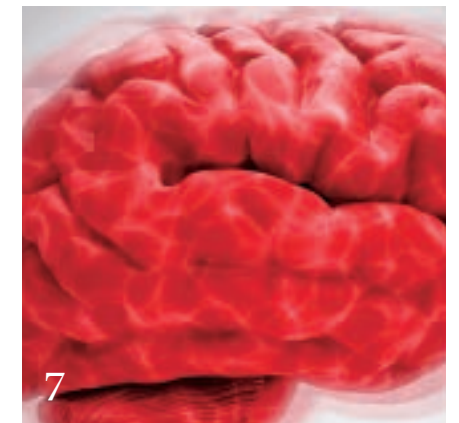
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CURRENTS



Cancer Researchers Honored

National awards have been bestowed on several faculty members. The Academy of the American Association of Cancer Research inducted two Fox Chase scientists into its inaugural class of Fellows: Alfred Knudson, MD, PhD, and Beatrice Mintz, PhD. Knudson is internationally known for his “two hit” theory of cancer causation – and Mintz for producing the first genetically modified mice. The Mesothelioma Applied Research Foundation honored Joseph Testa, PhD, of Fox Chase, with the 2013 Pioneer Award for his contributions to Mesothelioma research. The deadly

cancer is usually caused by exposure to asbestos, but has also been linked to the Bap1 gene mutation customarily linked with breast cancer. Robert Ozols, MD, PhD, received the American Society of Clinical Oncology’s Distinguished Achievement Award for extraordinary leadership in oncology. An internationally known ovarian cancer expert, Ozols recently retired following two decades at Fox Chase. He formerly headed the experimental therapeutics section of the National Cancer Institute. In addition, the Association of Community Cancer Centers selected Temple’s Cancer Program as one of ten nationwide Innovation Award winners in 2013.

National Rankings

Temple University Hospital and Fox Chase Cancer Center are again named in *U.S. News & World Report’s* Best Hospitals in America® list. In a *Consumer Reports* analysis of elective surgeries at U.S. hospitals from 2009 to 2011, Fox Chase posted the best surgical outcomes in Philadelphia. Eighty-five Temple physicians were named to the newest Best Doctors in America® list. Only five percent of physicians in America earn a spot. *Becker’s Hospital Review* named Larry R. Kaiser, MD, FACS, to its lists of top “Nonprofit Hospital and Health System Executives to Know” and “Physician Leaders of Hospitals and Health Systems to Know.” *Becker’s* also named Chief Operating Officer Verdi DiSesa, MD, MBA, and Robert Lux, Chief Financial Officer, to its national “top” lists.

MORE THAN
10,000
PEOPLE EARN A
LIVING AT
TEMPLE HEALTH

MOUSE: ISTOCK; © DRA. SCHWARTZ

New Leaders

Richard Fisher, MD, a leading cancer center administrator and nationally recognized hematology/oncology expert, has been appointed President and CEO of Fox Chase Cancer Center. He also holds the titles of Cancer Center Director and Senior Associate Dean for Cancer Programs. Michael Weaver, MD, was appointed Chair of the Department of Neurosurgery. A longtime faculty member and Medical Director of the Neurosurgical ICU, Weaver’s interests include neuro-oncology, intracranial procedures involving skull-base surgery, and cerebrovascular surgery. Gil Yosipovitch, MD, has joined Temple to re-establish a Department of Dermatology and serve as its Chair. He will also lead the dermatologic program at Fox Chase Cancer Center and develop a dedicated Center for Itch. Dubbed the “Godfather of Itch,” Yosipovitch is co-author of *Living with Itch: A Patient’s Guide* (Johns Hopkins University Press, 2013).

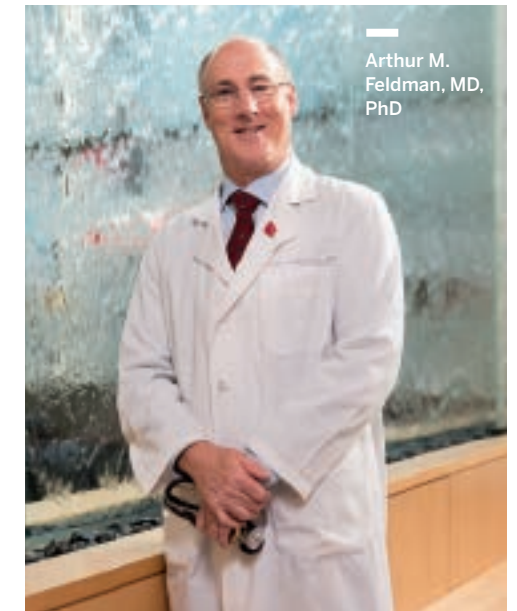


Richard Fisher, MD

FELDMAN AND FISHER: JOSEPH V. LABOLITO

Lifetime Achievement Award for Heart Research

Renowned cardiologist and cardiovascular researcher Arthur M. Feldman, MD, PhD, Executive Dean of Temple University School of Medicine and Chief Academic Officer of Temple University Health System, received the 2013 Lifetime Achievement Award of the Heart Failure Society of America, recognizing his contributions and leadership in the heart failure field. Feldman’s NIH-funded research targets the molecular pathobiology of heart failure. His groundbreaking work on the role of G proteins, pro-inflammatory cytokines and vasopressin receptors in the development of heart failure have been published in more than 250 peer-reviewed articles. He is the editor of two textbooks, *Heart Failure: Pharmacologic Management* (Blackwell Futura, 2006) and *Heart Failure: Device Management* (Wiley-Blackwell, 2010). He also serves as founding Editor-in-Chief of *Clinical and Translational Science*. Prior to joining Temple in 2011, Feldman was Magee Professor and Chair of the Department of Medicine at Jefferson Medical College in Philadelphia. Before that he held leadership roles at Johns Hopkins University and the



Arthur M. Feldman, MD, PhD

University of Pittsburgh School of Medicine. Feldman is a former president of the Heart Failure Society of America. “To receive this recognition is a humbling experience,” he said.

At the Helm

More than 100 faculty and professional staff serve in leadership capacities for professional societies in medicine and science. Recent elections and appointments among faculty include:

American Cancer Society	Enrique Hernandez, MD: Vice President/ Board Member
American College of Nuclear Medicine	Jian Q. Yu, MD: Treasurer/Board Member
American College of Physicians	Darilyn Moyer, MD: Chair-Elect, Board of Governors
American College of Rheumatology	Audrey Uknis, MD: President
American College of Surgeons	John Daly, MD: Vice President
	Enrique Hernandez, MD: Board of Regents
	Amy Goldberg, MD: Board of Governors
American Medical Association	Stephen Permut, MD, JD: Secretary, Board of Trustees
American Society of Echocardiography	Susan Wiegers, MD: Vice President
American Radium Society	Elin R. Sigurdson, MD, PhD: President
College of Physicians of Philadelphia	Bennett Lorber, MD: Immediate Past President
College on Problems of Drug Dependence	Toby Eisenstein, PhD: Board of Directors
International Cannabinoid Research Society	Mary Abood, PhD: Treasurer

New & Noteworthy

NEW RESEARCH CENTER:

Temple Health has launched a new Center for Metabolic Disease Research, aimed at discovering novel therapies for diseases such as diabetes and obesity. Hong Wang, MD, PhD, Director of the new Center, is world-renowned for pioneering research in hyperhomocysteinemia, a significant independent risk factor for cardiovascular disease. Metabolic disease is one of Temple's key research focus areas, along with cardiovascular, neuroscience, and cancer research.

SEPSIS:

Scientists at Temple are inching closer to solving a long-standing mystery in sepsis, a complex, potentially life-threatening condition that affects more than 400,000 people in the U.S. every year. By blocking the activity of the protein STIM1 in cells lining the blood vessels, they have halted a cascade of cellular events that culminates in the inflammation that characterizes sepsis. "More than 25% of sepsis patients die—but now we more fully understand the mechanisms behind it," said senior author Muniswamy Madesh, PhD. "Our results could lead to a whole range of new therapeutic research directions."

SPINAL CORD IMAGING:

With a \$1.7 million grant from the National Institute of Neurological Disorders and Stroke, Temple's Feroze Mohamed, PhD, and co-investigator Mary Jane Mulcahey of Thomas Jefferson University, are developing diffusion tensor imaging (DTI) to enhance diagnosis and treatment for children with spinal cord injury. Children constitute a significant portion of the 11,000 new cases of spinal cord injury diagnosed each year



Hong Wang, MD, PhD

in the U.S., and their small spinal cords pose a challenge for current imaging technology. DTI measures the diffusive transport of water in tissues, enabling the visualization of microscopic tissue structure. Mohamed is one of the first to apply it to pediatric spinal cord injury.

WORLDWIDE LUNG STUDY:

Temple University Hospital is participating in a worldwide clinical trial to test whether implanting miniature valves (the Pulmonx Zephyr™ Endobronchial Valve) in targeted regions of the lung can improve breathing for patients with emphysema. Gerard Criner, MD, Chief of Pulmonary Medicine, is the national co-principal investigator of the trial, which is called LIBERATE.

SOY FOR WOUNDS:

Peter Lelkes, PhD, Director of the Institute for Regenerative Medicine and Engineering at Temple, is developing a bioactive dressing composed of plant-derived soy proteins for hard-to-heal wounds. While the standard dressings on the market are quite costly, the soy plant is abundant and renewable. "It is inexpensive, bioactive, and accelerates wound healing," Lelkes says.



HeartWare®

The HeartWare® Ventricular Assist Device, a small apparatus designed to assume some — or all — of the heart's pumping function, is now available at Temple. The device is currently approved by the FDA for patients awaiting heart transplantation.

In the HeartWare® System, a golf ball-sized pump is connected directly to the heart. The pump is run by an external controller connected by a small cable passing through the skin. Totally portable, the 3.3-pound device affords patients great freedom of movement. Powered by battery or electricity, the device is worn in a carrying case around the waist or over the shoulder.

"Today's devices are much smaller and more durable than earlier generations of ventricular devices," said T. Sloane Guy, MD, MBA, Division Chief of Cardiovascular Surgery. "They also provide vital opportunity for use in children and smaller-framed adults with heart failure."

"This is the era of devices for patients with heart failure," added René Alvarez, MD, Vice Chief of Cardiology.

Such technology is a growing necessity, with the incidence of heart failure on the rise. Approximately 500,000 people are diagnosed with heart failure each year in the United States.

WANG: JOSEPH V. LABOLITO; HEART DEVICE: HEARTWARE INC.

Dangerous Trifecta

A Temple study has shown just how deadly the combination of colon cancer, diabetes, and high blood pressure can be. Analysis of more than 36,000 patients with colon cancer (the third leading cause of cancer death in the U.S.) reveals that patients with early-stage disease and diabetes or high blood pressure are at greater risk — not only for the cancer recurring, but for dying, compared to colon cancer patients who do not have diabetes or high blood pressure.

Diabetes and high blood pressure are components of metabolic syndrome, a cluster of conditions affecting one in five American adults that can also include obesity, low levels of HDL cholesterol, and high amounts of lipids in the blood.

"Our results suggest that patients with early-stage colon cancer who also have diabetes or hypertension may need to be followed more closely for recurrence and could potentially benefit from broader use of adjuvant chemotherapy," says senior author Nestor Esnaola, MD, MPH, MBA, Chief of Surgical Oncology at Temple. "Metabolic syndrome as a whole had no apparent effect on colon cancer recurrence or survival, but when we analyzed the effect of each of its components, the data told a different story."



HPV: Links to Lung Cancer and Epilepsy

The virus known to cause cervical and head and neck cancers may also trigger some cases of lung cancer — and could be linked to epilepsy. Researchers at Fox Chase examined tissue from lung cancer patients, and found that nearly 6% could be linked to a strain of human papillomavirus (HPV) known to cause cancer.

Studies from Asia have shown that lung tumors are frequently infected with HPV. This does not necessarily mean the infection caused

the tumors, cautions the study's author, Raneesh Mehra, MD, "but the integration of the virus into the tumor's DNA fuels the hypothesis that they are related."

Temple researchers have also found HPV in the brain, establishing its potential link to a common form of pediatric epilepsy. "Future treatment of cortical dysplasia could include targeted therapy against HPV-16 infection, with the goal of halting seizures," said Peter Crino, MD, PhD, Professor of Neurology at Temple.

Flash Freeze for Esophageal Disease



Temple recently became the first medical center in the world to offer cryotherapy

to patients with esophageal disease, including Barrett's esophagus and esophageal cancer. A minimally invasive technique, truFreeze® Spray Cryotherapy involves placing a catheter in an endoscope

to spray liquid nitrogen (-196°C) to eradicate diseased areas. A rapid freeze and slow thaw destroys targeted cells without disturbing the underlying connective tissue.



Dr. Larry Kaiser, Dean and CEO, with Dr. Weiping Li, President of Renji Hospital.

Temple Partners with Renji Hospital in Shanghai

In April 2013, Temple University School of Medicine's top academic leaders – Larry R. Kaiser, MD, Dean & CEO; Arthur Feldman, MD, PhD, Executive Dean; and Joseph Cheung, MD, PhD, Chair of Medicine (then Senior Associate Dean) – traveled to China to sign a partnership agreement with Renji Hospital for collaborative educational and research programs.

With 2,400 beds, Renji Hospital is one of the largest hospitals associated with Shanghai's Jiao Tong University School of Medicine in Shanghai, which works with 12 teaching hospitals totaling nearly 12,000 beds. The relationship will feature education, research and, by extension, patient care. Research collaborations and an exchange program for students and faculty have already begun.

"Although our two academic medical centers sit on the opposite sides of the planet, we have

much in common, in terms of the health issues of the patients we serve, the research challenges we face, and our goals for educating the medical professionals of tomorrow," Feldman said. "This robust partnership will benefit science and students."

While in Shanghai, the Temple leaders met Peter King, MD, a 1974 graduate of Temple University School of Medicine. King is Chief of Cardiology and Director of the Hong Kong Heart Center at Adventist Hospital, site of the country's first open heart surgery. King also serves as CEO of Global Health Care, which operates two clinics in Shanghai that cater to American expatriates and international travelers – admitting patients, when needed, to Renji Hospital.

King volunteered to help the two institutions plan a "Recent Advances in Medicine" symposium to be held in Shanghai in October 2014.

TEMPLE RANKED

6th

IN THE U.S. FOR THE NUMBER OF AFRICAN AMERICAN MEDICAL SCHOOL GRADUATES, 1978–2008

Event Honors New President

In October, Temple Health presented "Medicine in the 21st Century," a snapshot of the paradigm-changing research, technologies, and innovations that are moving medicine ahead. The talk celebrated the investiture of Temple University's new president, Dr. Neil Theobald.

Jonathan Chernoff, MD, PhD, Fox Chase Cancer Center's Chief Scientific Director, explained new techniques for identifying drugs to target cancer cell weakness. Howard Cohen, MD, Director of Temple's Interventional Heart and Vascular Institute, described approaches now transforming heart valve repair. Nora Engel, PhD, of Temple's Fels Institute for Cancer Research, explained how epigenetic modulation could revolutionize cancer treatment. Temple's Chief of Nephrology, Crystal Gadegbeku, MD, shed light on the heart-kidney connection. T. Sloane Guy, MD, MBA, Temple's Cardiothoracic Surgery Chief, previewed the devices and techniques at cardiac surgery's frontier. Jay Rappaport, PhD, Associate Neuroscience Chair, shared insights on AIDS-related dementia.

JOSEPH CHEUNG

Gift Establishes William Wikoff Smith Chair

The Philadelphia-based W.W. Smith Charitable Trust has established the William Wikoff Smith Chair in Cardiovascular Medicine at Temple University School of Medicine, with a \$2.5 million gift. Walter Koch, PhD, was installed as the Chair's inaugural holder. An internationally recognized scientist and educator dedicated to cardiovascular disease, Koch is Chair of Pharmacology and Director of the Center for Translational Medicine at Temple.

"The gift recognizes Temple as an elite institution advancing knowledge through translational research — as well as Dr. Koch's groundbreaking research," said Larry Kaiser, MD, Dean and CEO. "We are honored by the Smith family's commitment to advancing the treatment of cardiovascular disease."

"This gift speaks to the confidence we have in the trailblazing research being done by Dr. Koch and in Temple as a whole," said W.W. Smith Trustee Mary Smith.

Since 1977, the W.W. Smith Charitable Trust has distributed nearly \$185 million in gifts and grants to health and human service organizations — including more than \$15.2 million in support of scholarships and research at Temple.

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Jean Pierre Issa, MD

It's DNA, Not Destiny

Jean Pierre Issa, MD, Director of Temple's Fels Institute for Cancer Research, was one of four world experts invited to present "Destiny and DNA: Our Pliable Genome" at New York's annual World Science Festival last summer.

"When the human genome was sequenced," he said, "some scientists predicted it would enable us to understand every disease. But as it turns out, DNA isn't the total picture. Environment can play a role."

Issa, an expert in epigenetics, the factors influencing gene expression, notes that epigenetic traits themselves can be inherited.

A 2005 study found that pregnant women who witnessed the 9/11 attacks in New York passed on higher levels of the stress hormone cortisol to their infants. Other studies indicate that abuse, famine, and trauma can create epigenetic markers.

Issa calls the implications of epigenetics 'enormous.' He is currently investigating whether cancer patients can be treated with drugs that "reprogram" cancer cells by reconfiguring epigenetic markers. "Reshuffling the epigenome might prove a better alternative to chemotherapy — perhaps even cure cancer one day," he said.

Stellar Ratings for Education

U.S. News & World Report ranked Temple University School of Medicine sixth in the nation for number of applicants. The school received 10,600 applications for the 2012–2013 year.

Graduateprograms.com, a popular online guide to graduate schools, ranked Temple's medical and dental school programs 19th in the nation — and the best in Pennsylvania. The rankings are

based on survey responses from current and recent students on topics such as academic competitiveness, career support, financial aid, and quality of career-networking opportunities.



Hope
for
Broken

Hearts

Temple's heart research and patient care team is on a fast track to innovating next-generation therapies and treatments for heart patients. Without them, more than 23 million people will die from cardiovascular disease by 2030.

By GISELLE ZAYON
Illustrations by BRYAN CHRISTIE

Cardiovascular disease is like a tsunami—widespread and deadly. Thousands of researchers around the world are working to keep it at bay. Some are trying to build life preservers at the microscopic level in the body. Others are trying to build seawalls to minimize damage for entire populations.

“There’s no silver bullet for a disease this complicated,” says Arthur Feldman, MD, PhD, Executive Dean and Chief Academic Officer, a heart researcher and cardiologist himself. “Except in cases where a genetic mutation is causative, heart disease is not caused by a single molecule, nor can it be cured by one. Once a person has a syndrome like heart failure, thousands of things have already gone wrong.”

Feldman is not exaggerating. Thousands of things going haywire on a molecular level can gang up to pack a fatal punch. An initial insult such as a viral infection or heart attack can trigger a cascade of events that lead to eventual failure of the heart’s ability to pump.

Founded in the 1930s, Temple’s heart program has marshaled significant progress in heart medicine. Today, top scientists and physicians are leaving premier institutions all over the nation to come to one of the hottest places in the heart field today. More than four dozen world-class experts — like Feldman — have joined the team.

“It’s exciting. We are close to breakthroughs on a number of fronts,” Feldman says.

Two big research centers at Temple manage most of the heart research: the Center for Translational Medicine, headed by Walter Koch, PhD, the W.W. Smith Chair of Cardiovascular Medicine; and the Cardiovascular Research Center, headed by Steven Houser, PhD, Laura Carnell Chair of Physiology. Both researchers are internationally known.

Early in his graduate-school days, Houser studied neuroscience. Then his father, a heavy smoker, died of a heart attack at 51. Houser’s professional mission changed — and it was personal.

Koch decided to devote his career to the heart because he was “totally amazed” by his mentors. One of them, Dr. Robert Lefkowitz, won the 2012 Nobel prize in chemistry. Feldman, too, was inspired by his mentors. And then there was his dad, who suffered from rheumatic heart disease.

“It’s complex science that boils down to fundamental questions: What can we do to get heart muscle to work better? How can we build new muscle cells? What can we do for people with damaged hearts?” poses Koch.

Each researcher’s motivation is different, but they are all united in their goal: To add new therapeutics and treatments to the tool chest.

“It’s complex science that boils down to fundamental questions: What can we do to get heart muscle to work better? How can we build new muscle cells? What can we do for people with damaged hearts?” poses Koch.

Four main disease targets define the research. The first is arrhythmia. The intricate electrochemical processes that regulate heartbeat contain many mysteries to decipher. Serious rhythm problems can result in cardiac arrest, which can result in sudden death.

The second target is ischemic heart disease. Coronary arteries can clog with fat and plaque, robbing heart muscle of oxygen and blood. Sometimes vessels occlude altogether — and cause myocardial infarction, killing off heart muscle. Big heart attacks can be fatal. Lesser ones can still cause serious problems — including the third target: cardiomyopathy. Heart muscle disease, in turn, can lead to heart failure, the fourth target, which affects some 5.8 million people. Heart failure affects the entire body. It’s the primary reason older adults are hospitalized in the United States. Aside from heart transplantation — not appropriate in most cases — there’s no real cure.

“In fact, some heart drugs on the market today can actually kill cells and cause arrhythmias in some patients,” says Houser. “We need new approaches fast.”

To help speed progress, funders such as the National Institutes of Health and American Heart Association have

Dr. Walter Koch mentors future generations of researchers. Those who teach, learn.

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awarded more than \$116 million in competitive grants to Temple’s heart research program during the past decade. Many of the following studies are sponsored by these awards.

Straight to the Bone

After a heart attack, heart muscle dies. Scars form. Surviving cells enlarge, attempting to compensate for their dead neighbors — but bigger is not better when it comes to the heart. The body tries to repair itself through remodeling, but it often harms more than it helps. In fact, it can lead to heart failure.

Numerous approaches aimed at thwarting remodeling are under study at Temple. In one, scientists are trying to get healthy new cells to grow in the damaged area right after a heart attack.

“Heart cells do not regenerate as well as cells of other organs of the body,” says Houser. “So we’re sending in replacements. The general approach is called cell therapy.”

In one set of studies, the team compared the ability of different

types of stem cells to transform into functional heart cells. They tested stem cells from heart tissue and stem cells from cortical bone. The results were surprising. As detailed in the August 2013 issue of *Circulation Research*, bone stem cells worked best — even triggering the growth of new blood vessels. A small-scale clinical trial will be created to test the novel therapy in patients soon.

“This could be a real game changer,” says Daniel Edmundowicz, MD, Temple’s Chief of Cardiology. “The day is coming when delivery of reparative cells to injured heart tissue may be routine practice for heart attack patients in the emergency room.”

Calcium: Sometimes Less is Best

In certain pathways in the heart, excess calcium triggers remodeling. So researchers want to see if blocking it will prevent remodeling. But you have to be careful. If you block too much calcium, the heart won’t be able to contract. Eventually the team got just the right balance — with a gene therapy approach.



It's not just about doing research yourself. It's about empowering others to do research as well, says Dr. Steven Houser (center), who chairs the American Heart Association's Research Committee.

"The idea in gene therapy is to deliver new genes to overwrite defective programs in damaged areas. Genes are the software programs our systems operate on," Houser says.

Genes with specific actions are inserted into specially engineered (harmless) viruses that are very good at getting into cells. Like minuscule spies on a covert operation, the viruses slip in and put the new gene regime in command, blocking just the right amount of calcium.

"The success of this approach has been proven in the laboratory — and will be tested in patients as soon as safely possible," Houser says.

In Praise of Kinase

In heart failure, the electrochemical signals regulating the heart get out of whack — so scientists are looking for ways to normalize them. The signals are controlled, in part, by a group of regulatory enzymes called G protein-coupled

receptor kinases (GRKs). No one knows more about them than Wally Koch. He's the world's leading authority. What he's discovered about GRKs has the potential to transform the care of broken hearts.

A kinase called GRK2 helps regulate the strength and speed of heart muscle contraction. In precedent-setting studies, Koch's team showed that blocking excessive GRK improves the heart's contractile function. In fact, it actually reversed remodeling in a pre-clinical model of heart failure (*European Heart Journal*, 2013). Koch is working toward a gene therapy trial targeting GRK for heart failure that will be a "first-in-man."

In another heart failure study of GRK2, the team delivered a GRK2 blocking agent directly to the adrenal glands — and it reduced stress hormone output and improved the heart's ability to contract. Thus, adrenal GRK2 targeting is also headed toward human trials.

GRK2 can also get into the mitochondria of heart cells — and set off the cellular self-destruction program. "So the goal here is to keep it out," Koch says, "And so far we have found two different ways to do it."

Other kinases are being studied, too, including GRK5, which can get into the nuclei of heart cells and ultimately cause

hypertrophy. Again, perhaps GRK5 can be railroaded to help heal the troubled heart.

Several of these approaches are just steps from testing in humans," said one junior researcher. "It's amazing to think that treatments with potential to transform the world's approach to heart treatment are being created right here."

Exploring New Territory

Like kinase, there are other pathways and targets opening new avenues in heart research at Temple.

One is phospholemman, a small molecule with a big role in the heart. Phospholemman is good at getting heart rhythm problems under control and preserving the contractile strength of the heart under stress. It was discovered by Joseph Cheung, MD, PhD, Chair of the Department of Medicine and former Senior Associate Dean for Research at the School of Medicine. Now he's working to harness the benevolent powers of this molecule.

Another study targets the restorative potential of a little-studied vascular cell growth factor.

A novel, calcium-permeable ion channel called TRPM2 that activates to protect the heart from injury could lead to new treatments.

Proteins that play a role in regulation of vascular inflammation are under the microscope, too. They might be used to inhibit ischemic disease and promote new blood vessel growth.

In addition, Temple researchers recently discovered two previously unidentified pathways through which beta blockers work — pathways that could open up even more avenues for heart failure treatment.

Innovation in the Clinic

One of the most respected heart programs in the Delaware Valley, the Temple Heart and Vascular Institute offers a full range of treatments, for the most common heart conditions and the most complex.

"We make the most advanced techniques and tools available to patients," says T. Sloane Guy, MD, MBA, Chief of Cardiothoracic Surgery, "such as the HeartWare® Ventricular Assist Device — a portable, golf ball-sized technology designed

to assume some or all of the pumping action of the heart for patients awaiting a transplant."

With Guy and team at the helm, Temple has become an epicenter for robotic and minimally invasive heart surgery, as well as heart and lung transplantation.

"Physicians refer to us because we offer qualifying patients treatments not even commercially available yet," Edmundowicz says. For example, Temple is the only hospital in Philadelphia selected for the nationwide RENEW trial to evaluate a treatment that entails injecting cells from a patient's own bone marrow into the heart to see if it will reduce angina and improve blood flow. "Cell therapy has the potential to change the way medicine is actually delivered," Houser says.

"Physicians refer to us because we offer qualifying patients treatments not even commercially available yet," Edmundowicz says.

Temple is also the only medical center in Philadelphia in the TRIS trial (TandemHeart® to Reduce Infarct Size). The goal is to see if the device will produce better results for patients with acute heart attacks than standard treatments alone. "This trial could ultimately change the paradigm of therapy for large heart attacks," says Edmundowicz.

Temple is also testing the MitraClip Percutaneous Mitral Valve Repair System®. This new device could make a huge difference for patients considered too high-risk for valve repair surgery. It's deployed via catheter. No surgery needed.

Cardiovascular disease is a tough nut to crack. "But when I look at the creativity and innovation of teams like Temple's, I am optimistic," says Dr. Rose Marie Robertson, the American Heart Association's chief scientific and medical officer. "Better days for the heart lie just ahead." 📖

For an appointment with a heart specialist at Temple, call 1-800-TEMPLE MED.

Bryan Christie's illustrations have appeared in *Esquire*, *Time*, *Scientific American*, and the *New York Times*.

HIGHLIGHTS IN HEART HISTORY AT TEMPLE

- | | | | |
|-------------|---|-------------|--|
| 1937 | Produced early textbook on cardiovascular imaging. | 1990 | Performed the region's first successful heart-kidney transplant. |
| 1947 | Opened one of the first heart units in Pennsylvania. | 2003 | Deployed the first ventricular assist device in Philadelphia as a destination therapy. |
| 1948 | Perfecting the electrokymograph for early detection of heart disease. | 2009 | Surpassed 1,000 heart transplant surgeries — one of the largest totals anywhere. |
| 1960 | Revolutionized the treatment of heart attack with lytic therapy. | 2012 | Only center in Philadelphia selected to study stem cell therapy for heart (RENEW trial). |
| 1969 | Performed the tri-state region's first coronary bypass. | 2013 | Only center in Philadelphia selected to study Tandem Heart® device (TRIS trial). |
| 1984 | Performed the region's first heart transplant. | | |
| 1985 | Unveiled one of the earliest artificial hearts, the Philadelphia Heart. | | |

ED CUNCELLI

PATIENTS ON THE FRONTLINES OF RESEARCH MAKE JOURNEYS FUELED BY HOPE

THE FIRST HURDLE

BY JENNIFER LAIDMAN - ILLUSTRATION BY C.J. BURTON

It's a four-hour drive from Heidi Henn's home, south of Washington, D.C., to Fox Chase Cancer Center in Philadelphia. Every three weeks, her husband Harvey takes the wheel and guides their Infiniti up the Eastern Shore to northbound Interstate 95. The long commute is a no-brainer for Heidi. Every mile of clogged highway brings her closer to the drug that is keeping her alive.

Each year, some 200 patients come to Fox Chase to take part in a Phase 1 clinical drug trial (generally, 25 to 30 are active at any given time). And many, like Henn, make a long drive to do so. "Patients all over the East Coast are coming to us," says Anthony Olszanski, MD, RPh, Director of the Fox Chase Phase 1 program. They are on journeys powered by hope.

"Most Phase 1 patients have metastatic disease and are out of other options," Olszanski says. "Their physicians have often said, 'There is nothing more I can do for you.'" Phase 1

trials — of investigational medications — are their only option."

A Phase 1 trial is the first in a gauntlet of three that any new medication must run to be considered for approval by the U.S. Food & Drug Administration. In Phase 2 and Phase 3, investigators set out to demonstrate a drug's cancer-killing potency. But the goal of a Phase 1 trial is to be able to say the drug is safe and determine which dose produces the fewest side effects. That's it. The goal is not taming a cancer, shrinking a tumor, or zapping metastases. That's for later. The goal is finding the dose to use in subsequent trials that do aim to tame, shrink, and zap.

"Phase 1 is where drug development starts," says Hossein Borghaei, DO, head of thoracic medical oncology at Fox Chase, and Henn's oncologist. Borghaei is the lead investigator in about a dozen trials, including several in Phase 1. "Phase 1 trials give us the chance to find the best treatment for our patients."



THE LUCK OF THE MUTATION

When Henn came to Fox Chase, she knew that the treatment she signed on for came with no guarantees, but she was at the end of her tether. The standard course of treatment — including chemotherapy — had been a bust for the 50-year-old mother of two, who, in the fall of 2011, learned she had stage IIIb lung cancer. The diagnosis was the result of a medical workup to get to the source of breathing difficulties that had suddenly beset her. She thought it might be heart disease, which took both her father and mother at relatively young ages. “I never for a minute thought lung cancer,” Henn says.

Stage IIIb meant the cancer was advanced. It had already moved to her lymph nodes. The survival statistics are grim, with only about five percent of stage IIIb lung cancer patients surviving five years. Henn’s children were 16 and 13 at the time. No way was she ready to let them go. But her cancer had already eluded the chemotherapy. It had now moved to other areas of her body.

Henn’s tumor had been tested for specific genetic mutations. Genetic screening is a field of growing importance in the treatment of cancer, enabling oncologists to use drugs capable of targeting particular mutations. Henn did not have the most common lung cancer mutation, which occurs in a gene called Epidermal Growth Factor Receptor. She had a less common mutation on a gene labeled ALK, Anaplastic Lymphoma Kinase. ALK is mutated in three to five percent of lung cancers. The discovery was good news. It meant she could take a new drug called Xalkori (crizotinib), which is custom-made for ALK mutations.

The results of Xalkori treatment were immediate. It was like getting her life back — without the awful side effects of chemotherapy. Of course, cancer is never simple: she also received high-dose radiation to shrink a tumor that was beginning to strangle her, making it difficult to breathe and talk.

FAILED TREATMENT, NEW HOPE

But nine months into the regimen, Xalkori stopped working. Henn began searching online for experimental treatments for ALK mutations. She contacted several medical centers testing ALK-targeted drugs. “I got a response from Fox Chase really quickly,” she says. She was to start her new therapy, a novel drug called LDK378, the day after Christmas 2012.

Not just any hospital can offer a Phase 1 treatment of this kind, Olszanski says. “We are one of the few centers able to do so. Phase 1 trials are highly specialized. It takes a huge commitment — extensive resources, experienced physicians, nurses, and staff. We specialize in administering new agents. We know how to quickly detect any ill effects from treatment, and how to intervene when they occur. Having Phase 1 trials available means we can offer new hope to patients with innovative therapies not otherwise available. And being on a clinical trial adds up to better care across the board.”

Henn arrived at Fox Chase feeling miserable, but desperate to try the new drug. The cancer in her lungs had grown, and now



Hossein Borghaei, DO (above), head of thoracic medical oncology at Fox Chase, and Heidi Henn (at right).

there were tumors on her liver. “Much to my terror, they found four brain tumors,” she says.

But her treatment was delayed. She was too sick, with a temperature of 103, possibly brought on by the cancer itself. Borghaei admitted her as an inpatient to treat the fever. Eventually he ordered a blood transfusion. Finally, on January 7, 2013, feeling slightly stronger, she was able to take her first dose of LDK378.

“We’ve been able to put a lot of patients on this trial drug,” says Raneeh Mehra, MD, principal investigator for the LDK378 trial at Fox Chase. “We’re seeing response rates of 60 percent.”

Sixty percent is an excellent overall result, and Henn’s

individual results have been even better. But not every patient on a Phase 1 trial can expect such a turnaround.

MANAGING SIDE EFFECTS

Experimental treatments require close communication among medical professionals and careful attention to the patient’s health. There are always risks attendant with taking a drug that has not been tested for safety before. Vigilance is key.

“I sleep less when I have a patient on a Phase 1 trial. I worry about them,” Borghaei says. “You have to look at the trial protocol, and you have to look at the drug being tested, and you have to decide, ‘Would I feel comfortable putting my own family member on this?’”

Henn was undaunted by the risks. A few weeks into the trial,

“I SLEEP LESS WHEN I HAVE A PATIENT ON A PHASE 1 TRIAL. I WORRY ABOUT THEM,” BORGHAEI SAYS. “YOU HAVE TO DECIDE, ‘WOULD I FEEL COMFORTABLE PUTTING MY OWN FAMILY MEMBER ON THIS?’”

she started to feel better, despite the side effects the drug caused. “I struggled with severe GI issues for a while.” But her care team changed the timing of her dose from morning to evening, and that reduced the side effects. The treatment also causes fatigue. “But compared to chemotherapy, this is night and day. This is wonderful,” Henn says.

As her treatment progressed, Henn’s cancer retreated. Her brain tumors are now considered non-measurable. Her liver tumors are gone. The cancer in her lymph nodes vanished. And her lungs are much clearer. In fact, Kristen Kreamer, the nurse practitioner who works with Borghaei, told Henn that her recent lung x-rays were nearly as clear as the lungs of a patient who didn’t have lung cancer. “My breathing is so much better,” says Henn, who returned to work at the Naval Air Systems Command, putting in about 30 hours a week.

HELPING MORE PATIENTS

“It’s important to understand, scientifically, what we think is driving each patient’s cancer, and when a patient is no longer responding to standard of care — then immediately consider whether they might be a good clinical trial candidate,” Olszanski says.

Nationwide, about five percent of cancer patients enter clinical trials — a percentage Olszanski says is too low. “At Fox Chase, the rate is substantially higher,” he says. “We believe, and the National Comprehensive Cancer Network would agree, that the best care patients receive is often in the context of a clinical trial.”

As positive as her outcome has been so far, Henn tries to remain philosophical. “If this drug eventually stops working, even if it only helps me in the short run, I know it is still important for me to do this, because it will help others in the long run,” she says. “That’s been one of the silver linings for me, a way to give back some of what I have received.”

Jennifer Laidman’s work has appeared in *Reader’s Digest*, *Science Magazine* and the *Chicago Tribune*. For information on Fox Chase: www.fccc.edu/ 1-800-FOX-CHASE.

TOMMY LEONARDI

Lungs, (Un)plugged

A procedure requiring temporary stoppage of the heart and lungs — and the clinical cooling of the body to protect the brain — can save the lives of patients whose pulmonary blood vessels are chronically blocked by clots. Temple is the only Philadelphia-area academic medical center, and one of less than five in the nation, to offer this uncommon treatment.

By GISELLE ZAYON

“I was just trying to survive each day,” recalls Heather Frantz, a 45-year-old resident of Bucks County, PA, who, in June 2013, became the first patient to undergo a rare but potentially life-saving surgery called pulmonary thromboendarterectomy (PTE) at Temple.

A pulmonary embolism had been blocking blood flow to 90 percent of Frantz’s right lung. Another clot was lodged in her left. Over one million people in the U.S. suffer from this kind of acute pulmonary embolism per year, with fatal results in 10 to 20 percent of cases.

Most clots respond to blood-thinning medication or dissolve on their own. But Frantz fell into the two to five percent of patients whose clots do not respond to standard therapy. Instead, they continue to choke off blood flow, elevating blood pressure in lung vessels and putting extra strain on the heart.

When this situation persists for six months or more, the condition is called chronic thromboembolic pulmonary hypertension (CTEPH). It’s a diagnosis that robs approximately 5,000 people of breath — or life — every year.

For most patients with CTEPH, there is only one effective treatment: PTE. Frantz credits PTE, and physicians who performed it, with saving her life.

A complex surgery designed to remove chronic blood clots from major vessels in the lung, PTE was developed in the 1970s. It is still relatively rare. Less than 5,000 PTEs have been performed in the world. “That’s because PTE is such a serious undertaking,” says Paul Forfia, MD, who brought PTE to Temple. One of the world’s foremost experts in the diagnosis and treatment of CTEPH, Forfia directs the Pulmonary Hypertension and Right

Heart Failure Program at the Temple Heart and Vascular Institute.

When he came to Temple from the University of Pennsylvania in 2013, he worked with world-renowned thoracic surgeon Yoshiya Toyoda, MD, Temple’s Vice Chief of Cardiothoracic Surgery, to develop the PTE program at Temple.

“PTE is a highly specialized procedure that must be performed by an experienced team, calling on specialized knowledge and advanced technology,” emphasizes Forfia. “Proper preoperative diagnosis and patient selection, combined with high-level surgical expertise, are critical to optimal patient outcomes.”


Delicate and somewhat dramatic, PTE entails temporarily inducing “clinical death,” then bringing the patient back to life again. The patient’s chest is opened to give surgeons access to the heart and lungs. The surgeons then make a small incision in the pulmonary artery to insert special instruments to reach the clot.

Flowing blood would obscure the anatomy inside the vessel. Therefore, it

must be diverted. The patient is put on a heart-lung bypass machine — which is temporarily turned off when surgeons gently peel the clots away from vessel walls. To protect the brain during the procedure, the team reduces the patient’s temperature to 68 degrees Fahrenheit. After the incisions are closed, normal lung and heart function is restored, and the patient is gradually rewarmed.

Most PTE surgeries take about eight hours — and result in significant benefits for about 90 percent of patients. They no longer suffer shortness of breath. Lung blood pressure and heart function return to normal.

“We are on our way to making Temple a major PTE center regionally and nationally,” Forfia says.

Heather Frantz, Temple’s first PTE patient, was back to her “old self” within six weeks. “What joy to be back in the flow of air, the flow of humanity,” she says. 

For an appointment with a Temple clinician, call 1-800-TEMPLE-MED.

A Cool History: Temple’s Temple Fay

Coolness preserves. Refrigerators prove it daily. In the medical realm, coolness is neuroprotective. It spares the brain. Physicians use clinical cooling to reduce risk of damage when tissues are temporarily deprived of blood — as in PTE.

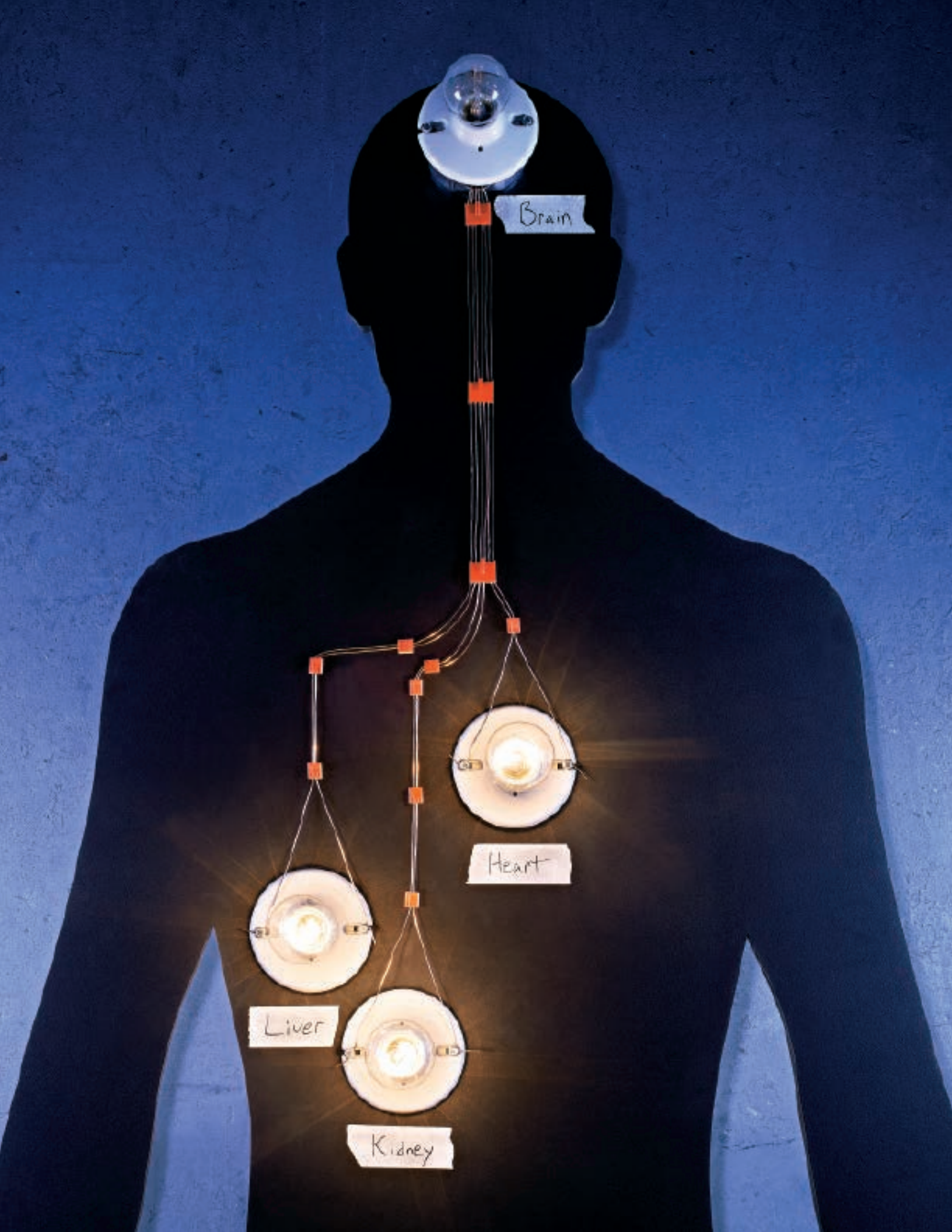
The physician credited with pioneering clinical cooling for modern times is Temple Fay, MD (1895–1963), once head of neurosurgery and neurology at Temple. In the 1930s and 40s, Fay demonstrated that clinical cooling controlled pain, slowed the growth of cancer, reduced inflammation, and inhibited bacterial growth. It was also well-tolerated by the brain. Ice-chip blankets were used daily on Fay’s “Refrigeration Service.”

The innovative Fay also devised new surgical techniques and instruments, such as a multifunctional brain retractor with illumination.



Temple Fay, MD

FAY: TEMPLE ARCHIVES

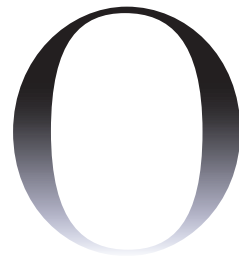


When
Death
Begets

LIFE

Every year, in hospitals across the United States, thousands of organs and tissues that could save lives do not get transplanted because many families of brain-dead patients do not say “yes” to organ donation. Now, a precedent-setting training program for physicians developed at Temple — poised to roll out nationally — has increased the family consent rate, saving more people on organ waiting lists, and providing families solace during a time of painful loss.

By GISELLE ZAYON
Photograph by CLINT BLOWERS



One of the most difficult things a physician will ever do is tell a family that their loved one has died. It's especially distressing when a young person is involved — and when the death is caused by a gun. This is all too-often the case in urban trauma centers, like Temple University Hospital.

"Something meaningful has got to come of this tragedy," says Amy Goldberg, MD, chief of trauma and surgical critical care at Temple University Hospital.

Something meaningful — from gun violence?

"Yes," Goldberg says. "Sometimes, when a person dies, other people can be saved — through organ donation — if we can help the grieving family to say 'yes.'"

More than 119,000 people in the United States are on the waiting list for organ transplants. Every 13 minutes, another name is added to the list. Every day, 18 people die waiting. The number of donors has not kept pace with the demand.

In 2003, as a result of persistently low rates of donor-organ availability, the federal government formed the U.S. Organ Donation Breakthrough Collaborative — a national initiative aimed at improving the nation's organ donor "conversion rate."

The conversion rate is the number of potential organ donors who actually *become* organ donors. That year, at a conference she attended, Goldberg heard the Secretary of the U.S. Department of Health and Human Services, Tommy Thompson, announce the goal himself. It was a lofty number: 75%.

"It was such a bold declaration. But I loved the vision," said Goldberg, who remembers the meeting as a "huge moment" in her life. Like Thompson, she knew she had to think "big."

An idea began to crystallize — an idea that would help Temple take up Thompson's challenge and cull meaning from the senseless violence taking so many young lives. Goldberg, who is also director of Temple's surgical residency program, would start with the young surgeons she trains. The national accrediting agency for resident education was rolling out new standards for resident professional communications skills at the time. Teaching residents how to handle the conversation about brain death with families would meet the new criteria. It was all coming together.

DEAD, BUT ON "LIFE" SUPPORT

When people die who are not registered as organ donors, the decision to donate their organs is left to the family.

Every day, potential organ donations are lost, because families refuse

to say "yes" — sometimes because they do not believe their loved one is truly dead. Brain death is the cause of the confusion.

As defined in the Uniform Determination of Death Act, brain death is the complete and irreversible cessation of brain function. Brain death *is* death. The patient cannot pull through. Nevertheless, critical care technology can keep a brain-dead patient's organs perfused with blood and oxygen for a while. Dead patients on ventilators appear to be breathing, though it's actually the machine doing the work. This concept can be difficult to grasp, especially for families in the acute stages of grief. Many families think their loved one is "asleep."

"It's easy for family members to misjudge the situation," Goldberg says. "Plus, physicians could create false hope by not giving a proper explanation of brain death. Physicians have got to be honest with the family. We must show compassion, but also be concise and clear. This is the only way families are going to understand."

"Research shows a statistically significant relationship between the understanding of brain death and authorization rates for organ donation," says Gweneth O'Shaughnessy, Director of Hospital Services at Gift of Life, the region's non-profit organ and tissue donor network, serving eastern Pennsylvania, southern New Jersey, and Delaware.

Last year, Temple had 39 potential organ donors — 19 of whom went on to donation. These are small numbers — and in many ways, that's the whole point. Only one to two percent of people die in a condition that makes them a suitable organ or tissue donor. That's why it's vital to get every possible "yes." When the conversation about brain death isn't handled properly, families don't understand their loved one is dead.



Something meaningful from gun violence? "Yes," Goldberg says. "Sometimes when a person dies, other people can be saved — through organ donation — if we can help the grieving family to say 'yes.'"



GETTING TO YES

After hearing Secretary Thompson's summons, Goldberg teamed up with Temple's organ procurement organization, Gift of Life, to create a first-of-its-kind venture to equip resident physicians with the skills, knowledge, and confidence to effectively and clearly communicate brain death to families. They launched the pilot program at Temple in 2006. To date, more than 200 surgical resident physicians at five hospitals in the Gift of Life region have been trained. Additional residents in other specialties, such as neurology, neurosurgery, and internal medicine, have also taken the training.

"Working with hospital staff to make sure they're able to communicate brain death effectively is a unique and essential strategy to help us prepare to ask families to donate — during one of the most



difficult times in their lives," says Gift of Life President and CEO Howard M. Nathan. "In 2012, only 34% of all potential organ donors in the Philadelphia region were registered organ donors, so the program can really make a difference to the more than 6,400 men, women, and children awaiting life-saving transplants in our region," he says.

The training features detailed explanations of brain death and the organ donation process. But its prime focus is on role-playing. In simulated family encounters, residents practice explaining brain death to Gift of Life staff, who serve as "family members." The sessions are videotaped and reviewed by the instructor and residents for immediate feedback.

"We do not make it easy. We provide realistic scenarios," Goldberg says. "We teach residents to use non-clinical language to explain brain death. Their manner must be compassionate, yet clear."

Residents learn that showing families the patient's radiographic scans or studies can help illustrate that the brain is no longer functioning.

"We urge the residents to never provide a sense of false hope. We educate them about the importance of providing the exact date and time of death — for example, 'I am so sorry to say that your loved one was declared dead at 1:45 pm today.' It is absolutely essential that the family understands, and typically, this takes time," Goldberg explains.

Residents are given a 12-point checklist that outlines how brain death should be explained. Senthil Jayarajan, MD, a senior resident at Temple who took the training five years ago,

says the program continues to help him today. "I don't need my checklist anymore," he says. "I know the steps by heart."

After the family has had a chance to absorb the news, Gift of Life Transplant Coordinators gently and compassionately introduce the subject of donation.

MAKING A DIFFERENCE

To enable program evaluators to determine what difference the training has made, all residents who participate complete pre- and post-training assessments of their experience, confidence, skills, and knowledge in explaining brain death to families.

The before-and-after data is very telling. Before participating in the training, only 51% of residents believed that brain death is synonymous with death. After the training, 93% said they understood that it is. Prior to the training, 31% of residents said they felt comfortable discussing brain death with families. Following the training, 98% said they felt comfortable. The benefits are clear. The training has improved residents' knowledge of brain death, and their skills and confidence in discussing it with families. Rates of organ donation have also improved.

Since 2006, in cases where trauma was the cause of death, rates of organ donation increased in cases managed by surgical residents who completed the training. The rate of organ donation in Temple University Hospital's surgical intensive care unit was 41% in 2006. Just one year after the program was implemented, the rate jumped to 67% — a marked improvement. The program continues to have a beneficial impact at every site, every year.

Goldberg and O'Shaughnessy have been invited to present talks about the program at a number of national meetings, including a recent National Learning Congress attended by nearly 1,500 acute care hospital personnel and organ procurement staff from across the U.S. "Our hope is to take this training across the country, collect more data, and publish the outcomes," Goldberg says.

"Literature indicates that families don't regret donating — they regret *not* donating," Goldberg explains. That's why our physician training program is so important. It helps families find some meaning at a time of otherwise tragic and senseless loss."

In 2011, Beverly Kendrick's son was a victim of gun violence. Despite exhaustive efforts to save him, he died at Temple University Hospital.

"Doctors said that Dereck was brain dead," Kendrick recalls. "I stayed overnight beside his bed. I prayed through the night, asking God to give me the strength to let go. That morning, I walked over to the Gift of Life coordinator to give her my consent. I said to her, 'I will do it, if it will save somebody else's life.'"

Photographer Clint Blowers' clients include Procter & Gamble and the University of Michigan.

DOMINIC EPISCOPO

Selwyn O. Rogers, Jr., MD SURGEON-IN-CHIEF

Q
&
A

In July 2012 you told the Philadelphia Tribune that you were called to Philadelphia by forces beyond you. What does that mean?

When Temple's offer came, I was at Harvard—serving as Chief of Trauma, Burn and Surgical Critical Care at Brigham and Women's Hospital. I wasn't thinking of leaving Boston, but how could I pass up the chance to build a world-class surgical program in one of the most underserved neighborhoods in the country? The state-of-the-art *and* the underserved speak to me at a core level. An opportunity so right, it felt destined in a way. Some see adversity in North Philadelphia. But I see opportunity to change the dialogue about how a hospital can partner with the community it serves.

Q: *Change the dialogue? How so?*

A: It's time to redefine "hospital." A hospital should be a beacon of wellness. A hospital should look beyond the patching of skin and bone to address social determinants of disease, poverty, homelessness, and helplessness. Take Philadelphia's high rate of homicides. We need campaigns to save the lives of young men. Violence is a health problem. The *Philadelphia CeaseFire* and *Cradle to Grave* programs at Temple give at-risk youth an unvarnished look at the aftermath of gun violence. Programs of substance and impact. That's what hospitals need to be about.

Q: *The U.S. Census Bureau lists Temple's zip code among the country's top five for diabetes and obesity.*

A: That's right. And diabetes and obesity are just two issues. Interventions such as bariatric surgery can play a transformative role in these problems, leading to weight loss and remission of diabetes.

Temple cares for a lot of critically ill patients, complex cases, trauma. Embracing the sickest people, bringing better care to those who need it most — that's what drives me.

Q: *Where did you get your altruistic ambitions?*

A: From my mother, mostly. She raised me and my four siblings herself, in the U.S. Virgin Islands. Never earned more than \$30,000 a year, but our house was big enough for each of us to have our own room. Her whole life was about my betterment. My teachers, too. Now I'm telling young people to dream large, aim high. I'm on a mission to increase the number of minority physicians in this country.

Q: *You are Temple's first black chair of surgery. What's that like?*

A: I've had my share of quizzical looks over the years. Even patients who assumed I had come for their meal tray. Once I was introduced to a surgeon who

stammered, "Oh. I didn't think you'd be so ... tall." Sure it's wrong. But you cannot let bitterness burn your life away.

Q: *You are interested in the impact of race and ethnicity on outcomes and quality of care.*

A: Yes. I characterize surgical outcomes among different populations. There are unwarranted variations in both process and outcomes of care. We must address them. In 2005, Hurricane Katrina put the national spotlight on poor people in New Orleans who needed medical care. Few realize it, but just as many of New Orleans' poor needed medical care *before* the storm. There are silent Katrinas every day.

Q: *Eliminating disparities: is this is your main objective?*

A: Larry Kaiser, our CEO and Dean, brought me to Philadelphia to elevate Temple surgery to a higher plane. To expand its range of surgical options, adopt new technologies, ensure high-quality outcomes, and establish a research program to distinguish our efforts at the national level.

Last year, six amazing surgeons joined the already stellar team in place — helping put Temple surgery on the map with procedures that are not being done anywhere else in the region — or the nation. All milestones, establishing Temple as an epicenter of minimally invasive surgery. Our capabilities are among the most advanced in the world.

It takes a team to advance an institution's stature. Likewise, it takes the heart and soul of many to serve the rich and the poor with equal levels of skill and compassion. The state-of-the-art and the underserved. They're intermingled, interwoven, in everything I care about, everything I do.

Selwyn O. Rogers, Jr., MD, MPH, FACS
Surgeon-in-Chief
Temple University Health System



Lupus

Systemic Lupus Erythematosus (SLE) is an autoimmune disease that affects nearly 500,000 Americans. Lupus means wolf in Latin. In the 13th century, the skin lesions characteristic of the disease were said to resemble a wolf's bite. In the 19th century, scientists recognized the lesions as part of a systemic autoimmune disease with serious consequences. In autoimmune disease, the body turns against itself, attacking healthy cells and tissues.

A short walk divides the offices of Stefania Gallucci, MD, and Roberto Caricchio, MD, at Temple University School of Medicine, making it easy for the married researchers to talk about their passion: Systemic Lupus Erythematosus (SLE).

"We talk about it all the time," says Gallucci. "We talk about it when we wash the dishes. Our children say, 'Please, let's talk about something else.'"

Gallucci and Caricchio are part of a team of physicians and scientists who treat lupus *and* study the puzzling disease.

Temple's Lupus Clinic was the first in the Greater Philadelphia region dedicated exclusively to patients with SLE.

"About 90% of SLE patients are women. African Americans and people of Hispanic descent are two to three times more likely to have SLE," says Philip Cohen, MD, Chief of the Section of Rheumatology. Internationally known for helping to characterize the role of B cells in autoimmune disease, Cohen is one of the rheumatologists who staff the Lupus Clinic.

Nearly 40% of SLE patients have renal disease. Therefore, the clinic also includes an expert in kidney care.

Temple has more SLE researchers than any other organization in the tri-state region, with more than \$1.5 million in funded research underway. Cohen says to have so many scientists and physicians focused on lupus treatment and research is rare — and necessary. Over the past 56 years, only a single new drug, Benlysta, has been approved for SLE.

While all the SLE researchers at Temple collaborate, each looks at a different aspect of the disease.

Caricchio studies how dead cells fuel the autoimmune system to keep it working against the body. "We can work on stopping that process," he says.

He also examines why kidney disease is more severe in male SLE patients than female. Hormonal links could be the key. "We might actually have male and female versions of the disease — and end up treating them differently," he says.

Caricchio is also refining a new test to determine the severity of kidney disease with a simple urine sample. If developed commercially, this diagnostic tool could spare patients the need to undergo the invasive kidney biopsy procedure standard in the field.

Gallucci studies the factors that trigger the faulty autoimmune response inherent in SLE. She is studying a group of inflammatory mediators, the interferons, that are over-expressed in SLE patients and that are normally part of the immune response to a viral infection — although no virus is found in SLE patients. Estrogens, she suspects, play a part in triggering the response. "If this is confirmed," she says, "we could identify new drug targets."

Caricchio, Gallucci, and Cohen are members of the Temple Autoimmunity Research Center. The 15 physicians and scientists in this group collaborate to advance medical science's ability to treat and perhaps someday prevent SLE and a wide range of autoimmune diseases, including rheumatoid arthritis and Sjogren's syndrome. They also mentor the postdoctoral fellows, students and other junior researchers who will lead the field in the future.

Italian-born physicians who studied medicine in Italy, Caricchio and Gallucci have been together since their first date, on Roberto's 18th birthday. They immigrated to the U.S. in 1996.

After more than a decade of lupus research, intent on becoming licensed to see patients in the U.S., Caricchio put in five additional years of training, which he completed at Temple last year. Gallucci is a full-time researcher.

"Roberto may be one of the few, if not the only, physician in the U.S. ever to get a National Institutes of Health grant while in Internal Medicine residency training," says Cohen.

And as for those children protesting their parents' obsession with science? "One plans to be a scientist, the other a physician," says Gallucci with a smile.



Roberto Caricchio, MD, and Stefania Gallucci, MD: A professional and personal partnership.

Advancing Robotic Surgery

Minimally invasive and ultra-advanced, robotic surgery is setting a new standard for procedures once performed solely through “open” surgery. The technology permits a virtually scarless result — with reduced blood loss and pain, faster recovery, and a shorter hospital stay. Certain procedures can be performed through just one “port” in the body.

During robotic surgery, the surgeon sits at a cockpit-like computer console to control robotic instruments inside the patient. A camera on a robotic arm magnifies the patient’s internal anatomy in three dimensions on a high-definition screen.

“We are doing cases at Temple that cannot be done anywhere else in the region,” says Daniel Eun, MD, Vice Chief of Robotic Surgery, who collaborates with colleagues across a spectrum of specialties to bring innovative procedures to patients, with excellent results.

Temple has pioneered many robotic surgery “firsts,” including the nation’s first robotic kidney blockage repair — and the region’s first robotic kidney and gallbladder removal — using the daVinci® Single Site platform.

Designed with the input of Eun and colleagues, Temple University Hospital’s new \$5.7 million robotic surgery operating suite features a central-command center and two spacious operating rooms. It is one of the most sophisticated in the world. A total of six daVinci® robots are utilized. Each costs between \$1.75 and \$2.5 million. In addition, Temple operates the only robotic surgery training center in the region — attracting surgeons seeking advanced training from throughout the Greater Delaware Valley and beyond.



“Temple is setting a new standard in robotic surgery. We have the most sophisticated robotic operating rooms in the world.”

—DANIEL EUN, MD, VICE CHIEF OF ROBOTIC SURGERY



LARGER THAN LIFE, IN THREE DIMENSIONS. At Temple, members of the surgical team — and students — can watch the procedure on high-definition, high-magnification 3-D monitors (as large as 72 inches). Temple broadcasts procedures to surgeons-in-training across the nation in real time, and sessions can be videotaped for later review and education.



LIKE TINY ACROBATS. Slim-profile, telescoping instruments, equipped with dozens of interchangeable parts with specialized functions, do the work the surgeon commands: cauterizing, retracting, suturing, suctioning, etc. Instruments are replaced frequently at an average cost of \$2,000 per replacement part.



VISION WHERE EYES CANNOT GO. A stereoscopic camera on the robot’s instrument arm virtually extends the surgeon’s vision into the patient’s body. What the surgeon sees (and does) is projected onto a 3-D monitor at the console at high magnification.



BETTER THAN THE HUMAN HAND. The surgeon operates the robot at a computer console, using hand and finger controls to manipulate instruments inside the patient — with precision of movement surpassing the abilities of the human hand alone. Small-scale and agile, the instruments permit entry into tiny spaces.

TIMELINE

Episcopal Hospital

Founded in 1852, Episcopal Hospital, now known as Temple University Hospital-Episcopal Campus, is the second-longest continually operated hospital in Philadelphia. The oldest, Pennsylvania Hospital, was founded in 1751.

Episcopal's history is storied. It cared for Union soldiers during the Civil War, weathered the polio epidemic of 1916, and staffed field hospitals overseas during

World Wars I and II. In 1945 it attracted international attention for pioneering the world's first surgical technique to remove scar tissue from the heart's mitral valve.

Episcopal was a training site or base of practice for many prominent figures in American medicine, including Howard Kelly, MD (1858–1943), one of the four founding physicians of Johns Hopkins University School of Medicine, and Charles Harrison Frazier, MD (1870–1936), who,

with Harvey Cushing, developed neurosurgery in the United States.

Today, with a busy emergency department, a general medical telemetry inpatient unit, outpatient services in several specialties, and 118 beds for psychiatric care, Episcopal serves as Temple's main site for behavioral health services. Its Crisis Response Center sees more than 11,000 psychiatric outpatients annually. In recent years, Episcopal has won

national awards, such as the Press Ganey Compass Award for excellence in patient satisfaction. It is also home to Temple's highly respected resident physician training program in psychiatry.

While most of the campus has been modernized, two landmark structures remain: a chapel designed by John Sloan in the 1850s, and the Tower building, designed by the famed Philadelphia architect Horace Trumbauer in 1933.



2013 Episcopal's Emergency Department logs nearly 50,000 annual visits and its Crisis Response Center sees more than 11,000 patients.

1845 Episcopal Rev. Alonzo Potter (left) and Philadelphia physician Caspar Morris (right) lobby to create a new hospital. With only 200 charity care beds combined, the city's two hospitals, Philadelphia General and Pennsylvania Hospital, cannot serve all the city's chronically ill and poor.

1851 Ann Leamy and Elizabeth Stout offer their 5.5-acre property for the new hospital — an offer initially opposed due to its "remoteness" from the city. In 1852, the renovated mansion opens as the Hospital of the Protestant Episcopal Church. The first patients are treated on Christmas Eve.

1860 Construction on a new hospital building gets underway as the Civil War intervenes. The first casualties from the Virginia campaigns arrive in 1862, with the wounded overtaking military hospitals.

1862 Philadelphia General and Pennsylvania Hospital, cannot serve all the city's chronically ill and poor.

1881 Ann Leamy and Elizabeth Stout offer their 5.5-acre property for the new hospital — an offer initially opposed due to its "remoteness" from the city. In 1852, the renovated mansion opens as the Hospital of the Protestant Episcopal Church. The first patients are treated on Christmas Eve.

1888 Episcopal founds its nursing school. Later, its graduates help establish the organization now known as the American Nurses Association.

1913 The hospital treats its first auto accident victims. Three years later, it responds to a severe outbreak of poliomyelitis in Philadelphia.

1916 The hospital responds to a severe outbreak of poliomyelitis in Philadelphia.

1917 Episcopal authorizes the formation of a base hospital in France under the auspices of the Army Red Cross.

1924 Episcopal serves as a training site for medical students of the University of Pennsylvania, and later, Temple University School of Medicine (1933). Demand for services grows. In 1928, the hospital logs 6,700 inpatient stays and 31,000 outpatient visits.

1945 Episcopal performs the world's first mitral commissurotomy, a surgery to remove scar tissue from the heart's mitral valve, attracting international attention.

1948 Episcopal performs the world's first mitral commissurotomy, a surgery to remove scar tissue from the heart's mitral valve, attracting international attention.

1998 Episcopal Hospital becomes part of Temple University Health System. Two years later, restructuring and renovations re-focus Episcopal primarily on behavioral health. The facility is renamed the Temple University Hospital-Episcopal Campus.

2006 With more than 9,000 visits, Episcopal's Crisis Response Center is the busiest in Philadelphia — and one of the busiest on the East Coast. Patient satisfaction scores soar to the 98th percentile.

2009 Episcopal's nursing school graduates its final class.

2013 Episcopal's Emergency Department logs nearly 50,000 annual visits and its Crisis Response Center sees more than 11,000 patients.

IMAGES: TEMPLE ARCHIVES; 1860: MPI/GETTY IMAGES

2013: ELIZABETH MANNING

ALUMNI NEWS

Temple's 10,000+ medical school graduates are advancing health and social welfare across the globe.



1



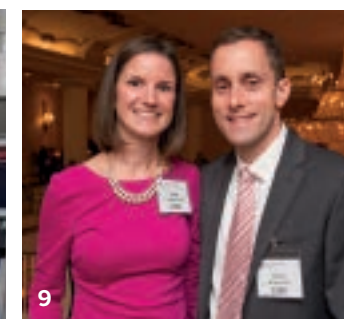
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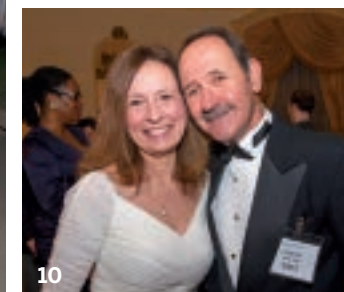
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Reunion Was a Blast!

More than 300 alumni and guests flocked to campus on November 16, 2013. Put simply, Class Reunion rocked.

The celebration kicked off with breakfast at Philadelphia's historic Bellevue Hotel, followed by a series of on-campus events. First, a panel discussion by distinguished faculty: "Transforming Medical Care at Temple." Next a luncheon, capped off by campus tours. Interactive sessions in the robotic and hybrid operating rooms were big hits.

Later, it was back to the Bellevue for the Reunion Banquet, with Alumni Association President Darilyn Moyer, MD '85, presiding. Temple University President Dr. Neil Theobald and Dean/CEO Dr. Larry Kaiser welcomed the returning graduates and guests, expressing gratitude for their support. "I am proud to say

that, together, we have done much to expand the reach of the "Temple T," Kaiser said.

Exemplary individuals were honored that night. The Honored Professor Award went to Ellen Tedaldi, MD, Professor of Medicine, for her dedication to medical education at Temple. Theodore Wagner, MD '68, a Seattle-based spine specialist, received the Alumni Service Award for his generosity to Temple. Jonathan Ellen, MD '88, president of All Children's Hospital, in St. Petersburg, FL, received the Alumni Achievement Award for his accomplishments. The Henry P. Laughlin Alumnus of the Year Award went to Alfred Michael, MD '53, Emeritus Dean of the University of Minnesota Medical School. Dining and dancing followed.

"It was a blast," said Eugene Kern, MD '63, of upstate New York. "We did not want to leave."

SAVE THE DATE
> NOVEMBER 8, 2014
 Reunion for School of Medicine graduates of class years ending in 4 and 9. Mark your calendar now, and watch the mail for your official invitation.

ALUMNI, SHARE YOUR NEWS
medalum@temple.edu
 215-707-4868
 800-331-2839



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7



8

1. Dr. Larry Kaiser, Dean/CEO (center), with reunion honorees (L-R) Jonathan Ellen, MD '88, (Alumni Achievement Award); Alfred Michael, MD '53 (Alumnus of the Year); Ellen Tedaldi, MD (Honored Professor); and Theodore Wagner, MD '68 (Alumni Service Award).

2. Alumni on tour. In the background, the Medical Education and Research Building, home base for the medical school.

3. Florida Oliveri, MD '73 (left) and Cynthia Hunt, MD '73.

4. Decked out for sessions in the hybrid and robotic ORs.

5. (L-R) Michael Zeibelman, MD '83, Patricia Marshall, Sheona Mackenzie and Temple University President Neil Theobald, PhD.

6. (L-R) Geoffrey Moorer, MD '03, Marc Hopkins, MD '03, and Erica Yoon Hopkins, MD '03.

7. John Jagerman, MD '73 (blue shirt).

8. The faculty who presented "Transforming Medical Care at Temple" (L-R): Daniel Eun, MD '01 (robotics); René Alvarez, Jr., MD (cardiology); Eric Choi, MD (vascular surgery); and Paul Forfia, MD (pulmonary hypertension/right heart failure).

9. Sarah Goodyear, MD '03, and Cyrus Morgan, MD '99.

10. Eugene Kern, MD '63, and Ruth Kern.

11. From the Class of 1993 (L-R): Drs. Melanie Koehler, Linda Bogar, Taiwen Chen, Maria Gaydos, and Heather Ruddock.

“SURGERY IS A PERFORMANCE-TO-WIN SPORT. YOU DON’T GET A TROPHY FOR PARTICIPATION.”

—T. SLOANE GUY, MD, MBA (CHIEF, CARDIOVASCULAR SURGERY)

“WHEN I LEFT TEMPLE MEDICAL SCHOOL WITH MY M.D. DEGREE, I HAD EARNED A SOCIAL CONSCIENCE AS WELL.”

—FREDERICK HARTMAN, MD, MPH (ALUMNUS)

“Whatever changes may occur in healthcare in this country, we must maintain the sacred doctor-patient bond. Nothing is more important.”

—LARRY KAISER, MD, FACS (DEAN AND CEO)

“A disease has only one name, but each person who suffers from it is different.”

—HANNAH RAVREBY, MD, (INTERNIST)

“We are charged with reducing the burden of disease in our society, with making sure that patients have access to care that is effective, safe, and humane. We do this by continually questioning, refining, and improving what we do. This type of applied research enables us to provide better care to more patients.”

—NESTOR ESNAOLA, MD, MPH, MBA (CHIEF, SURGICAL ONCOLOGY)

“Today we sometimes hear, ‘medicine is not like it used to be.’ To this, I say thank goodness. Does anyone want to go back to epidemics of polio or the time before we could fix blocked arteries in the heart?”

—BENNETT LORBER, MD, MACP (PROFESSOR OF MEDICINE)

Temple University School of Medicine ranks

5th in the nation in National Institutes of Health grant funding per faculty member.

“To some, medicine means mastering biochemistry and beta-blockers. But for most of us, such things are simply stepping stones in our quest to become the ultimate givers.”

—STELLA LUO, MD (ALUMNA)

37% of physicians in Pennsylvania graduated from Temple’s medical school.

“EVERY SCIENTIST THINKS THEIR WORK IS GOING TO BE EARTH-SHATTERING. SOMETIMES IT ACTUALLY IS.”

—STEVEN HOUSER, PHD (DIRECTOR, CARDIOVASCULAR RESEARCH CENTER)

“It is a universal truth: Patients have the right to have healthcare matters presented in a culturally sensitive way.”

—CURTIS MIYAMOTO, MD (CHAIR, RADIATION ONCOLOGY)

Break Out the Bubbly

A living fibroblast cell—at 630x magnification—effervescent with activity.

The red bubbles are coated with Ras proteins, which stimulate growth. Ras proteins traffic through the cell’s vesicle membranes (blue), which bud off the Golgi of the cell (green).

In normal growth, Ras proteins travel from the Golgi to the outer plasma membrane. Uncontrolled cell growth—and tumor formation—may be linked to abnormal patterns of Ras movement.

“Location and direction mean everything,” says Assistant Professor Lawrence E. Goldfinger, PhD, who studies Ras intracellular trafficking. “Elucidating the patterns might help us determine how to inhibit the hyperactive growth linked with cancer and other diseases,” he says.

CONFOCAL FLUORESCENCE MICROGRAPH: JEREMY G.T. WURTZEL AND LAWRENCE GOLDFINGER, PHD

Temple Health

Magazine

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