# PENN Medicine

SPRING 2014

# MICROBIOMICS:
## THE NEXT BIG THING?

**What Lies Ahead for Penn Medicine**
**From Philadelphia to the World: Medical Missions**
**Master Clinicians, Then and Now**

# The Coming of Hope

Since March, a new art installation has greeted visitors as they entered the Perelman Center for Advanced Medicine. Suspended from the center's glass atrium, *Homologous Hope* was created especially for the Basser Research Center for BRCA by Mara G. Haseltine. With its ribbon diagram form, the sculpture is meant to illustrate how a healthy cell repairs DNA that causes breast, ovarian, and pancreatic cancers. It depicts the part of the BRCA2 gene that is responsible for DNA repair. The repair occurs in three stages, as illustrated by a light show within portions of the piece.

The full-scale piece took nearly three months to create. Its features include:

- Nearly 560 pounds of carbon fiber twisted into three separate parts that together form the 15' x 6' x 12' piece
- Roughly 600 programmable LED lights
- A stainless steel ring weighing nearly 400 pounds from which the sculpture is suspended

*Homologous Hope* was installed in the Perelman Center over a period of six weeks and took four days to be lifted from the ground.

Located within the Abramson Cancer Center, the Basser Research Center for BRCA is the first comprehensive center of its kind focused on BRCA. Its mission is to use the newest research in basic and clinical sciences to advance the care of individuals living with BRCA1 and BRCA2 mutations.

In 2012, Mindy and Jon Gray, alumni of the University of Pennsylvania, gave a $25 million gift to establish the Basser Center in honor of Mindy's sister, Faith Basser, who passed away of ovarian cancer at the age of 44. Recently, the Grays c ommitted an additional $5 million gift to support research on BRCA-related pancreatic cancer and to launch a program of external grants to help advance BRCA-related research around the globe.

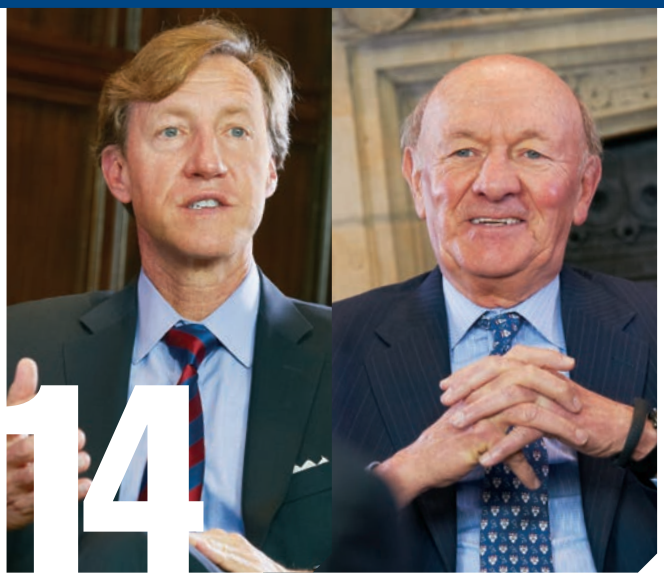
PENNMEDICINE SPRING 2014 / VOLUME XXV NUMBER 2

8

## MICROBIOMICS: THE NEXT BIG THING?

*By Lisa J. Bain*

**Researchers in the rapidly expanding research field of microbiomics have shown that the human body is home to an entire ecosystem of bacteria, viruses, fungi, and other microbes. What's more, they play an important role in regulating many physiological processes. All microbiome research is very multidisciplinary by virtue of its complexity, so Penn is an ideal place to study it.**



14

## TWO VIEWS FROM THE TOP

**The rising costs of health care. The potential of precision medicine. Shrinking federal funding for biomedical research. Innovative ways of teaching the medical curriculum. Recently, J. Larry Jameson, M.D., Ph.D., executive vice president of the University of Pennsylvania for the Health System and dean of the Perelman School of Medicine, and Ralph Muller, M.A., chief executive officer of the Health System, sat down to discuss these topics and more.**

## Departments



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22

## A LOOK BEHIND THE MASK

*By John Shea*

**An alumnus and eye surgeon combines an account of his own professional experiences – which range from the routine to the more technically and emotionally demanding – with stories of some of his heroes in the field.**

24

## ON A MISSION: PENN DOCTORS LEND THEIR TALENTS AROUND THE WORLD

*By Carole Bernstein*

**Many Penn doctors, in addition to their workload here at home, make time in their schedules and their lives to embark on medical missions. The sites vary widely: Haiti, Vietnam, Nicaragua, a hospital ship docked at an African port. The conditions they work in are often very different from those at home, and they often face challenges. But their help is needed – and very welcome.**


29

## MASTER CLINICIANS, THEN AND NOW

*By John Shea*

**A new honor recognizes a select group of clinicians throughout the institution's many clinical settings whose clinical abilities are matched by their compassion and interpersonal skills. These "ambassadors" for Penn Medicine commit to helping improve its culture of clinical excellence.**

**Penn Medicine** is published for the alumni and friends of Penn Medicine by the Office of Public Affairs.  Address all correspondence to John Shea, **Penn Medicine**, 3535 Market Street, Suite 60 Mezzanine, Philadelphia, PA 19104-3309, or call (215) 662-4802, or e-mail john.shea@uphs.upenn.edu.

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## Penn Medicine Researchers Show How Lost Sleep Leads to Lost Neurons


Most people appreciate that not getting enough sleep impairs their cognitive performance. For the chronically sleep-deprived such as shift workers, students, or truckers, a common strategy is simply to catch up on missed sleep on the weekends. But a Penn Medicine study, published this spring in *The Journal of Neuroscience*, shows evidence that chronic sleep loss may be more serious than previously thought.

Using a mouse model of chronic sleep loss, a team of researchers from Penn and Peking University have determined that extended wakefulness is linked to irreversible physical damage to – and loss of – neurons that are essential for alertness and optimal cognition. These are the locus coeruleus (LC) neurons. Sigrid Veasey, M.D., associate professor of medicine and a member of the Center for Sleep and Circadian Neurobiology at the Perelman School of Medicine, is senior author of the study.

"In general, we've always assumed full recovery of cognition following short- and long-term sleep loss," Veasey says. "But some of the research in humans has shown that attention span and several other aspects of cognition may not normalize even with three days of recovery sleep, raising the question of lasting injury in the brain. We wanted to figure out exactly whether chronic sleep loss injures neurons, whether the injury is reversible, and which neurons are involved."

Mice were examined following periods of normal rest, short wakefulness, or extended wakefulness, modeling a shift worker's typical sleep pattern. The Veasey lab found that in response to short-term sleep loss, LC neurons upregulate the sirtuin type 3 (SirT3) protein, which is important for producing mitochondrial energy and redox responses, and protect the neurons from metabolic injury. SirT3 is essential across short-term sleep loss to maintain metabolic homeostasis, but in extended wakefulness, the SirT3 response is missing. After several days of shift-worker sleep patterns, LC neurons in the mice began to display reduced SirT3 and increased cell death. In addition, the mice lost 25 percent of these neurons.

"This is the first report that sleep loss can actually result in a loss of neurons," Veasey notes. Particularly intriguing is that the findings suggest that mitochondria in LC neurons respond to sleep loss and can adapt to short-term sleep loss but not to extended wakefulness. This discovery raises the possibility that somehow increasing SirT3 levels in the mitochondria may help rescue neurons or protect them across chronic or extended loss of sleep. The study also demonstrates the importance of sleep for restoring metabolic homeostasis in mitochondria in the LC neurons and possibly other important brain areas, to ensure their optimal functioning during waking hours.

Veasey stresses that more work needs to be done to establish whether a similar phenomenon occurs in humans and to determine what durations of wakefulness place individuals at risk of neural injury. In addition, aging, diabetes, high-fat diet and sedentary lifestyle may all reduce SirT3.

The next step will be putting the SirT3 model to the test. "If we can show that we can protect the cells and wakefulness, then we're launched in the direction of a promising therapeutic target for millions of shift workers."

The team also plans to examine shift workers post-mortem for evidence of increased LC neuron loss and signs of neurodegenerative disorders such as Alzheimer's and Parkinson's. While not directly causing these diseases, Veasey notes that "injuring LC neurons due to sleep loss could potentially facilitate or accelerate neurodegeneration in individuals who already have these disorders."

*– Jessica Mikulski*

## A Pathway to . . . Hair Growth?

A molecular pathway known for its role in regulating adult stem cells has been shown to be important for the proliferation of hair follicles. But contrary to previous studies, it is not required within hair follicle stem cells for them to survive. Those are the findings of research-

ers at the Perelman School of Medicine. Their study in *Cell Stem Cell* identifies a molecular pathway that can be activated to prompt the hair growth of dormant hair follicles – or, on the other hand, to block the growth of unwanted hair.

The team examined the functions of Wnt proteins, which are small molecular messengers that convey information between cells and activate signaling via the intracellular molecule ß-catenin. By disrupting Wnt signaling in an animal model with an inhibitor Dkk1, the team was able to prevent hair growth. At the same time, stem cells were still maintained within the dormant hair follicles. When Dkk1 was removed, the Wnt/ß-catenin pathway resumed normal function, the stem cells were activated, and hair growth was restored.

The researchers also unexpectedly found that the Wnt/ß-catenin pathway is normally active in non-hairy regions, such as on the palms of hands, the soles of feet, and the tongue, as well as between hair follicles on the surface of the skin. This finding is consistent with previous results showing that removing ß-catenin prevents the growth of skin tumors.

According to Sarah Millar, Ph.D., a professor in the departments of Dermatology and of Cell and Developmental Biology, "While more research is needed to improve our understanding of this pathway, our results suggest that therapeutics capable of decreasing levels of Wnt/ß-catenin signaling in the skin could potentially be used to block growth of unwanted hair and/or to treat certain skin tumors." She added that if they are delivered in a limited, safe, and controlled way, the agents that activate Wnt signaling "might be used to promote hair growth in dormant hair follicles in conditions such as male pattern baldness."

The research team includes co-corresponding author Edward E. Morrisey, Ph.D., professor of medicine, along with co-first authors Yeon Sook Choi and Yuhang Zhang, and Mingang Xu, Mayumi Ito, Thomas Andl, and George Cotsarelis from Penn's Department of Dermatology; Tien Peng and Zheng Cio from Penn Cardiology; and colleagues from the University of Cincinnati, Cincinnati Children's Hospital Medical Center, Mount Sinai Hospital in Toronto, and Sloan Kettering Institute in New York.

The research was funded by the National Institute of Arthritis and Musculoskeletal and Skin Diseases.

*– Kim Menard*

## Honors & Awards

**Alexander J. Brucker, M.D.**, professor of ophthalmology and a retina specialist, delivered the 2013 Gian Battista Bietti SOI Medal Lecture at the 11th International Congress of the Società Oftalmologica Italiana in Milan, Italy. He has been consistently recognized in *Philadelphia* magazine's Top Docs issue and was included in Castle Connolly's *America's Top Doctors*.

**Jeffrey A. Drebin, M.D., Ph.D.**, chair of the Department of Surgery and the John Rhea Barton Professor of Surgery, was elected the 2014 president of the Philadelphia Academy of Surgery, the oldest surgical society in the United States. Drebin's research has contributed significantly to the understanding of the genetic origins of cancer. His classic work with monoclonal antibodies directed against the HER2/neu protein provided the scientific foundation for the evolution of targeted therapeutics for cancer and led to the development of the first generation of targeted monoclonal antibody drugs for the treatment of breast cancer. He is currently the co-principal investigator on a $22 million dollar clinical and translational "dream team" award from the Stand Up to Cancer Foundation for innovative studies in pancreatic cancer. Last

## Another Top 5 Showing

For the 17th year in a row, the Perelman School of Medicine at the University of Pennsylvania has ranked among the top five research-oriented medical schools in the United States. According to the annual survey by *U.S. News & World Report*, Penn's school is ranked #4. It was tied with the University of California at San Francisco. The three highest-ranked medical schools were at Harvard University, Stanford University, and Johns Hopkins University.

The Perelman School of Medicine also ranked among the nation's top medical schools in four areas of specialty training, including a first-place ranking in pediatrics, drug/alcohol abuse (#4), women's health (#5), and internal medicine (#5). In addition, the School of Medicine ranked #13 among schools focused on primary care.

"The *U.S. News & World Report* rankings underscore the commitment by the Perelman School of Medicine faculty and staff to provide an exceptional educational environment for our students as they prepare for challenging careers in medicine and science," said J. Larry Jameson, M.D., Ph.D., dean of the Perelman School of Medicine and executive vice president of the University of Pennsylvania for the Health System.

The annual medical school rankings are based on statistical indicators that measure the quality of a school's faculty, research, and students. Information is obtained through surveys of program directors, academics, and professionals. Criteria used in the rankings include peer assessment surveys, research activity, grade-point averages, MCAT scores, and NIH funding.

## Hugs and High Fives

After some initial tension and uncertainty earlier this spring, members of this year's graduating class celebrated with classmates, families, and friends on Match Day. That was when they learned – from the National Residency Match Program – where they'd be doing their residency training.

This year, 161 Penn medical students (82 men and 79 women) took part in the program. Fifty-two matched in Pennsylvania, and 49 will train at Penn and CHOP. The top three specialties are: internal medicine, emergency medicine, and pediatrics.

year, Drebin was elected to the Institute of Medicine of the National Academy of Sciences.

**Chris Feudtner, M.D. '95, Ph.D., M.P.H.**, associate professor of pediatrics in the Perelman School of Medicine and the Steven D. Handler Endowed Chair of Medical Ethics at the Children's Hospital of Philadelphia, received the 2014 Hastings Center Cunniff-Dixon Physician Award in the mid-career category. The awards recognize five physicians who have distinguished themselves in advancing the practice of palliative care and have shown model exemplary skill and compassion at the bedside.

In nominating Feudtner for the award, Ezekiel Emanuel, M.D., Ph.D., the Diane v.S. Levy and Robert M. Levy University Professor and chair of the Department of Medical Ethics and Health Policy at the Perelman School of Medicine, wrote that Feudtner's "plural excellences – extraordinary success as a nationally recognized researcher and ethicist combined with exceptional face-to-face skills – make him, in my mind, the epitome of the kind of doctor all worried parents would want for their sick children and the embodiment of the clinical leader needed by complex health-care organizations serving sick children and their families."

Feudtner is also director of research for the Pediatric Advanced Care Team at CHOP.

**Garret FitzGerald, M.D.**, chair of the Department of Pharmacology and director of the Institute for Translational Medicine and Therapeutics, was the 2013 recipient of the Jay and Jeanine Schottenstein Prize in Cardiovascular Sciences, presented by the Wexner Medical Center at Ohio State University. The prize is given to an international leader in the clinical sciences of cardiovascular medicine, cardiothoracic surgery, or the basic sciences of molecular or cellular cardiology. FitzGerald's research takes an integrative approach to elucidating the mechanisms of drug action, drawing on work in cells, model organisms, and humans. With the gift, the Schottenstein Laureate receives an honorarium of at least $100,000.

**Jing Guo, Ph.D.**, now a postdoctoral researcher in the Center for Neurodegenerative Disease Research, received the 2013-2014 Doctoral Dissertation Award in Health Sciences from the Northeastern Association of Graduate Schools. Each year, there can be only one nominee from each member institution. Guo, who had been in Penn's Neuroscience Graduate Group, completed her dissertation under the supervision of Virginia M.-Y. Lee, Ph.D., the John H. Ware 3rd Professor in Alzheimer's Research in the Department of Pathology and Laboratory Medicine and director of the Center for Neurodegenerative Disease Research. According to Lee, "Jing has done an outstanding job in a completely uncharted area, breaking new ground in providing novel insights on the mechanism of progression as well as clinical diversities in Alzheimer's and Parkinson's disease."

Guo was also the recipient of the 2013 Flexner Award, for the Best Neuroscience Dissertation, given annually by Penn's Mahoney Institute for Neurosciences.

**Stephen M. Hahn, M.D.**, chair of the Department of Radiation Oncology, was named among the ten 2013 Fellows of the American Society for Radiation Oncology. ASTRO's Fellows Program honors radiation oncology leaders who have made

substantial contributions to the field in the areas of research, education, patient care or service, and leadership. Hahn's research and clinical care concentrate on cancers of the lung and genitourinary system, as well as radiation biology and photodynamic therapy. During his tenure as chair, he has overseen the opening of the Roberts Proton Therapy Center, the

world's largest and most advanced center integrating both proton beam radiation therapy and conventional radiation.

**Katherine A. High, M.D.**, the William H. Bennett Professor of Pediatrics at the Perelman School of Medicine and director of the Center for Cellular and Molecular Therapeutics at The Children's Hospital of Philadelphia, received the 2013 E. Donnall Thomas Prize from the American Society of Hematology. She was honored for her trailblazing scientific and clinical research on hemophilia. Over the past two decades, High has developed novel approaches to correcting hemophilia with gene therapy in studies. Her studies continue today in a current clinical trial for hemophilia funded by the National Institutes of Health.

In presenting the Prize, the society's president, Janis L. Abkowitz, M.D., said, "Through her countless discoveries, Dr. High has transformed the notion of utilizing genetically engineered mechanisms for treatment of incurable inherited disorders from a distant vision to reality."

High is also a Howard Hughes Medical Institute Investigator and former president of the American Society of Gene and Cell Therapy.

**John D. Lambris, Ph.D.**, the Dr. Ralph and Sallie Weaver Professor of Research Medicine in the Department of Pathology and Laboratory Medicine, received an honorary doctorate from Sweden's Uppsala University. He conducts research on the complement system and is the editor of several books on the subject. Lambris's laboratory was among the first to map the critical sites on the complement component 3 (C3) responsible for its diverse functions and also to define its complex binding dynamics to various C3 natural ligands, viral proteins, complement receptors, and regulators. His laboratory contributed to the development of complement-based anti-inflammatory therapeutics through the discovery of the first small-size complement inhibitor, termed Compstatin. In 2006, Lambris received an honorary doctorate from the University of Kalmar, also in Sweden.

**Daniel J. Powell Jr., Ph.D.**, research associate professor in the Department of Pathology & Laboratory Medicine and a member of the Penn Ovarian Cancer Research Center, was selected for a 2014 Outstanding New Investigator Award by the American Society of Gene & Cell Therapy. He was recognized for significant contributions to the field. The Powell lab is developing innovative immunotherapy strategies built upon clinical observations and studies in basic T cell biology. Adoptive T cell therapy using naturally occurring tumor infiltrating lymphocytes (TILs) or peripheral blood T cells that have been genetically modified to express a chimeric antigen receptor (CAR) can mediate comprehensive cancer elimination in patients, provided that highly avid, tumor-antigen-specific T cells with the ability to proliferate and persist after infusion can be identified.

For the past six years, the Powell Lab, their colleagues, and friends have joined to participate in the annual Sandy Sprint Run/Walk, hosted by the Sandy Rollman Ovarian Cancer Foundation. The event attempts to spread the word about its mission and raise funds to advance research. This year's event was in April at the Philadelphia Museum of Art. For fifth time, Powell's team of nearly 50 members won the overall team event, helping raise close to $250,000, part of which will be for grants awarded to the Powell Lab and various other labs in the Ovarian Cancer Research Center.

**Jennifer Prah Ruger, Ph.D., M.Sc., M.A., M.S.L.**, associate professor in the Department of Medical Ethics & Health Policy and senior fellow at the Leonard Davis Institute of Health Economics, has been elected a member of the Council on Foreign Relations. The nonpartisan organi-

zation is dedicated to providing resources that help members, government agencies, and other interested citizens better understand the world and the choices in foreign policy facing the United States and other countries.

Ruger received a doctoral degree from Harvard University. After finishing a postdoctoral fellowship at Harvard's Center for Population and Development Studies, she worked at the World Health Organization and the World Bank.

A member of the Institute of Medicine's Board on Global Health, Ruger was the recipient of the Greenwall Faculty Scholar Award in Bioethics and a Donaghue Investigator Award in the ethics and economics of health disparities. In 2011, she received a John Simon Guggenheim Fellowship, which allowed her to write her forthcoming book, "Global Health Justice and Governance" (Oxford University Press).

## The Academy Welcomes Three More

Three researchers from the Perelman School of Medicine have been elected members of the American Academy of Arts and Sciences, one of the nation's most prestigious honorary societies and a leading center for independent policy research.

The new honorees, who join 20 other Penn Medicine experts previously elected, are:

**Garret A. FitzGerald, M.D.**, the Robert L. McNeil Jr. Professor of Translational Medicine and Therapeutics, chair of the Department of Pharmacology, and director of the Institute for Translational Medicine and Therapeutics.

**Carl H. June, M.D.**, the Richard W. Vague Professor in Immunotherapy in the Department of Pathology and Laboratory Medicine and director of translational research in the Abramson Cancer Center.

**M. Celeste Simon, Ph.D.**, a professor of Cell and Developmental Biology, scientific director and investigator for the Abramson Family Cancer Research Institute, and an investigator of the Howard Hughes Medical Institute.

**Nancy Bonini, Ph.D.**, professor of biology in Penn's School of Arts and Sciences and an investigator of the Howard Hughes Medical Institute, is also among the Penn faculty elected to the Academy.

Among the Academy's Fellows are more than 250 Nobel laureates and 60 Pulitzer Prize winners.

## Serving the Society

**Susan Mandel, M.D., M.P.H.**, professor of medicine and of radiology and associate chief of the Division of Endocrinology, Diabetes, and Metabolism, was elected vice president, Physician-in-Practice, of The Endocrine Society. In addition, **Mitchell Lazar, M.D., Ph.D.**, the Sylvan Eisman Professor of Medicine, chief of the Division of Endocrinology, Diabetes, and Metabolism, and director of the Institute for Diabetes, Obesity, and Metabolism, was elected to serve as an at-large council member of the Society. They will collaborate with other newly elected officers and council members to lead the world's oldest, largest, and most active organization devoted to research on hormones and the clinical practice of endocrinology.

Mandel will serve a three-year term. Active in the Society for more than two decades, she has received numerous honors, including the Society's Distinguished Educator Award.

Lazar will serve a three-year term. Since joining the Society in 1989, Lazar has provided editorial leadership to numerous journals, including *Endocrine Reviews, Endocrinology*, and *Molecular Endocrinology*. Among his many honors, Lazar has most recently been recognized with the Society's Gerald D. Aurbach Lecture Award.

## Transitions

### A Change of Leaders at the Center for Studies of Addiction

**Henry R. Kranzler, M.D.**, professor of psychiatry, has been named director of Penn's Center for Studies of Addiction. He came to Penn Medicine in 2010 after a lengthy career at the University of Connecticut, where he was an associate scientific director of the Alcohol Research Center, program director of the Lowell P. Weicker General Clinical Research Center, and associate dean for Clinical and Translational Research.

Since 1987, Kranzler's research has been funded by the National Institute on Alcohol Abuse and Alcoholism and National Institute on Drug Abuse. His contributions to the field of alcohol research include advancing clinical trials methodology as it relates to pharmacological treatment, the identification of interactive effects of serotonergic medications with alcoholism subtypes, the use of a targeted approach to naltrexone treatment of heavy drinkers, and the development of long-acting naltrexone as a treatment option. In addition, his work has contributed to identifying or characterizing specific genes that influence the risk for dependence on alcohol, nicotine, cocaine, and opioids.

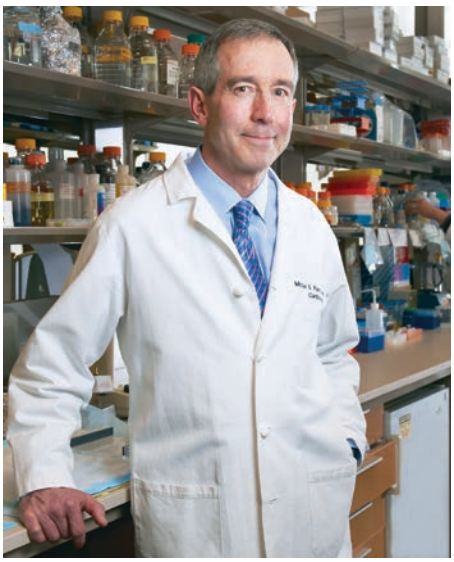
Kranzler received his medical degree from the Robert Wood Johnson Medical School and completed a psychiatric residency and a fellowship in alcohol research at the University of Connecticut.

**Charles P. O'Brien, M.D., Ph.D.**, the Kenneth E. Appel Professor of Psychiatry, is the founding director of the Center for Studies of Addiction. Under his leadership, the center, which began at the Philadelphia VA Medical Center and expanded to its current prominent position at Penn, has served as a national resource for the empirical validation of assessment and treatment methods and training in these methods. O'Brien will continue his funded research and will serve as a collaborator and mentor to his many colleagues in the Center.

In October, while serving as honorary president during the 2013 European and

International Congress on Addiction, Hepatitis, AIDS in Biarritz, France, O'Brien was named a Chevalier [knight] of France's National Order of the Legion of Honor. O'Brien's discoveries over the past 30 years have helped form the standard of care in addiction treatment throughout the world. O'Brien received two other international awards in 2013 for discoveries in the treatment of alcoholism: the Jellinek Award in Canada and the Isaacson Award in Japan.

**Michael S. Parmacek, M.D.**, the Herbert C. Rorer Professor of Medical Sciences, was appointed chair of the medical school's largest department, the Department of Medicine. He had been serving as interim chair. Parmacek came to Penn as chief of the Division of Cardiovascular Medicine in 1998, following successful roles at the University of Michigan and the University of Chicago. He is also the



founding director of the Penn Cardiovascular Institute. A nationally recognized expert in cardiovascular biology and medicine, he has distinguished himself at Penn with significant research advances and has built one of the nation's leading cardiovascular medicine divisions. In addition, he has been named to several important clinical and administrative leadership roles, including the advisory council of the National Heart, Blood, and Lung Institute.

Over the course of his career, Parmacek has made many seminal discoveries that have had an impact on the understanding the molecular and genetic basis of congenital heart disease, atherosclerosis, aortic aneurysm and dissection and heart failure. He has published a substantial body of scholarly work in high-impact journals. Named an Established Investigator by the American Heart Association (AHA), he was elected to the American Society of Clinical Investigation and the Association of American Physicians. He has been president of the Association of Professors of Cardiology and is a Fellow of the AHA and of the American College of Cardiology.

Parmacek earned his medical degree from Northwestern University. He completed residency training in internal medicine at the University of Michigan and did a fellowship in cardiovascular disease at Northwestern University. Following his clinical training, Parmacek was a postdoctoral fellow in molecular cardiology at the Howard Hughes Medical Institute at the University of Michigan.

**Daniel J. Rader, M.D.**, has been named chair of the Department of Genetics. A widely recognized international leader in the human genetics of lipoprotein biology and cardiovascular disease, he has been a faculty member at Penn for 20 years. Currently he is the Edward S. Cooper, M.D./Norman Roosevelt and Elizabeth Meriwether McLure Professor of Medicine and chief of the department's Division of Translational Medicine and Human Genetics.

In addition, Rader serves as associate director of the Institute for Translational Medicine and Therapeutics. He also co-directs the new Penn Medicine BioBank, an integrated, centralized resource for consenting, collecting, processing, and storing

DNA, plasma/serum, and tissue for human genetics and translational research.

Rader's lab discovered and characterized the enzyme endothelial lipase, demonstrated its effects on high density lipoproteins (HDL) in mice, and then found that loss-of-function mutations in the gene cause high levels of HDL in humans. He was also involved in identifying the molecular defect in a rare genetic disorder causing very low levels of low-density lipoproteins (LDL), which spurred the development of inhibitors of this protein to reduce levels of LDL. Indeed, when one such drug was abandoned by a pharmaceutical firm, he went on to oversee its development for the orphan disease homozygous familial hypercholesterolemia, characterized by extremely high levels of LDL and heart disease in childhood.

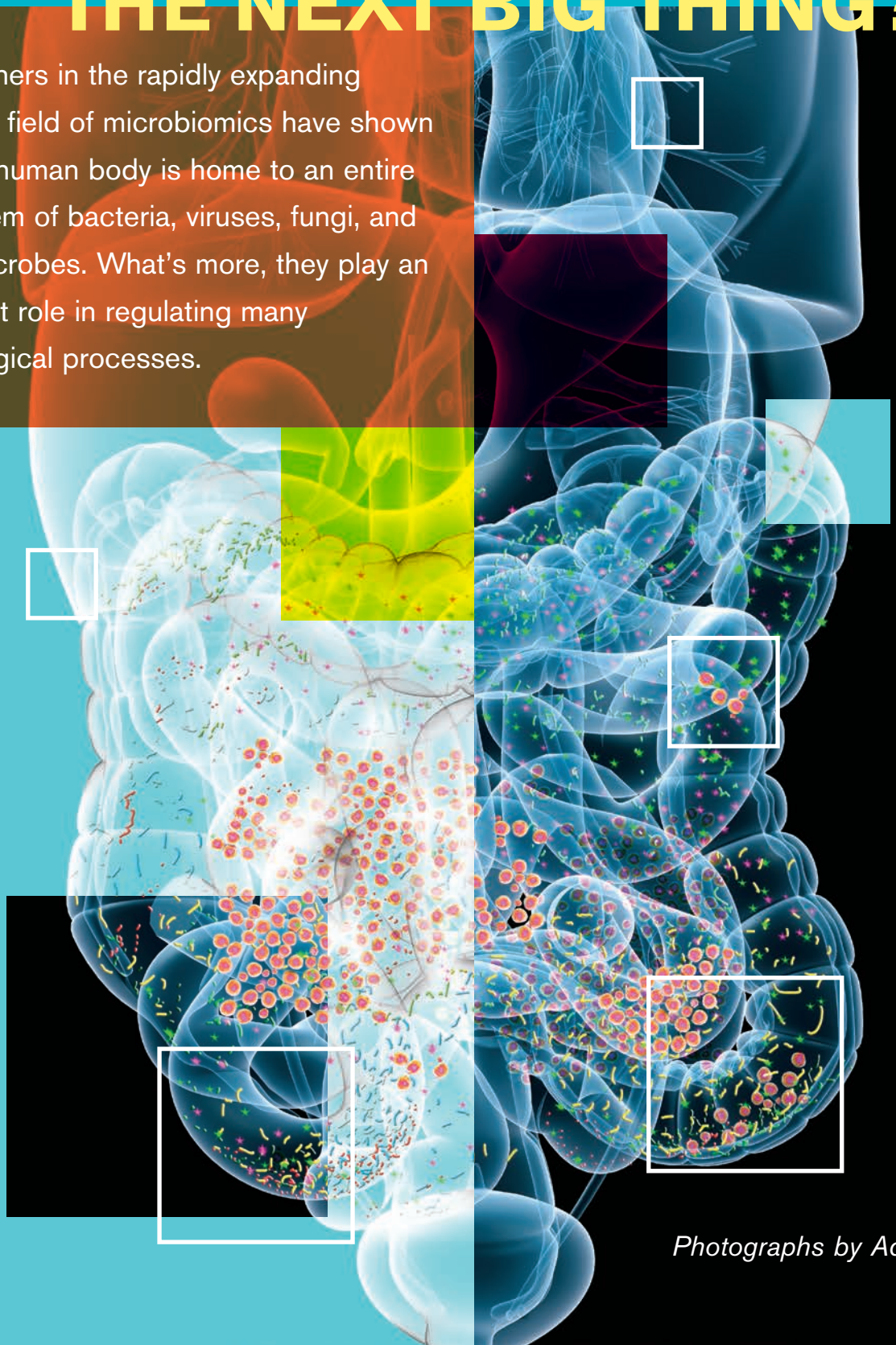
Rader has received numerous awards as a physician-scientist, including the Burroughs Wellcome Fund Clinical Scientist Award in Translational Research and the Doris Duke Charitable Foundation Distinguished Clinical Investigator Award. He has been elected to the American Society of Clinical Investigation and to the Association of American Physicians. In 2011, he was elected to the Institute of Medicine.

He has also been honored with the William Osler Patient-Oriented Research Award, one of the Perelman School's Awards of Excellence. ■

# MICROBIOMICS: THE NEXT BIG THING?

*By Lisa J. Bain*

Researchers in the rapidly expanding research field of microbiomics have shown that the human body is home to an entire ecosystem of bacteria, viruses, fungi, and other microbes. What's more, they play an important role in regulating many physiological processes.



*Photographs by Addison Geary*

Although it may sound weird, unappealing, even disgusting, fecal transplantation has piqued the interest of gastroenterologists and infectious disease specialists around the world. Meanwhile, patients suffering from severe diarrhea are demanding the procedure and the FDA has weighed in with restrictions on how this "unapproved therapy" can be delivered.

Why all the excitement? Fecal transplantation is not new: Ben Eiseman, a surgeon at the University of Colorado, described it more than 50 years ago to treat a life-threatening diarrheal disease caused by a bacterium called *pseudomonas enterocolitis*. But until a few years ago, Eiseman's unconventional treatment was largely dismissed by the medical community, at least in the United States (it has been much more widely used in Australia). Then, in 2010, The New York Times ran a story about a doctor in Minnesota using fecal transplantation to successfully treat a patient with a severe infection caused by a bacterium called *Clostridium difficile,* or *"C. diff."* And this year, a randomized controlled trial of the treatment was stopped early when an interim review of the data showed not only that it worked, but that it was far superior to the standard treatment with powerful antibiotics. Fecal transplantation, also known as fecal microbiota transplantation (FMT) or bacteriotherapy, had arrived.

The acceptance of FMT for the treatment of diarrheal disease caused by *C. diff* exemplifies a paradigm shift in how many diseases are viewed, as well as a translational application of the science of microbiomics – a rapidly expanding research field that *Science* magazine dubbed "The Germ Theory of Everything." Microbiomics researchers have shown that the human body is home to an entire ecosystem of bacteria, viruses, fungi, and other microbes, and that these bugs play important roles in keeping us healthy and regulating all sorts of physiologic processes. When the gut microbiota (the population of microbes) is disrupted, for example by overuse of antibiotics, the consequences can be lethal, as is the case with *C. diff*. It infects as many as 3 million people worldwide each year and in recent years these infections have become less and less responsive to antibiotic treatment. In the U.S. alone, medical costs to treat *C. diff* infections exceed $1 billion per year, and some 14,000 Americans die from the infections.

## Big Science and the Microbiome

Following on the heels of the massive Human Genome Project, which identified about 22,000 protein-coding genes in humans, the National Institutes of Health launched the Human Microbiome Project (HMP) in 2007 to map the collective genomes of the human microbiota. HMP researchers at nearly 80 institutions, including Penn, analyzed tissue from 242 healthy individuals, sampling 15 body sites in men and 18 in women. The findings made the genome project look modest in comparison: the human gut microbiome alone is home to 100 trillion bacteria – ten times the number of cells in the human body – with somewhere around 8 million protein-coding genes, 360 times as many as in the human genome.

The same gene sequencing technology that fueled the genome project also made mapping the microbiome possible. "You literally can get more than a hundred billion bases of sequence information from a single instrument run these days," says Frederic Bushman, Ph.D., professor of microbiology. "It's astounding. We're analyzing a dataset of over a trillion bases of sequence information. When I was a student, it would be a few days' work to get a few reads of a hundred bases each. Today, I have a little machine in my lab that will do a hundred thousand sequence reads of about 250 bases each in a day." One of the changes the new technology has brought about in Bushman's research is the makeup of his laboratory personnel: "We now have four programmers in the lab and lots of collaborating statisticians to work with that kind of data. That's all new in the last ten years."

Indeed, gene sequencing has brought about a transformation in the entire field of microbiology, as it has in many other areas of biomedical research. David Artis, Ph.D., associate

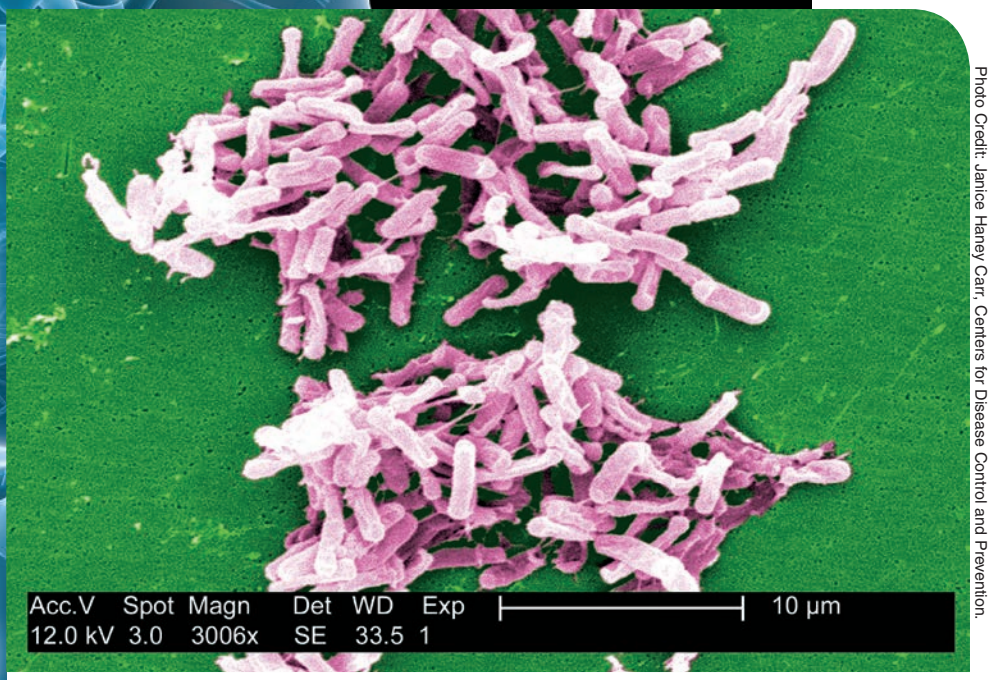



Photo Credit: Janice Haney Carr, Centers for Disease Control and Prevention.

Micrograph depicting Gram-positive *C. difficile* bacteria from a stool sample culture.

professor of microbiology, says that when he completed his training in immunology back in the mid-'90s, he was advised not to be concerned about the microbiota or what was then referred to as the commensal bacteria (bacteria that live harmoniously with the host) that colonized the intestine. "We were told, 'don't worry about it – it's too complicated, you can't culture the bugs, and you can't phenotype what they are.' What has been an incredible journey for us has been the rapidity with which we've been able to engage and interrogate the role of the microbiome in the last decade or so."

Artis explains that before the advent of gene sequencing, the only way to study bacteria was to grow them in the laboratory, but perhaps as many as 90 percent of the commensal bacteria in the human intestine cannot be cultured. "We took a quantum leap from those culture-based assays to sequencing-based approaches," he says. With Bushman as one of the leaders in this effort, these new technologies have enabled scientists to profile complex microbial communities and map the evolutionary relationships of diverse species of commensal bacteria. According to Artis, "What we've learned is that disorganization or change in the composition of the commensal bacteria can be associated with many human diseases, from inflammatory bowel disease to asthma, to arthritis, to multiple sclerosis." One of the fundamental questions has been: are those changes in bacterial diversity a consequence of the disease, or could they have perhaps participated at some level in the development of these diseases?

Gene sequencing is not the only new tool that has fueled progress in answering some of these questions about the microbiome. "In addition to profiling microbial communities in human health and disease, we have been able to adopt animal model systems – flies, fish, and mice – where we can deliberately manipulate the diversity of commensal bacteria and ask if that influences the immune system, the physiology of the heart, liver function, the enteric nervous system, or whatever organ system that we might be interested in," explains Artis. He directs the Penn Gnotobiotic Mouse Facility, where mice that have never been exposed to live microbes are housed in germ-free conditions, enabling scientists to introduce a single organism or group of organisms to the mice to study the colonization of different body sites and how it affects disease resistance or susceptibility. "We're finding remarkable effects indicating that changes you see in human diseases may not just be a consequence of the disease; the microbes may actually participate in the development or progression of these diseases," Artis continues. He notes that Penn's germ-free mouse facility was one of the first of its kind in the United States. Germ-free mice, for example, have been used at Penn to study the role of commensal bacteria in the development of the immune system and other tissue systems, as well as the role of specific organisms in a range of diseases that affect organs from the skin to the gut.

## "All Diseases Begin in the Gut"

Back around 460 B.C., Hippocrates himself identified the human gut as the gateway to the rest of the body, yet 25 centuries later, scientists are still only beginning to understand what commensal bacteria do in the healthy human gut, much less in a disease state. Evidence suggests that this ecosystem within our bodies plays an important role in keeping us healthy by producing vitamins, enzymes, and other compounds that help us digest and metabolize food and regulate the immune system. In addition, many of the advances in hygiene over the past decades – including improved refrigeration, sanitation, vaccination, increased antibiotic use, and food processing – are thought to have upset the mutual balance between the microbes and their human hosts.

Bushman, an internationally recognized expert on the microbiome, is working with Gary Wu, M.D., and James Lewis, M.D., M.S.C.E, both professors in

gastroenterology, on one of 15 demonstration projects for the Human Microbiome Project. They are examining how diet influences the gut microbiome in people with Crohn's disease, a particularly insidious type of intestinal bowel disease (IBD). Like all microbiome research, this work is very multidisciplinary by virtue of its complexity, so Penn is an ideal place to study it: Wu investigates the microbiome in mouse models; Lewis does the human translational work; and Bushman performs the detailed gene sequencing that produces the reams and reams of data to be analyzed by bioinformaticians and computational biologists.

The HMP project followed earlier studies in which the Penn team assessed the effect of diet on the gut microbiome. The project comprised an observational component, where the microbiomes from 98 healthy volunteers were analyzed in relation to their diets as reported on a questionnaire. The second component compared two dietary interventions – high fat, low fiber vs. low fat, high fiber – in 10 volunteers sequestered for 10 days at Penn's Clinical Trial Research Center.

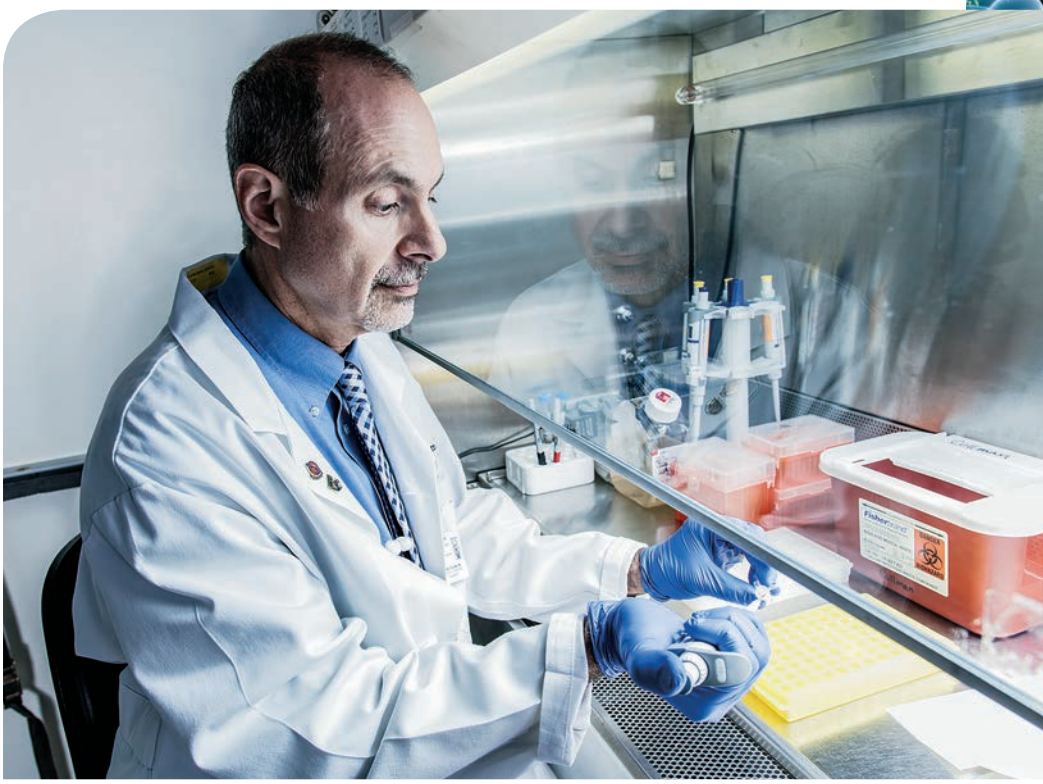
As Wu puts it, "We found a couple of interesting things. First, there was a significant impact of a change of diet on the gut microbiome within 24 hours." They also found that individuals change in different ways, and that even if they are forced to eat the same thing, the composition of the microbiome does not converge. "Our hypothesis going into the study was that the intersubject variability was in part due to the fact that we are all eating different things. But we didn't observe that at all. Short-term diet is not the explanation for why people have different compositions of the microbiota." But the observation that diet affects the human microbiome led the HMP to examine the impact on the microbiome of defined formula diets, which are used as therapy for IBD.

"We got into this because we were particularly interested in inflammatory bowel disease, where we know that for children in Europe, a nutrition-based therapy is actually one of the first-line treatments for Crohn's disease," said Lewis. "It's been known for decades that this approach worked, but nobody knew how." Known as enteral therapy, the procedure involves delivering a defined formula diet through a naso-gastric tube. It is used very little use in the United States, with the possible exception of the Children's Hospital of Philadelphia.

One reason for the limited use of these diets, as Wu points out, is that they are unpalatable. "You can't really drink them, but even if you could – and there are some palatable forms of the diet – it's very difficult to be compliant with just drinking those diets and not eating anything else."

Lewis, Wu, and Bushman started a collaboration with Robert N. Baldassano, M.D., director of the Center for Pediatric Inflammatory Bowel Disease at CHOP, and the other members of his team, as a unique opportunity to understand how nutritional therapy works. "One of our hypotheses has always been that it had an impact on the gut microbiome," says Lewis. The researchers designed a study that compared the gut microbiome in children receiving enteral therapy to those receiving a completely different but often-used type of therapy that suppresses the immune system with injections of monoclonal antibodies against a protein called tumor necrosis factor (TNF). Anti-TNF therapy is highly effective as a treatment for Crohn's disease but is associated with an increased risk of infection. The phase of the study for collecting data is complete; however, results are not yet available.

"The question is, 'What's the mechanism?' and that's what we're trying to find out," says Wu. "We don't know if it's the bacteria, or what's responsible. We just know that diet does influence bacteria, and we know that bacteria are important



Ronald Collman, M.D., became interested in the microbiome as a means to better understand how HIV triggers lung complications in infected people.

Frederic Bushman, Ph.D., James Lewis, M.D., M.S.C.E., and Gary Wu, M.D., are examining how diet influences the gut microbiome in people with Crohn's disease.

for the development of IBD. And we know that the composition of the microbiota is abnormal in patients with IBD."

One way that the gut microbiome may influence the development of intestinal bowel disease is through the immune system. "A significant portion of our total immune system is associated with the gastrointestinal tract, so it's an interaction between commensal microbes and the mammalian immune system that plays a critical role in balancing whether there is a state of health or a state of disease in the GI tract," says Gregory Sonnenberg, Ph.D., research associate in the Division of Gastroenterology and the Institute for Immunology. And it's not only the gut that is affected, he continues. "What's going on in the gut also plays a key role in the health of the cardiovascular system, the liver, spleen, central nervous system, and other body systems." Sonnenberg's lab, in collaboration with the Artis lab, is studying how balance is maintained between commensal bacteria and the immune system. When this balance is disrupted, notes Sonnenberg, the immune system attacks commensal bacteria with an inflammatory response that may underlie many chronic diseases such as IBD, diabetes, cancer, and cardiovascular disease. His lab recently identified a previously unrecognized innate immune cell that appears to play a central role in regulating the balance between commensal bacteria and the host. He believes that a better understanding of how this cell functions could lead to new therapies for chronic diseases.

## Beyond bacteria in the gut

Bacteria are not, of course, the only commensal organisms in the human gut. Viruses, fungi, and archaea (a distinct type of microorganism similar in some ways to bacteria) also inhabit the intestinal ecosystem. Bushman is especially interested in studying the predators that eat gut bacteria – a group of viruses called bacteriophage. Bacteriophage (or "phage") are perhaps the most abundant organisms on the planet, far exceeding the number of bacteria. While humans carry around huge and diverse populations of bacteria in their guts, the number and diversity of gut bacteriophage particles is potentially even greater. Researchers like Bushman are just beginning to clarify the importance of phage in human disease. They are known to carry genes for toxins and antibiotics – and probably many other important genes involved in physiological processes, including metabolism. And because they move easily between different strains of bacteria, they are likely to have an enormous influence on the composition of the microbiota as well as the pathogenicity of various organisms.

In addition, it's not just the gut microbiome that is important in human disease. Microbes colonize every barrier surface in the body. Even the lung, which was thought to be a sterile environment in healthy people, harbors low levels of bacteria, according to Ronald Collman, M.D. Collman, professor of medicine and co-director of the Penn Center for AIDS Research, became interested in the microbiome as a means of better understanding how HIV triggers lung complications in infected people. New technologies developed for studying the gut microbiome enabled Collman and colleagues to ask whether the immunodeficiency in AIDS patients may lead to changes in bacterial or fungal populations that could contribute to lung disease. But to answer these questions, the researchers first had to develop another new set of sampling and bioanalytic techniques to ensure that the gene sequences being analyzed came from the lung and not from cross-contamination from the upper respiratory tract or reagents.

"These techniques enabled us to open up this set of questions and apply it not only to HIV infection but also the impact of bacteria in lung transplantation," says Collman. "And we're also using it to look for potential novel pathogens in diseases of unknown origin," such as sarcoidosis, an inflammatory disease that can affect almost any organ but most commonly the lungs. Although research on the lung microbiome lags far behind that of the gut microbiome, the field is evolving quickly. As he says, "There's a growing sense that even in diseases such as asthma, there may be changes in the microbiome with consequences for patients, but we aren't there yet in terms of an overarching new vision."

Studies of the skin microbiome also lag behind the gut but are beginning to catch up, according to Elizabeth Grice, Ph.D., assistant professor of dermatology.

"I think people are beginning to realize that the microbiome may be involved in a lot of different disease processes," she says. "There is an increased understanding in our field that the diversity of what is on the skin is much greater than we ever would have thought. And with that comes a realization that perhaps even those diseases that do not have overt infectious types of pathologies may, in part, be modulated, triggered, or influenced by the microbiome."

For example, Grice recently showed, in collaboration with John Lambris, Ph.D., the Dr. Ralph and Allie Weaver Professor of Research Medicine in the Department of Pathology and Laboratory Medicine, that the skin microbiome is regulated in part by the complement system, an evolutionarily ancient part of the immune system that works with antibodies to destroy bacteria. The proteins that make up the complement cascade have many other functions as well, including inducing inflammation. Because complement activation is known to be involved in several different diseases of the skin, such as psoriasis, a better understanding of the relationship between the skin microbiome and complement may lead to new therapeutic strategies to combat these diseases.

Grice envisions changes in how skin diseases are treated to emerge from this research. "Can we transplant a skin microbiome in the same way that they're doing fecal microbiome? To me, that would be much less disgusting and easier. It's very real in the future that those types of things will be part of our arsenal."

## The Germ Theory of Everything?

The popular press has embraced the microbiome in a big way, with prominent features in *The New York Times, The New Yorker, The Economist, Forbes,* and *Mother Jones*, among others. Pharmaceutical and biotech companies are also climbing aboard the bandwagon. So was *Science* magazine right when it suggested that "the microbiomic theory of life" may be true? Changes in the microbiome have been linked not only to obesity and many of the major diseases of humankind – heart disease, diabetes, and cancer – but also to autoimmune diseases and complex brain diseases such as Alzheimer's and autism.

"In a fairly short space of time, there has really been a revolution in biomedical research, encompassing not just the inflammatory and metabolic disease, but cancer and even behavioral diseases," says Artis. "We have to go beyond identifying that organism A regulates processes B, C, and D, or these groups of organisms are associated and can cause this disease. I think the challenge of molecular medicine is to define the molecules that control these relationships. That knowledge is going to allow us to develop drugs or intervention strategies that will allow us to either mimic a healthy microbiome or limit the signals being generated by an unhealthy microbiome. And I think that is where the field is shifting."

In Collman's view, Penn is ideally situated to lead this new field. "This is a really unique place in that we have great interactions and collaborations between clinical/translational microbiologists like me, and more basic molecular/computational microbiologists like Rick Bushman. It's a very synergistic collaboration."

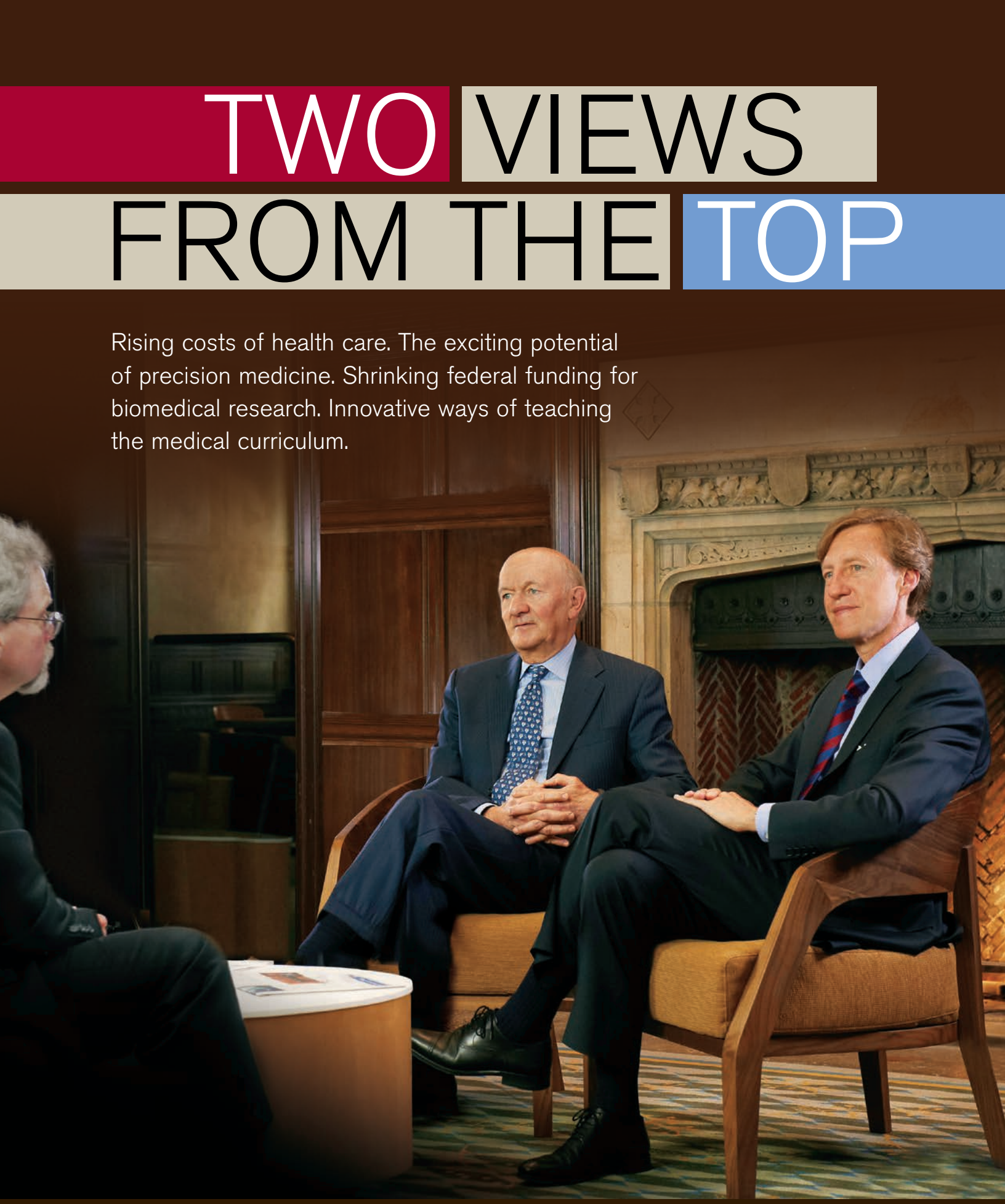
That view is shared by Glen Gaulton, Ph.D., executive vice dean and chief scientific officer at the School of Medicine. He notes that Penn scientists are ideally positioned to develop a better mechanistic understanding of the microbiome and to tie observations about different bacterial populations back to what is happening in patients. "We have the ability to do that because we are so closely linked between researchers in the school and physicians who interact with patients in the hospital and outpatient clinics," he said. "We're working now to determine how this key initiative might benefit from formation of a center that would coalesce these teams and strategically guide project development."

As Bushman puts it, "I think the sky's the limit." There are technical challenges to solve, "but it gets better with each passing year," with increased knowledge, better methods, and more rigorous statistics. ■

Dermatologist Elizabeth Grice, Ph.D., left, notes that "the diversity of what is on the skin is much greater than we ever thought." With her is Jacquelyn Meisel, a doctoral student in her lab.

# TWO VIEWS FROM THE TOP

Rising costs of health care. The exciting potential of precision medicine. Shrinking federal funding for biomedical research. Innovative ways of teaching the medical curriculum.



*Photographs by Peggy Peterson Photography*

**This spring,** J. Larry Jameson, M.D., Ph.D., executive vice president of the University of Pennsylvania for the Health System and dean of the Perelman School of Medicine (at right in the photo), and Ralph Muller, M.A., chief executive officer of the Health System, sat down to discuss these topics and more. With Kevin Ferris, an editor and columnist at *The Philadelphia Inquirer*, moderating, they shared their views about the future of health care, potential concerns, new trends, and Penn Medicine's role in caring for patients and producing the next generations of physicians. Following is an edited transcript of the discussion.

## What are the reasons to be optimistic about the future of health care?

**Jameson:** First of all, recent data shows that the health-care cost curve is being bent, for the first time in decades. This is critically important for the good of the U.S. economy because health-care costs place a huge burden on businesses and the federal government, as well as individuals.

While the recent recession may explain this in part, I think an under-recognized component has been focus on quality and safety, along with efforts to reduce variations in care and unnecessary testing.

Thus, the profession of medicine is changing. This largely began after the Institute of Medicine launched a series of reports on quality and safety a little over a decade ago. There's been a real focus by health systems to improve the quality of care, to reduce hospital-acquired infections, and develop a variety of very specific strategies to eliminate medical errors.

You combine these efforts with the new technologies, such as minimally invasive surgery that reduces length of stay, or advanced imaging capabilities that improve our diagnostic skills, and I believe we can continue to blunt the rising costs of health care.

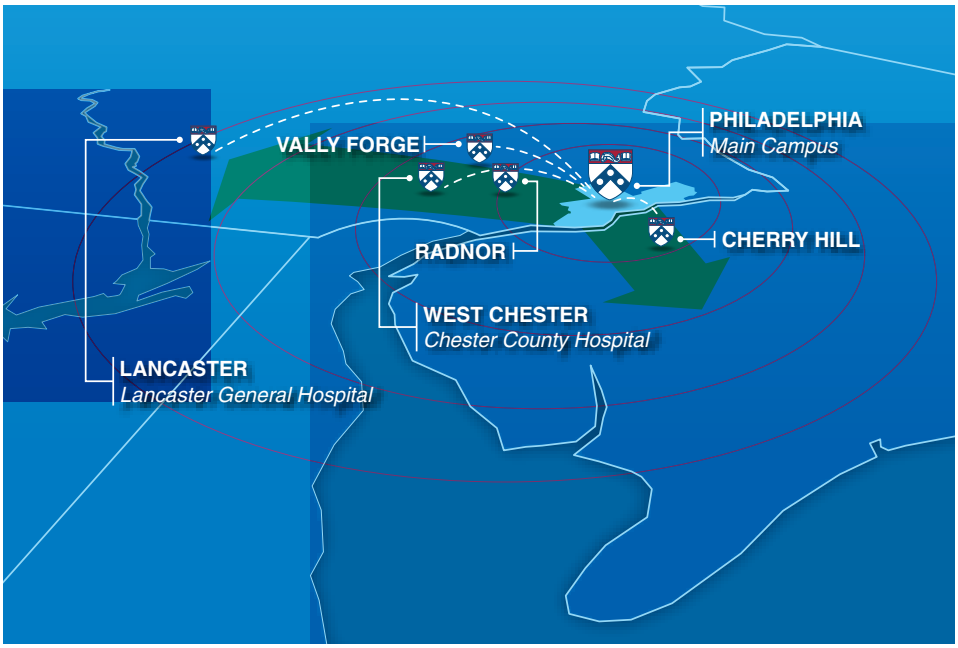
**Muller:** As the controversy over the Affordable Care Act shows, health care and its related politics are central to our society. In many ways this reflects not just the fact that it's such a big part of the economy, but having access to health care directly reflects the core values we have as a country. The conditions under which people get access to health care, who pays for health care, and the associated obligations and rights – for example, the controversy over the mandate – are central political questions of our time. Health care is an exciting field to be a part of because all the issues that get raised in our life every day get raised in our job as well.

> "Health care is an exciting field to be a part of because all the issues that get raised in our life every day get raised in our job as well."

**Jameson:** Two examples of policy changes that are critically important: The first is a policy that prevents discrimination based on genetics. With the development of the human genome project and our rapidly developing capabilities to sequence the human genes, this is a critically important policy to allow us to diagnose genetic disorders and provide better treatments when these are available. The second example that Ralph has alluded to is part of the Patient Protection and Affordable Care Act. This is the ability for people to get insured, independent of pre-existing conditions. This is a fundamental change in health insurance and will provide patients with better access to the health-care system, allowing more effective management of chronic disease.

## Does the larger health-care debate affect how you do your jobs?

**Muller:** The debate affects the kind of health-care services that we offer to patients. For example, Pennsylvania is one of the states that has chosen so far to not expand its Medicaid program. A large component of the Affordable Care Act was to expand the insured population, in part through the expansion of the Medicaid program. As one of the largest states, Pennsylvania – and, specifically, the Philadelphia region where we are located – has a significant number of people that could




be eligible for Medicaid. Thus, the fact that the state so far has chosen not to go forward with its Medicaid expansion is a big challenge for both us and some of our patients. For example, we've been asked many times by the city, by the state, and others to expand the health-care services we offer in our region. However, for us to expand our services, we need to have more people insured than are currently insured, so the decision not to expand Medicaid yet has had some effect on the kind of services we can offer in different settings of the city. That is just one example.

**Jameson:** We are expecting, over the long term, for more patients to enroll in the health-care system. As we consider primary care – Clinical Care Associates in the case of Penn Medicine – we're anticipating the need to have more providers and improved access to primary care. The emergency department anticipates having a greater proportion of patients coming in with urgent health-care problems, with some of the lower-acuity activity moving into the primary care arena. We're beginning to plan for these types of changes as a result of the Affordable Care Act but we anticipate that they will occur over years rather than months.

**Muller:** Another part of the Affordable Care Act is experimenting with new kinds of payment systems. For example, accountable care organizations, called ACOs, or bundled care, ask hospitals and doctors and settings like ours to organize ourselves in different ways to provide more integrated and coordinated care for our patients. These new organizational changes are already evident. For example, in the last year, Chester County Hospital, which is about 30 miles west of Philadelphia, joined the University of Pennsylvania Health System, enabling us to expand the depth and breadth of quality health-care services that Penn Medicine provides. We recently announced a major alliance with Lancaster General Hospital, which is about 80 miles west of Philadelphia, to develop innovative programs and initiatives to improve patient care. We've also expanded our facilities at Penn Medicine at Valley Forge and in New Jersey. As a result of these organizational changes, we're becoming a more regional system.

**Jameson:** We're very keen to organize care around diagnoses and needs of patients. And, as Ralph says, we would have done this anyway, without the Affordable Care Act. But it certainly positions us to be ready for more bundled and coordinated kinds of payment systems. So, for example, when a patient with breast cancer comes to Penn Medicine, they see a highly coordinated team that includes medical oncologists, breast surgeons, radiation oncologists, and plastic surgeons if reconstruction is needed. We coordinate the biopsy process, the pathology review, including molecular testing, all focused on the nature of the disease, so that our specialists recommend the optimal treatment approach. Even how you access the system is much more coordinated than it was a few years ago. Many of our clinical services are now organized as Centers, such as the Lung Center, the Heart and Vascular Center, or the Diabetes Center. We're expanding this model to most of our clinical service lines, and our new clinical buildings at the Perelman Center for Advanced Medicine (PCAM), or at Penn Medicine at Washington Square, Radnor, or Valley Forge allow us to design spaces around the needs of patients.

**Muller:** As of this January, we have initiated what are called bundles, for heart failure, cardiac procedures, and joint replacement procedures for Medicare patients. Under these bundles, when a patient arrives suffering from heart failure or needing a knee replacement, we're now financially responsible not just for the care inside our hospital, but also the care the patient receives for 90 days after the hospitalization. One of the advantages of how Penn Medicine is organized is we not only have hospitals and doctors within Penn Medicine, but we also have home care, rehabilitation hospitals, and a nursing home facility that enables us to

provide the full continuum of care for patients in these bundles.

Another advantage of Penn Medicine's integrated care model is if patients need to visit these various facilities over the course of their treatment, they are served in one common electronic medical record. For example, if a patient undergoes knee replacements at Presbyterian Hospital or Pennsylvania Hospital, they will receive home care after they are discharged. The nurse in home care has immediate access to the patient's records, right in their system. Similarly, the same patient records are available if the patient then needs some kind of physical therapy at our rehabilitation hospital. This immediate and ubiquitous access to the patient's medical records across all of Penn Medicine's providers makes it much easier for that patient and the caregiver, not just in terms of the next caregiver knowing what the previous caregiver did, but also providing information about the patient's allergies, their current medications, their images, and their previous lab results. Having all this information in one electronic system makes a big difference in improving patient care.

**Jameson:** It sounds like a great place, Ralph. I don't know why anybody would go anywhere else!

## What does medical school need to do to prepare graduates for this new world of medicine?

**Jameson:** This is a really important question. We have a big project under way to actually design our medical education space for the future needs of students. We've decided to move most of the facilities for medical education over to the Perelman Center for Advanced Medicine, so that the medical school space, named the Jordan Medical Education Center, will now be located on top of the clinics and adjacent to the Smilow Center for Translational Research. That physical location will place the medical students in the clinical environment – mostly the outpatient environment – but also in the research environment. If you've ever come up into the Perelman Center, the first floor has become Main Street, where you see the doctors and the scientists crossing paths in the main lobby.

First, I feel it is important to immerse the medical students in this new dynamic environment that will expose them to more of their faculty role models. Second, we can design the space for medical education of the future. Classrooms have been designed to be very flexible and to accommodate new classes that include interprofessional education, with nursing students, nurse practitioners, pharmacists, and social workers. The curriculum is evolving to really prepare the students for what they'll encounter in the clinics, the operating rooms, and in the intensive care units, in the future.

For example, we have courses now where nurse practitioners and first-year medical students take classes together. They have complementary backgrounds and skills. The nurse practitioners have been in the clinical environment for some time, they have a lot of experience with the clinical world that medical students will soon be entering. The medical students have a very quantitative background in math, physics, information technology, the life sciences, and they can bring that type of background to the nurse practitioners as they study pathophysiology. We're training them together, knowing that only a few years later, they'll be immersed in the clinical environment together.

**Muller:** Penn Medicine, like the rest of the world, has transitioned to an Internet model where almost all of our classes now are available online, so the students can get access to course material without having to have the professor up in front of the classroom. That's a huge difference in medical school coursework from 10 years ago.

The medical students now work in teams and develop experience in team learning and team problem-solving. We're preparing them for taking care of patients over a period of time – what we call longitudinal care – which is increasingly moving to team-based models of care. For example, patients with chronic disease need access not just to doctors and nurses but

other kinds of caregivers such as therapists, pharmacists, etc. Students need to learn this team-based approach to providing care starting in school, rather than magically figuring it out once they get out of medical school or nursing school.

**Jameson:** Penn Medicine is really pioneering what we call the "flipped classroom." This began in some respects with Coursera, but it builds on a legacy of having recorded a lot of our lectures and CME

courses in the past. The idea is that medical students and other health-care providers can learn a lot of fundamental information online. Then, when they come into the classroom, it's intended to be very dynamic and interactive. It's team learning, student and lecturer learning together. But also, as Ralph says, team dynamics are a critical skill for what they're going to encounter later in the health-care system.

## Are there advantages or disadvantages to shortening medical school?

**Jameson:** I really think about medical education as continuous learning throughout your career. Before you get to medical school, in the pre-medical curriculum, you need to be taking courses that prepare you for the rest of your career, and after you finish, you need to be learning continuously because the field of medicine will change in a very dynamic way.

Whether you think about ending medical school at three years or extending it out to five will be debated for decades. Our group of medical students is quite different from those at other schools. Our students are training to be leaders in various fields. Over 50% of our students receive a second degree, such as a Ph.D. or master's degree, or a certificate based on additional training. Thus, many of our students elect to spend more than four years in medical school. Personally, given the amount of information and skills needed to practice medicine, I wouldn't advocate shortening medical school. However, I do think there are opportunities to achieve some of these additional forms of training in less time, thereby reducing the costs as well as the time for medical education. The real challenge – from medical school, through residency, and 30 to 50 years of practice – is to keep up with the burgeoning amount of information that's out there.

## What are younger alumni doing after graduation and training?

**Jameson:** Our new alumni are not altogether different from a decade before. I feel very proud that we're graduating doctors who are among the most talented leaders in the country. They go into internal medicine, pediatrics, neurosurgery, dermatology, obstetrics, orthopaedics, and other specialties as they have before. And, within those general fields, our students tend to further specialize in oncology, cardiology, infectious disease, and the like. If there is one change, we see our alumni are joining more coordinated health-care systems rather than small group practices, but this is a national trend. We also have a significant number of alumni who transition into other fields such as the investment world, biotech, and health policy.

**Muller:** Four or five years ago, I noticed some of our medical students, who were not directly practicing medicine, might have worked on Wall Street, and now they're all going into software development. That's a major change.

These apps that are being developed have the potential to transform patient care. For example, one app allows the care team to create a private social network, so to speak, around the patient so the doctors, nurses, pharmacist, therapist, and all the allied health professionals can instantly share information by their mobile phones about the patient and the next steps in her care. While the primary system to coordinate care uses the electronic medical records that we've invested in over the the last 10 to 15 years, our care providers are also using smart phone technology to to have a kind of instant, real-time information-sharing as to what happened with that patient five seconds ago, where that patient is going next, and what kind of responsibilities the next caregiver has for that patient.

## Where do you see research support coming from? Government, private donors, industry?

**Jameson:** Here we have a paradox. The paradox is that we've never been better positioned for research advances in our history. The human genome project has been completed and we have sequencing technology that is rapid and becoming less expensive. We've trained a large generation of graduate students and postdocs who are more talented than ever before. However, unfortunately, there has been a flattening of the federal research budget, and it's not keeping pace with

our scientific opportunities or with the scale of our trained scientists. It's also not growing at the rate of biomedical inflation. The impact of this is a sharp curtailing of new research support, and trainees who planned a career in science or medicine are asking, "Can I sustain my career if there is no long-term commitment to research?" So we see a lot of young people who are now pursuing careers outside of science instead of staying with the field where they've been highly trained. That's our greatest risk – that we're going to lose a generation of very talented people, who have wonderful tools to work with.

**Muller:** The next generation of young scholars and doctors is going to have to learn how to get money from different sources. The generations before us were able to largely rely on the National Institutes of Health for their research support. They spent time learning how to apply for and achieve those grants. With the lack of growth in NIH research budgets, researchers have to really diversify their funding streams. This change requires learning new funding models and is accompanied by more work, which adds to the overhead of research. This is an unfortunate change, but it reflects the world we're in right now.

**Jameson:** If you look at this in a Penn-specific way, we've still been able to maintain our research support from the federal government. This mainly reflects the quality of our creative faculty and their aggressive efforts to seek funding, often working as teams to put together innovative grants. As Ralph said, we're looking for new sources of funding by partnering with industry. Again, to do investigator-initiated work at Penn, but to focus on a research problem with the potential to impact patient care in the future. We call this translational research, where we're trying to take the discoveries at Penn and convert them into practical treatments for patients.

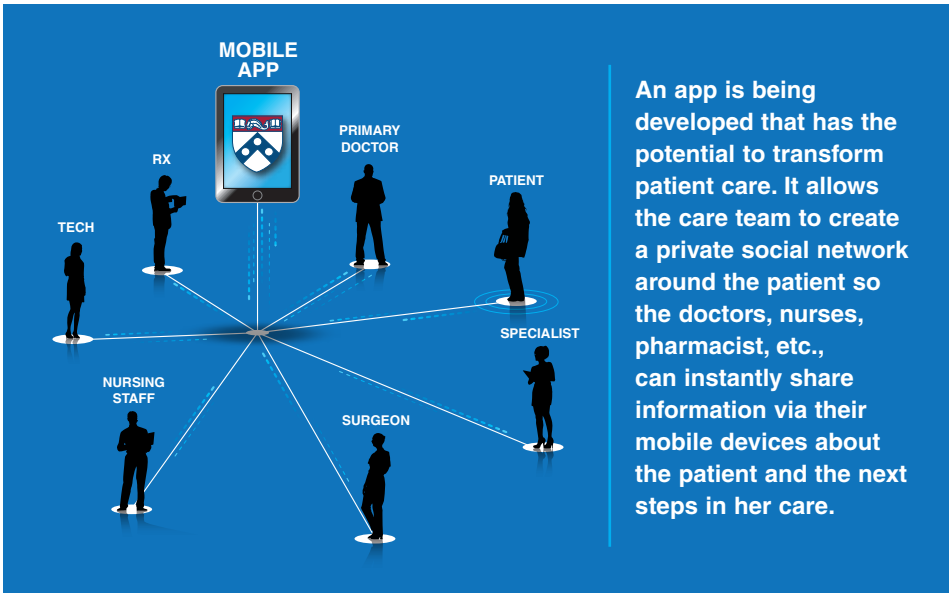
A recent example that people have heard about is in the area of gene therapy and cell therapy. For example, Dr. Carl June's work, looking at the ability to modify the immune system so that it can target certain types of cancer, is a wonderful example of translational research. This work began in the laboratory 15 years ago but is in clinical trials today to treat chronic lymphocytic leukemia, acute lymphoblastic leukemia, mesothelioma, and certain forms of lymphoma.

> "We're graduating doctors who are among the most talented leaders in the country. They go into internal medicine, pediatrics, neurosurgery, dermatology, obstetrics, orthopaedics, and other specialties as they have before."

## What about Penn's partnerships with industry?

**Jameson:** We have partnerships with most pharmaceutical companies, including Novartis, GlaxoSmithKline, AstraZeneca, Merck, to name a few, each focused on a different disease area. The most recent example is the Novartis partnership, which supports the research of Dr. June and his team. It's a wonderful example of synergy. Novartis is making capital investments in our ability to scale up the production of the immune cells that are used to treat cancer. But they are also bringing their own team of scientists to collaborate with ours to identify new targets for treatment. Novartis also has a lot of experience with the FDA regulatory process and, if this is successful, they have an international platform that can be used to scale up the system for producing the immune cells so that patients can be treated around the world.

**Muller:** Part of the changes in Big Pharma over the last 15 years is that the companies are investing far less in basic science than they were 20, 30, 40 years ago. Therefore, industry is increasingly relying on universities, such as Penn




**An app is being developed that has the potential to transform patient care. It allows the care team to create a private social network around the patient so the doctors, nurses, pharmacist, etc., can instantly share information via their mobile devices about the patient and the next steps in her care.**

Medicine, to be its partner in developing new forms of therapy. This represents a significant change in how drug development is done inside this country. I expect we'll see more and more of these partnerships in the next 15 to 20 years. We really see this change as an opportunity for Penn Medicine to fill an important societal need.

**Jameson:** The other strategy that we use at Penn is to collaborate across the schools and take advantage of the fact that Penn has many schools that are physically close to one another. For example, collaborations between the faculty at the medical school and the engineering school only require crossing Spruce Street. This allows us to think about how to use bioengineering or nanotechnology in medicine. Or we can easily collaborate with the vet school to explore early-stage research on new approaches to surgery or cancer. Having the nursing school embedded on the medical campus facilitates interprofessional education as well as collaborative research. The Leonard Davis Institute (LDI), has joined almost every school at Penn in health-care economists and policy.

## How is precision medicine affecting Penn Medicine?

**Muller:** We're investing heavily in precision medicine right now. Some of this investment comes from the genome project that Larry referenced earlier. We have made a conscious effort across our various disciplines to have leaders in personalized medicine. I'll discuss two of them: Dr. David B. Roth, who leads our Center for Personalized Diagnostics, has been with Penn Medicine for about three years. The center is increasingly performing genetic testings, both within Philadelphia and now, for example, from China. We've also brought in a senior scientist from Merck, Dr. Gary Gilliland, vice dean for precision medicine, and his role is to foster all the parts of Penn Medicine that are making efforts in precision medicine. We really see our opportunity to be a world-leading individualized patient diagnostics center.

By and large, patients come to a place like Penn Medicine not just for what we can do in a particular therapy, but also for how well we diagnose disease. Increasing that capacity to differentially diagnose through imaging, through pathology, through genetic analysis, is part of what makes us unique and what we hold out to Pennsylvania and beyond as a reason to come to Penn Medicine. We're investing in precision medicine leaders who will then foster the next generation of people and technologies that will make those diagnostic capabilities available to people on the East Coast.

**Jameson:** When most people hear about a new effort in personalized medicine, they ask the question, "I thought medicine was always personalized?" So one of the things we have to do, as Ralph was explaining, is to define what we mean by personalized medicine or precision medicine. I think it's an interesting contrast between our effort to take care of the population as a whole and to manage the individual patient. In the former, we have an obligation to make sure that preventive strategies and clinical pathways are put in place to ensure that everyone has access to the best practices in medicine.

But at the same time, we know that every patient is indeed an individual who has a distinct past medical history and a current set of symptoms or diagnostic challenges. The point of precision medicine is to be able to efficiently make the right diagnosis for this individual patient and identify the optimal treatment for them. We believe this actually has the potential to also reduce costs in the future. With the Center for Personalized Diagnostics, the main effort is to make sure that a patient with lung cancer, for example, is not put on a chemotherapy regimen that will not work effectively but could still cause side effects. Why expose that patient to a treatment that's not likely to be effective if instead we can identify a drug that may have better outcome and lower side effects?

**Muller:** The investments we've made in electronic medical records have helped

us in this area as well. For example, in addition to this kind of diagnostic capacity, we also perform gene sequencing. The fact that we now have electronic records on thousands of patients enables us to match those patients with our diagnostic capacity, so we can follow these patients over a period of time.

Thinking back to just 20 or 30 years ago, if a patient sought care in three different settings, each of those three different sets of doctors or nurses wouldn't know what the other doctor or nurse knew. Now, by having the same electronic record available in all settings, it allows us to mirror this personalized diagnostic information with their electronic record we have containing their history, their medications, and all the other illnesses for which they've been treated. One way through which we really differentiate ourselves, in addition to this kind of precision medicine, is by having the most powerful electronic record in the whole 100-mile region.

**Jameson:** We've identified certain patients who we know are at high risk of colon cancer, for example, and through the electronic health records, as Ralph is describing, we can ask, "when was the last time they had a screening colonoscopy?" And if it's been too long, how can we reach out and encourage them to have that appropriate screening? Particularly for patient populations who are reluctant to access the health-care system, we can be more proactive in reaching out to them and making sure they have the best care.

**Muller:** When a patient comes to us, the electronic record goes into this big database file where it is de-identified so that patients are not at personal risk of being identified around that data. This data allows us then to do the type of studies that we referenced. We're finding, increasingly, that with what's called "big data," we have the potential to ask questions that weren't previously possible to answer. Part of the learning curve to take advantage of this new data involves asking questions in a different way and seeing what the information we have stored on millions of patients allows us to answer.

**Jameson:** We have a distinct advantage as a fully integrated academic medical center to link big data, in a clinical environment, with the research environment. A related effort over the last few years has been to create a biobank, where we collect samples on patients who have given consent. The biobank has blood samples, DNA samples, tissue specimens, and these can be linked with the clinical information in a de-identified manner that allows us to make discoveries based entirely on mining databases.

> "With the Center for Personalized Diagnostics, the main effort is to make sure that a patient with lung cancer, for example, is not put on a chemotherapy regimen that will not work effectively but could still cause side effects."

## What's the best thing you get to do every day?

**Muller:** For me it's seeing all the young people coming through Penn Medicine, whether they are young doctors or young nurses or the students that we see in training. They all bring an important kind of energy to our campus, our hallways, and our discussions. I think their enthusiasm actually regenerates all of us.

**Jameson:** The best thing I get to do is meet with our faculty and hear about the exciting things that they're doing. Whether it's the research in a laboratory or taking care of patients or teaching, our faculty have a wide range of interests. Each week I learn about something brand new that's really exciting. I would say, second to that are the wonderful letters that we get from patients who have received care in the Penn Medicine system. It's amazing to me that people take the time to write about the experience they've had, the quality of care they've received, and how grateful they are to Penn Medicine.

## The challenges?

**Muller:** The regulatory climate is getting more and more dense every year. It's in the nature of working in a large, complex system involving both the government and other large institutions. However, the result is that there is "red tape" everywhere and too many resources are being spent dealing with these regulatory complexities.

**Jameson:** I think the hardest – and it relates to what Ralph was describing – is helping people with time management, given all the pressures. Whether it's coming from the regulatory environment, or just the need to write more grants. Our faculty struggle with time management as they try to balance creativity and productivity with the other demands on their time. It's a mentoring process, really, so I wouldn't say it's a negative thing, but it's a challenging thing for all of us. ■

# A Look Behind the Mask

An eye surgeon combines an account of his own professional experiences with stories of his heroes in the field.

*By John Shea*

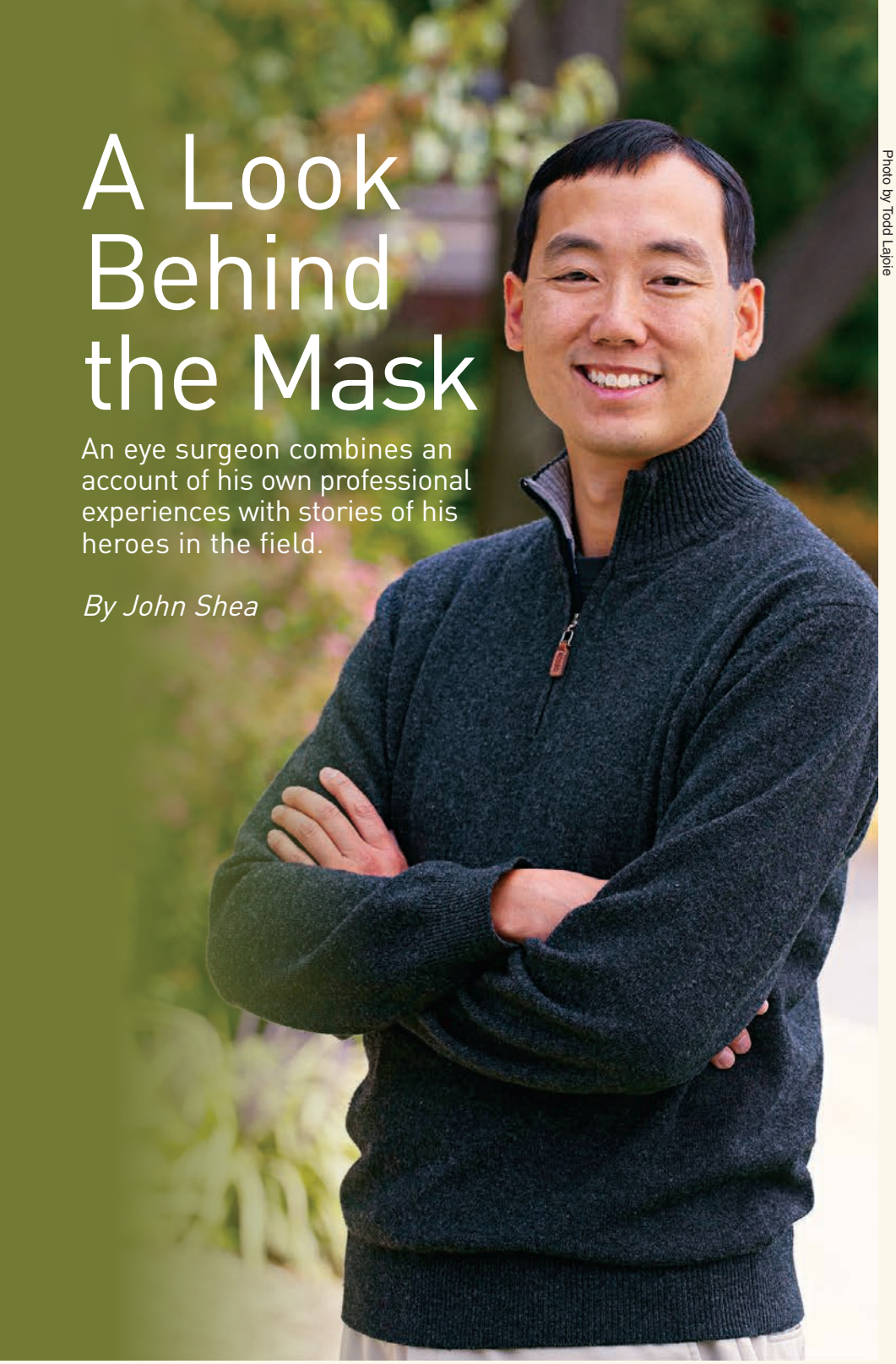


Photo by Todd Lajoie

For a practicing eye surgeon and assistant professor of ophthalmology at Tufts University School of Medicine, Andrew Lam, M.D. '02, knows a thing or two about writing a tense, vivid scene. Indeed, he appears to have learned well from the masters of suspense. Even when presenting the more historical sections of *Saving Sight: An Eye Surgeon's Look at Life Behind the Mask and the Heroes Who Changed the Way We See* (2013), Lam paces his narratives well. It is no surprise that he went on to publish a novel in December, set in China during World War Two. For *Saving Sight*, he decided that the best way to draw readers in was to intersperse his sketches of some innovators and inventors in the field of ophthalmology with his own experiences as a surgeon.

And for Lam, the experiences range from the routine – as routine as delicate surgery can ever be – to the more technically and emotionally demanding. The book covers eye trauma, cataracts, LASIK, retinal detachments, macular degeneration, and more. In the first chapter, here's how he describes an emergency operation he had to handle as a retina fellow at Wills Eye Hospital. Jacob, the young worker he is treating, had been grinding metal without safety glasses:

> I gently opened his lids and looked through the scope.
>
> *Oh no.*
>
> At first I thought the cornea was missing. All I saw was a black blob mixed with some dark brown iris tissue. Had the contents of the eye been expulsed? I'd never seen that before, but I knew it could happen if the patient coughed violently or vomited while his eye was ruptured like this.
>
> I drew a deep breath and looked closer. *Wait.* Now I could make out the torn edges of a huge laceration, starting in the center of the cornea and extending laterally, beyond the edge of the cornea and into the sclera. How far back did it go? I couldn't tell; it was a bloody mess. The normally white sclera and the conjunctiva of the eye were torn, swollen and beefy red. . . .
>
> *The metal.*
>
> It looked huge in my view through the operating microscope, jagged, at least five millimeters across. It was lying on a bed of bruised retina, looking like a meteor that had just cratered the moon.
>
> *How the hell am I going to get this out?*
>
> It was too big for forceps. No intraocular forceps would have jaws that opened wide enough. There was a special basket-like instrument for scooping BBs out of

the eye, but this shard was too oddly shaped to use that. . . . There was only one way: to take it out the way it had gone in, through the gaping wound in the front of the eye.

"Get the magnet," I told my assistant.

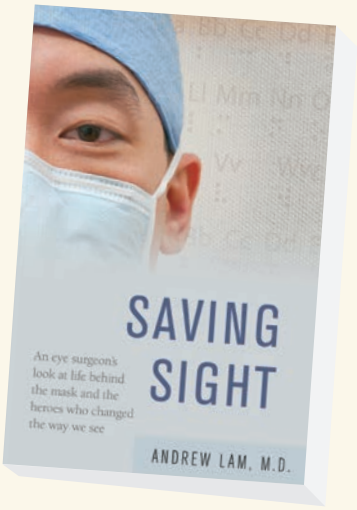
## Advances in the Field

Here and in other places in the book, Lam effectively describes the professional tools and the parts of the eye that most of us never think of. I read those pages with keen interest and, I admit, a certain amount of queasiness – and I suspect other readers may feel the same way. To some extent, Lam expects that kind of ambivalent response. As he puts it in *Saving Sight*: "The eye freaks a lot of people out. Come at the eye with something as simple as an eye dropper and some patients lurch back or, worse, faint. Medical students are often no better. Most of my classmates wouldn't have dreamed of going into ophthalmology."

But readers who proceed will find interesting accounts of some "heroes" of ophthalmology. Among them is Sir Harold Ridley, a British doctor whose serendipitous encounter with a pilot of the Royal Air Force during the Battle of Britain led to his invention of the artificial intraocular lens. Another is Charles Kelman, an American ophthalmologist whose trip to the dentist gave him an idea for radically improving how cataracts are removed: through phacoemulsification, which emits ultrasonic energy to emulsify the cataract and allow it to be removed through a small incision, involving less recovery time.

"There was only one way to take it out. Get the magnet."

The story of Charles Schepens almost seems the work of a novelist. A Belgian ophthalmologist who was forced to flee to occupied France during World War II, Schepens for a while managed a lumber mill there under an assumed name, pretended to be friendly with the Gestapo – and helped refugees escape across the border. He invented the binocular indirect ophthalmoscope, which, as Lam points out, "revolutionized our ability to diagnose and treat diseases located inside the eye." For Lam, viewing the retina through the instrument for the first time was a moving experience: "I gasped. It was incredibly beautiful."




## The Limits of the Profession

Although Lam the surgeon managed to save Jacob's eye in the first chapter, Lam as writer acknowledges limitations. Jacob regained "vision good enough to count fingers at one foot. No one would claim that this level of vision was very good. If I was making this story up, I might say that he had a miraculous recovery: 20/20 vision, after a corneal transplant and an artificial lens." In addition, Lam also recounts a touching experience in his last chapter, when he determines that Ann, a shy 18-year-old Asian American, has a detached retina in her left eye. One of the steps he has to take is to flatten the retina – which is, he points out, "delicate neural tissue packed with sight-giving photoreceptors. It's only 250 microns thick, just one-fourth of one millimeter. Any manipulation of it is certain to cause some damage."

For a while, the left retina improves, and Lam also corrects the right one. But a month after that, the left retina begins to detach again. Finally, while inspecting Ann's retina again during a subsequent operation, Lam decides not to proceed. "Some areas were barely recognizable as retina at all – distorted by traction or charred from previous laser treatment." It was, he says, "the first time I'd been unable to fix a retinal detachment."

## Some History of the Personal Sort

Born in Philadelphia, Lam is also part of a Penn tradition. His father, Wilfred Lam, graduated in 1973; his uncle, Victor Lam, in 1971. Two other uncles, Thomas J. Braciale Jr. and Isaac T. Tam, an internist at Penn Primary Care in West Chester, graduated in 1975. In addition, a cousin graduated last year.

Lam did his undergraduate work at Yale University, where he graduated *summa cum laude*. His degree in history no doubt helped him in writing his new novel, *Two Sons of China*. It focuses on an American lieutenant and a Communist Chinese guerilla leader who become great friends, united – at least for a time – in the fight against the Japanese.

Lam's second career has started well. *Saving Sight* has sold well on Amazon, and it recently received Honorable Mention Awards in the biography/autobiography category of two competitions, the New England Book Festival and the London Book Festival. ■

# ON A MISSION:

# Penn Doctors Lend Their Talents Around the World

*By Carole Bernstein*

The hardy Penn Medicine doctors and nurses who traveled to Haiti after the devastating earthquake in 2010 found only two operating rooms in the hospital in Cange – and their cases started by 9:30 a.m. and often continued until 7:00 or 8:00 at night.

D. Scot Malay, D.P.M., G.M.E. '03, M.S.C.E. '05, director of the Perelman School of Medicine's podiatric residency program, was on a medical mission to El Salvador last year. The hospital had no steam autoclaves. Instead, to treat the many children with deformities of their lower extremities, Malay and his colleagues had to soak their instruments in glutaraldehyde to make them sterile.

On a medical mission to Nicaragua last year, Jaimo Ahn, M.D. '03, Ph.D. '99, assistant professor of orthopaedic surgery, noticed some unexpected things while doing rounds in one of the largest public hospitals in the nation: "Two of the patients are in skeletal traction – pins in their bone pulled by a string attached to water jugs."

On one of his visits to Vietnam, James Kirkpatrick, M.D., assistant professor of cardiovascular medicine, remembers seeing three or four patients to a single bed on the cardiology floor of a Vietnamese hospital – some of them suffering from uncontrolled hypertension.

Many Penn doctors, in addition to their workload here at home, manage to find time in their schedules and their lives to embark on medical missions. The conditions they work in are often very different from those at home, and they often face challenges. But their help is needed – and very welcome.

## Listening to the Heart: James Kirkpatrick in Vietnam

When James Kirkpatrick, M.D., talks about how his Vietnamese wife came to this country, his voice is matter-of-fact: the facts themselves are dramatic enough. "She came here in 1975. She was on the last flight out of Saigon – the runway was destroyed a few minutes after the plane took off. She was three years old and has very few memories of it – just being on a dark, crowded plane with explosions going on around her."

It was partly his wife's heritage that would lead Kirkpatrick, years later, to embark on a medical mission. An assistant professor of cardiovascular medicine at Penn, Kirkpatrick traveled to Vietnam in April 2013, where his echocardiography skills helped diagnose cardiovascular conditions in patients in some of the poorest areas. His wife (Thanh Kirkpatrick, M.D., now a pediatrician, who did her residency at the Children's Hospital of Philadelphia) accompanied him, along with her sister and the Kirkpatricks' three young children.

Kirkpatrick has a longstanding interest in the use of echocardiography in underserved countries to identify disease, a subject that's received increasing attention from the medical community over the past decade. In Penn's echo lab, surrounded by shelves of black boxes housing patients' echocardiogram DVDs, another physician pulls up an image on a computer screen; the familiar *lub lub* of a human heart is heard. "Echo is important for finding a lot of things, such as fluid that can accumulate in the sac around the heart and squish the heart," explains Kirkpatrick. "This happens in infectious diseases like tuberculosis. Echo can also guide the placement of a needle to suck that fluid out. There's also a disease common in the developing world called rheumatic fever, which can damage

the heart valves and heart muscle. And a lot of congenital heart diseases can be found by echo."

The main obstacle to the use of echocardiography in Vietnam, however, was that an echo machine wasn't exactly something you could pack in your suitcase. The older machines weighed almost a ton and cost about $250,000. But recently, the machines have been miniaturized to the size of a laptop and even an iPhone. Says Kirkpatrick, "The image quality is really quite amazing."

As Kirkpatrick began contemplating his trip, he became aware through the American Society of Echocardiography that another physician, Jose Banchs, M.D. – director of the echocardiography lab at M. D. Anderson Cancer Center – was also interested in taking the new echo technology to Vietnam. Banchs's wife, like Kirkpatrick's, is Vietnamese. The physicians decided to pool their efforts. While the trip was not officially sponsored by any organization, some funding came from the American Society of Echocardiography, which helped defray costs for the echocardiography stenographers and trainees who came along. Echo machines the size of laptops were borrowed from an ultrasound equipment company, and the doctors paid their own way.

The team scanned an impressive 200 people in two days, working at three community health clinics in Hue, a city in central Vietnam. The clinics did not have full-time workers, Kirkpatrick recounts, but were basically large triage tents set up by personnel from the central hospital. To Kirkpatrick's team came people who had any complaint relating to the chest, such as chest pain or shortness of breath. Banchs's wife, originally from Hue, acted as primary translator, since she is fluent in the specific dialect spoken in the center of the country.

Photo: James Kirkpatrick

**Outside the Clinic.** James and Thanh Kirkpatrick with two of their children: Katriona Tam and Kason Tai (front).

The team found many conditions requiring medical intervention. "Vietnam is industrializing rapidly, so they're starting to see all the Western diseases. We did find some cases of pretty severe atherosclerotic plaque in the aorta" – a condition frequently caused by a high level of "bad" cholesterol. And many patients had thickening of the heart from high blood pressure. "It's really an epidemic in the country. Their diet now is even worse now than it ever was, and smoking is pretty prevalent." Kirkpatrick explains that the traditional diet is itself high in salt, which makes a dangerous combination with Western-style fast food.

Kirkpatrick's group partnered with Hue General Hospital to make sure all the patients needing medical intervention received follow-up, either by being referred to the pharmacist on site or being advised to make the trip to the hospital. "Transportation is very expensive in Vietnam," notes Kirkpatrick. "If people don't have to go to the central hospital, which is a long bus ride away, it saves them a lot of money." Patients had to be assured that going to the hospital was crucial.

A disease that we think of as "rare" in the U.S. may not be rare in another country. The echocardiography team diagnosed many cases of rheumatic mitral disease. The disease is common in Vietnam because of the spread of untreated strep throat. Kirkpatrick explains that the body can have a reaction to strep throat and damage the heart valves. When strep throat is eradicated quickly with antibiotics, as is typical in the U.S., injury to the heart is prevented. But in Vietnam, antibiotics aren't as widely used or readily available. According to Kirkpatrick, many young Vietnamese people – especially young women who seem particularly vulnerable to the disease – can develop thick, encalcified mitral valves, leading to lightheadedness, dizziness, and arrhythmias. "You end up with bad heart rhythms in these young women, and once they get to that point of arrhythmias – if they have a tight enough valve – that can be it." Echocardiography plays an important role in screening and finding these cases early on, when antibiotic therapy can still make a difference.

Kirkpatrick's two older children, aged ten and seven, were of help to their parents. Before leaving for Vietnam, they collected donations of crayons, gum, and toothbrushes from classmates. They handed out items to the kids waiting to be seen. "We wanted them to do something, not just sit at the hotel," says Kirkpatrick. "I think the trip was a really good experience for them, and a connection with their heritage."

Photo: James Kirkpatrick

**Inside the Clinic.** The portable echocardiography unit checks the heart of a Vietnamese child.

Kirkpatrick plans to return to Vietnam, and he speaks animatedly about the long list of initiatives in clinical care, teaching, and research he would like to see become a reality: refurbishing used devices such as pacemakers for re-use overseas, a concept about which he has written several papers; further academic interchange with the staff of Hue General Hospital, who on this trip responded with great interest to lectures such as his wife's on pediatric Kawasaki disease; expanding the trip to include other specialists, such as Kirkpatrick's brother-in-law, an interventional cardiologist who could help treat the many cases of rheumatic mitral disease; helping to integrate the concept of palliative and end-of-life care into Vietnamese society; and partnering with experts in resuscitation science about Sudden Unexpected Death Syndrome, which strikes many young Vietnamese men, often in their sleep.

"Now that they're not having wars over there, it's the number-one killer," says Kirkpatrick. "It's most likely a variant of something worldwide: the electricity of the heart gets messed up. So we're thinking of doing a study of training the Vietnamese people in CPR, which they really don't have there. It's possible with these arrhythmias that if they could be resuscitated quickly, they might do OK, even if they can't get to an ambulance or a hospital right away. . . . Most people won't, but saving even one life is worth it."

## Aboard a Hospital Ship: Joli Chou in Africa

Spending two weeks on a cruise ship seems like the perfect escape from winter, but for Joli Chou, D.M.D., M.D. '04, G.M.E. '07, it was a "working" vacation. She spent most of her time performing surgical procedures on African patients who couldn't otherwise get them.

Chou is an assistant professor of oral and maxillofacial surgery who practices at the Hospital of the University of Pennsylvania, Penn Presbyterian Medical Center, the Children's Hospital of Philadelphia, Penn's Center for Human Appearance, and Penn's School of Dental Medicine. For the past two years, she has volunteered her time – and skills – aboard the *Africa Mercy*, said to be the world's largest floating hospital. Operated by the Mercy Ships organization, the ship stays docked at an African port for 10 months, providing an array of medical services. During Chou's stay, the ship was docked at Conakry, Guinea. Volunteers customarily pay their own way for the flight to the nearest airport, as well as room and board. Chou was in part supported by a scholarship awarded by the American Association of Oral and Maxillofacial Surgeons.

During her stint on *Africa Mercy*, Chou performed three, four, or five cases each weekday, depending on their complexity. "I'm usually operating on my own but, if it's a big case, I'll work with another surgeon," she said. Chou also teaches local surgeons who assist in the surgeries. In addition, she shows the local nurses how to use the medical equipment that's donated to Mercy Ships.

Many of Chou's more complex cases stem from a lack of access to treatment. For example, last year an 18-year-old showed up with a huge benign tumor on his jaw. "It weighed five pounds!" reports Chou. Because it had been left to grow untreated, the young man had to undergo multiple surgeries to remove and reconstruct his jaw. In the United States, Chou pointed out, "we'd diagnose it much earlier and try to shrink it with injections. But he did very well – he actually smiled."

Several patients suffered from ankylosis (fused jaw joints). In one memorable case, the patient had not been able to open his mouth for more than 10 years. The condition results from infection or trauma that was not treated properly, explained Chou. "I did many of these procedures while I was there, and it was so rewarding. Patients can now eat real food."

Although Chou did take some excursions to land on weekends, the floating hospital was really like a small town, with a bank, shops for necessities – even a

Starbucks. "We get coffee for a $1 because they donate it," she said with a smile.

Volunteering to help others has been a part of Chou's life for many years. Before graduate school, she went to South America to help build houses with an organization similar to Habitat for Humanity. She also goes to Mexico every year to do maxillofacial surgery on children. She explains that she loves the work on the *Africa Mercy* because "everyone goes to help – surgeons, nurses, even the cooks – and they go out of their way to do what they can. I feel like everyone works hard to support the same goal."

Photo: Ruben Plomp. © Mercy Ships

**On the *Africa Mercy*.** Joli Chou, an oral and maxillofacial surgeon, tends to a patient.

The ship's limited resources prevent her from doing all she wants to for the patients, she admits. Still, she goes on to say, "it's such a positive environment to work in. I plan to go back next year as well. I'm very grateful to members of my department, who are so supportive."

*– Sally Sapega*

## Learning to Do Without: Derek Donegan in Nicaragua

The patient was 30 years old, with a both-bone forearm fracture, recalls Derek Donegan, M.D., an assistant professor of orthopaedic surgery at Penn. Donegan spent two weeks on a medical mission to Nicaragua in September 2012. In the United States, Donegan explains, they would be able to fix such an injury within three to five days and often would admit the patient to the hospital. "This patient, unfortunately, because of resources and finances, was splinted and sent home."

As Donegan recalls it, the patient was told that the injury probably needed fixing "but we don't have the implants to do it," referring to the pins, rods, screws and plates used to anchor fractured bones while they heal. Instead, the patient was told to get his own. Donegan recounts how it took the patient nearly three months to obtain his own implants from a local supplier. When the case eventually came to Donegan, the man had brought with him two plates and 16 screws, but the screws were all the same size – an unworkable situation. On top of that, resources at the public hospital where Donegan was assisting were limited. "We had no depth gauge to measure how long the screws needed to be. So we took a needle, bent the tip, and used it to hook the bone." The next step was to fix it in place with a clamp, take out the needle, then line up the screw beside it. "And then we'd actually take bolt cutters and cut the screws to the appropriate length. That to me was truly an eye-opening experience."

This particular patient's story was not unusual for Nicaragua, Donegan discovered. He says the trip opened his eyes about all that he took for granted about surgery in the U.S.: access to care, to surgical implants, to OR availability and resources. In Nicaragua, limited resources and implant ability means that a patient may lie in the hospital, or have to wait at home, for several weeks before receiving surgery. During which time the fracture start to heal – but often incorrectly. "A lot of what we dealt with were malunions – or non-unions – of broken bones." To make matters worse, Nicaragua has a high rate of traumatic injury because of the large number of motor vehicle accidents – an unfortunate combination of many motorcycles on the road and few enforced traffic laws.

The 2012 Nicaragua trip was the result of an initiative by Penn's Department of Orthopaedic Surgery to provide their residents with overseas experiences. Donegan served as a faculty supervisor, traveling with one resident. Two fellow trauma sur-


Photo: Derek Donegan

**In Nicaragua.** Tools of the trade for orthopaedic surgeons.

Photo: Derek Donegan

**In the OR.** One of many surgeries during Derek Donegan's mission to Nicaragua.

geons also went – Jaimo Ahn, M.D. '03, Ph.D., '99, and Samir Mehta, M.D. – each paired with a resident and based at one of two public hospitals in Managua. The department worked with Orthopaedics Overseas, part of the organization Health Volunteers Overseas, a network of healthcare professionals, organizations, corporations and donors. Orthopaedics Overseas helped the department identify areas of the world with the greatest need for trauma surgery. The Nicaragua program, after its inception last year, has been made a permanent part of the department's resident curriculum, and four trips have been completed to date.

Donegan and his resident were assigned to Roberto Calderón Hospital: "They basically take care of people without insurance, anybody and everybody who comes there." Making the best of limited resources colored every aspect of Donegan's trip. "What surprised me was how good the surgeons were at using what they had," he says. "The cases were not dissimilar to the ones we have here, but they had probably a third of the resources. To me it was, honestly, amazing."

Besides having to do things like the aforementioned trimming of implant screws with bolt cutters, Donegan had to perform all his surgeries without the aid of intraoperative fluoroscopy, using X-rays. The hospital didn't have the equipment. Operating without it was very challenging, especially when dealing with hip fractures, a procedure during which a surgeon in the United States would rely heavily on X-ray guidance. But he adapted. "You have to learn to use different landmarks" on the bones.

Donegan's time in Nicaragua included a daily morning conference with residents, during which he would give lectures. In the afternoon after clinical work was concluded, he would sit down with the surgeons and residents he'd been working alongside that day, pull up a presentation on his laptop about a type of case encountered during the day, and have the group review the basic treatment procedures. "It was interesting," commented Donegan. "Part of our mission was not only helping to take care of patients, but also to educate the surgeons about practicing more up-to-date techniques for fracture fixation. But I realized very quickly that we were learning just as much – or even more – from them," for cases in which the standard high-tech surroundings would not be available.

"I still keep in touch with a couple of the surgeons that I met down there, over e-mail. They get in touch about cases, or sometimes just to say hi."

## Returning Home with New Perspectives

Writing about a later mission to Nicaragua, Jaimo Ahn and Adam T. Griska, M.D., a resident in the Department of Orthopaedic Surgery, noted their mixed emotions upon leaving. Their two weeks in Managua exhausted them and they looked forward to "the relative luxury of our hospitals at home." At the same time, the trip "has been eye-opening in many ways. The patients, the staff, the techniques (and the lack thereof) have given us a new perspective on our specialty and have made us consider for the first time *what is the essence of what we do*? What is required to do what we do successfully? What can we do to help the patients here?"

For his part, Scot Malay was also kept very busy during his podiatric mission to El Salvador, sponsored by the Greater Philadelphia Chapter of Healing the Children and the San Salvador branch of Rotary International. Right after arrival, he and his team triaged 95 children in one day. When they began operating, they kept two or three Ors busy. "We finished by rounding our patients and changing dressings and casts, finalizing discharge plans, and saying farewell to our patients and their families, whose sincerity and gratitude made me feel better than anything that I did for them over the course of the mission." ●

# MASTER CLINICIANS, THEN AND NOW

A new honor recognizes a select group whose clinical abilities are matched by their compassion and interpersonal skills.

*By John Shea*

Last year, all three of the University of Pennsylvania Health System's hospitals were recognized by *U.S. News & World Report* as among the top 10 hospitals in Pennsylvania. To achieve that kind of recognition, it follows that Penn Medicine has plenty of highly skilled clinicians. A new program, supported by a major gift from Independence Blue Cross and institutional funding, explicitly seeks to foster clinical excellence – and to acknowledge those who stand out even among their fellows. Earlier this year, the inaugural class of the Academy of Master Clinicians, drawn from throughout Penn's Health System, was officially honored at a banquet.

The 22 new members come from the Hospital of the University of Pennsylvania, Penn Presbyterian Medical Center, Pennsylvania Hospital, the Abramson Cancer Center, the Children's Hospital of Philadelphia, the Philadelphia VA Medical Center, and Penn Medicine Radnor. Each receives a one-time financial award of $10,000. As members, each makes a commitment to serve as "ambassadors for Penn Medicine" and to help "improve the culture of clinical excellence in general and to promote the ideal patient experience in particular."

What are the characteristics of a Master Clinician? According to the selection/executive committee of the new program, they are: superior depth of knowledge in a field and a willingness to pursue new knowledge; excellent judgment, integrity, and exemplary interpersonal and communication skills; and compassion and empathy for patients. In addition, they must be team players, willing to help others toward the same high standards.

The clinicians who selected the inaugural class and make up the original members of the Academy have themselves been honored in the past for clinical excellence. Several are recipients of one of the Perelman School of Medicine's Awards of Excellence – especially the I. S. Ravdin Master Clinician Award, which is presented to a single person each year. The award was created in 1998, named in honor of the former surgeon-in-chief at HUP who later became the John Rhea Barton Professor of Surgery. Although he could be a demanding leader, Ravdin, M.D. 1918, was also known for his warm bedside manner with patients.

Jonathan E. Rhoads, M.D., G.M.E. '40, succeeded Ravdin as chair of the Department of Surgery. In his later years, Rhoads, himself a legendary figure in the annals of the University of Pennsylvania, published a piece modestly called "My Teacher and Chief: I. S. Ravdin." In the essay, he recalled some episodes that stood out in his memory. In one case, Rhoads had performed surgery on a patient who had suffered a fracture of the tibia. With a

Members of the inaugural class of the Academy of Master Clinicians are joined by founding members, Dean J. Larry Jameson, and CEO Ralph Muller.

cast on, the patient was sitting in the ward when Ravdin came by during rounds. Despite what Rhoads believed was a successful procedure, the man was not eating and was clearly not thriving.

Ravdin asked the patient what his occupation was. The man answered that he was a carpenter but added that he was worried he would never be able to work again. At once, Rav, as Rhoads called him, assured him that he'd be able to return to work – because Ravdin needed a porch built on his summer house at the Jersey shore and wanted the man to build it.

As Rhoads put it: "The whole attitude of the patient changed: he began to take an interest in life and ate heartily. The fracture healed, and he built the porch. It was typical of Rav's humanity and insight that he inquired into the patient's mind, grasped the fact that the depression was due to the patient's impression that he was helpless. It was characteristic of Rav to do something positive about it immediately."

Rhoads's anecdote illustrates the importance of humanity and insight – essential qualities for a great clinician. Over the years, similar traits have been noted in the descriptions of those who have re-

## THE INAUGURAL CLASS

**Louis M. Bell Jr., M.D., G.M.E. '85**
Professor of Pediatrics and Chief of the Division of General Pediatrics at The Children's Hospital of Philadelphia

**Susan C. Brozena, M.D.**
Associate Professor of Medicine and Medical Director of Penn Cardiac Care Radnor

**E. Cabrina Campbell, M.D., G.M.E. '93**
Associate Professor of Psychiatry at the VA Medical Center

**Emily F. Conant, M.D. '84, G.M.E. '89**
Professor of Radiology and Chief of Breast Imaging at HUP

**Edward T. Dickinson III, M.D.**
Associate Professor of Emergency Medicine at HUP and Director of EMS Field Operations

**Jack Ende, M.D.**
The Adele and Harold Schaeffer Professor in Medicine and Assistant Vice President, UPHS, and Assistant Dean in the Perelman School of Medicine

**Jody Foster, M.D., M.B.A.**
Clinical Associate Professor of Psychiatry and Chair of Psychiatry at Pennsylvania Hospital

**Gary Freedman, M.D.**
Associate Professor of Radiation Oncology at HUP

**Ellen J. Kim, M.D. '96**
The Sandra J. Lazarus Associate Professor in Dermatology at HUP

**Najjia N. Mahmoud, M.D.**
Associate Professor of Surgery at HUP and Chief of the Division of Colon and Rectal Surgery

**Natasha Mirza, M.D.**
Professor of Otorhinolaryngology: Head & Neck Surgery at HUP and the VA Medical Center; Director of the Penn Center for Voice and Swallowing

**Mark A. Morgan, M.D., G.M.E. '86**
The John J. Mikuta, M.D., Professor of Gynecologic Oncology; Chief of Gynecologic Oncology at the Abramson Cancer Center; Director of Gynecologic Oncology at Pennsylvania Hospital

**Amy A. Pruitt, M.D.**
Professor of Neurology at HUP and Chief of the Division of General Neurology

**Patrick M. Reilly, M.D., G.M.E. '95**
Professor of Surgery at HUP and Chief of the Division of Traumatology, Surgical Critical Care, and Emergency Surgery

**Anthony L. Rostain, M.D., G.M.E. '87**
Professor of Psychiatry and Pediatrics at HUP and Medical Director of Adult Developmental Disorders

**Joseph S. Savino, M.D., G.M.E. '87**
Professor of Anesthesiology and Critical Care at HUP

**Brian J. Sennett, M.D. '88, G.M.E. '93**
Associate Professor of Orthopaedic Surgery at HUP and Chief of Sports Medicine

**Donald L. Siegel, M.D. '87, Ph.D.. G.M.E. '90**
Professor of Pathology and Laboratory Medicine at HUP and Director of the Division of Transfusion Medicine and Therapeutic Pathology

**John J. Stern, M.D.**
Clinical Professor of Medicine and Chief of the Division of Infectious Diseases at Pennsylvania Hospital

**Matthew B. Stern, M.D., G.M.E. '82**
The Parker Family Professor of Neurology at Pennsylvania Hospital and Director of the Penn Parkinson's Disease and Movement Disorders Center

**Gregory Tino, M.D., G.M.E. '89**
Associate Professor of Medicine and Chief of Medicine at Penn Presbyterian Medical Center

**David J. Vaughn, M.D.**
Professor of Medicine in Hematology Oncology and Director of the Clinical Research Unit at the Abramson Cancer Center

ceived the I. S. Ravdin Master Clinician Award. For example:

- He epitomizes the ideal clinician. He has a broad base of knowledge and a wide range of experience which he shares with everyone who has the fortune of being in his presence, including allied medical personnel, nurses, students, housestaff, and attending or primary-care physicians." (Patrick S. Pasquariello Jr., M.D., G.M.E. '63, professor of pediatrics – 1998)
- He continually demonstrates "the three A's of a master clinician: availability, affability, and ability." He treats, calms, and reassures his patients, he inspires his students and residents, and he leads his colleagues by example. (Howard I. Hurtig, M.D., G.M.E. '73, professor of neurology – 2003)
- She is a superb diagnostician, and her colleagues across the region seek her opinion on difficult cases. It is her dedication to her patients that truly sets her apart. She is among the most respected faculty members at Penn. (Laurie Loevner, M.D. '88, G.M.E. '94, professor of radiology – 2009)
- He is beloved as a teacher by the trainees and students at Penn. At the cutting edge of cancer care, "he is the epitome of the sensitive, concerned, and highly knowledgeable physician that any of us would want to care for one of our family members." (Kevin R. Fox, M.D., G.M.E. '85, the Mariann T. and Robert J. MacDonald Professor in Breast Cancer Care Excellence – 2002)
- She is the consummate physician. In the clinic, she is known to be calm, compassionate, thoughtful, and insightful, with a remarkable fund of knowledge and an evidence-based approach to patient care. (Anne F. Reilly, M.D., professor of clinical pediatrics – 2013)

The very first recipient of the Ravdin Award was the late Wallace T. Miller Sr., M.D., G.M. '58. (See p. 39.) When he was recognized for his clinical skills, he was professor of radiology. In his 40 years at Penn, Miller was known as a "doctor's doctor." He was continually sought after by physicians at HUP and elsewhere for his radiological expertise and highly valued medical opinions. His original nomination stated it clearly: "Wally is unique in his ability to combine accurate radiological diagnoses with insightful recommendations regarding proper patient management based upon a patient's entire clinical picture."

As is true of many other recipients of the Ravdin Award, Miller also received several teaching honors, such as the Medical Student Government Teaching Award and the University's Lindback Award for Distinguished Teaching.

In 2012, Penn Medicine lost another Ravdin Award recipient, Ernest F. Rosato, M.D. '62, professor of surgery. Like Miller, Rosato was also a recipient of the Lindback Award. According to the Ravdin Award's selection committee in 2008: "Implementing innovative, non-traditional, and highly sophisticated approaches to the most complex surgical problems has become his trademark, and, as such, Dr. Rosato is frequently sought out by surgeons who have reached their clinical limit."

Rosato also exemplified one of the characteristics of the new honorees as "master clinicians" – he served as a kind of ambassador for the institution, willing to share his expertise to all. He was well known for his readiness to mentor medical students.

Ravdin, Miller, Rosato, and the other recipients above – a pattern seems to be emerging!

Another Penn clinician widely admired by both his patients and his colleagues is John Glick, M.D., an acknowledged leader in the areas of breast cancer, Hodgkin's disease, and non-Hodgkin's lymphoma. After 21 years as director of the Abramson Cancer Center, he continues as president of the Abramson Family Cancer Research Institute, as a vice president of UPHS, and as associate dean for resource development at the medical school. His newest role is as chair of the selection/executive committee of the Academy of Master Clinicians. More than 25 years ago, in *Penn Medicine* magazine, one of his colleagues had this to say about Glick: "He always gives every one of his patients his essence. He really sets

John Glick, M.D.

a standard on how one should best take care of a patient both physically and psychologically." Glick, too, is a winner of the I. S. Ravdin Master Clinician Award. According to one of the supporting letters, "he defines the very nature of a master clinician."

It is no surprise, then, that Glick would be one of major forces behind the creation of the Academy, ably helped by Victoria Mulhern, director of Faculty Affairs and Professional Development. With Glick, the other founding members of the Academy of Master Clinicians, and the inaugural class, the tradition of clinical excellence lives on at Penn Medicine. As Glick has stated: "What we do for our patients is of critical importance to our missions of research, clinical care, and education." ■

# Development Matters

# BASIC SCIENCES AT PENN:

## PHILANTHROPY NEEDS TO LEAD THE CHARGE

**It's a common and disturbing theme in 21st century biomedical research: Funding for the sciences, especially basic science, is under constant threat. Overall spending on biomedical research – from both the public and private sectors – continues to fall. According to a report in *The Economist*, spending in U.S. pharmaceutical companies fell by 15% over six years, and the National Institutes of Health budget is 22% less than it was a decade ago.**

**"While the scientific opportunities have never been more exciting than right now, the stress on the biomedical community in the U.S. has never been more severe," NIH director Francis Collins commented this April. "We are throwing away probably half of the innovative, talented research proposals that the nation's finest biomedical community has produced."**

**Yet basic scientific knowledge is at the root of why the once-deadly threat of childhood diseases is a distant memory. It's why so many patients are surviving cancer, living with diabetes, thriving after organ transplants, and enjoying longer, healthier lives.**

**Penn Medicine was one of the first to embrace and integrate science with its mission of care and education. We have played an important role in the research, testing, and teaching that have made these medical advances a standard of care.**

**With 15 departments in the top 10 for NIH funding and one of the best graduate education programs in the nation, Penn continues at the forefront of biomedical research. While dollars are dwindling, the supply of novel ideas arising from emerging areas of science and technology has never been more abundant.**

**Five leaders in the basic sciences at Penn share their thoughts about how philanthropic support can help.**

## GENETICS: MOVING FROM PROMISE TO PRESCRIPTIONS

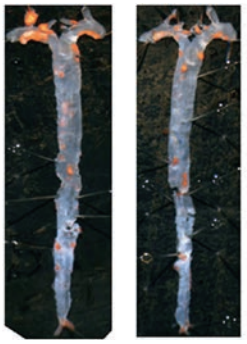
You simply cannot underestimate the effect of government budget cuts on biomedical research – and the future of our nation's health. We're already facing tremendous challenges getting promising new drugs to market, and yet, because of the sequester, I had to shelve a significant proposal that would have accelerated the commercialization process. At Penn, we know it can be done – we had success with launching a new drug for a rare genetic disorder that results in high cholesterol – but the need across all medical conditions is tremendous. **Philanthropy is the only way we'll be able to bridge the gap in development and meet that need.**

– Daniel J. Rader, M.D.
*Chair, Department of Genetics*
*Associate Director, Institute for Translational Medicine and Therapeutics*

In a recent paper written with Dr. E. John Wherry – highlighted later in this article – Dr. Rader identified a gene and its expressed protein that could have implications for atherosclerosis.

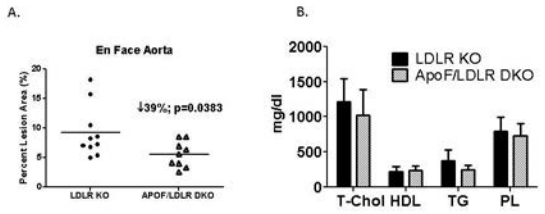
These photos show the aortas of mice, stained to show the lesions caused by atherosclerosis (in red). In both samples, the gene *Ldlr* was turned off, or "knocked out" (KO). The right-hand photo shows the study gene, *ApoF*, also turned off or "double knock out" (DKO).

Seeing is believing: there is less atherosclerosis in the mouse with the *ApoF* gene also turned off. Growing understanding about this gene, and which pathways it uses to cause disease, could reveal multiple future drug targets.



***LDLR* KO** ***ApoF/LDLR* DKO**

Figure 1




## GIVING INFORMATION

*You can join us in our drive to enhance medical education, research, and patient care by supporting any or all of these exciting projects.*

*To learn more or to make a gift today, visit PennMedicine.org/giving*, call (215) 898-0578, or send your check made out to the "Trustees of the University of Pennsylvania" to:

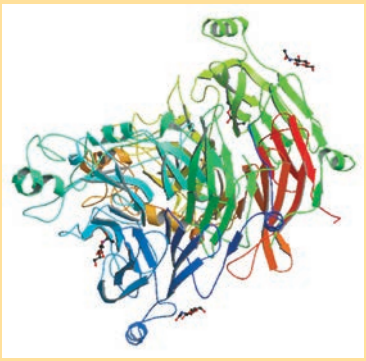
**Penn Medicine Development & Alumni Relations**
**3535 Market St., Suite 750, Philadelphia, PA 19104-3309**

# MEDICINE'S FRONT LINE

## STEM CELL BIOLOGY: THE KEY TO THE BODY'S REGROWTH AND REPAIR

The past decade has seen hope, hype, and controversy surrounding stem cell research. Understanding the basic science of how organs grow is an important key to realizing the full potential of stem cells to regenerate damaged tissues. For example, now that we know more about how stem cells influence the way the heart develops, more babies born with heart defects are surviving to adulthood and we are developing methods to rejuvenate failing hearts. These successes offer opportunities for transformational new treatments and care, yet government restrictions on funding remain – even while other nations have been able to advance their research programs. **We need philanthropic support to keep Penn at the forefront.**

– Jonathan A. Epstein, M.D.
*William Wikoff Smith Professor of Medicine*
*Chair, Department of Cell and Developmental Biology*



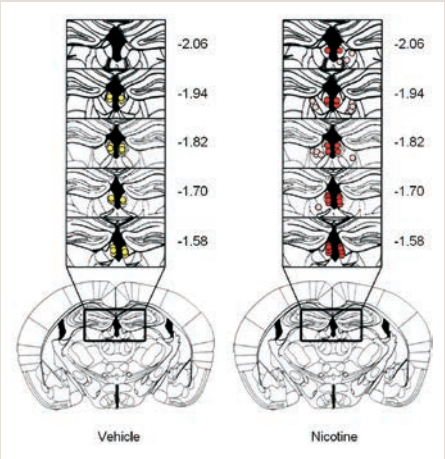
Dr. Epstein's recent *Nature Medicine* paper identified a "guidance" molecule, appropriately named semaphorin 3d, which is crucial for the normal patterning of pulmonary veins – a new model for explaining abnormalities.

Pulmonary veins normally enter the left atrium of the heart. In mice who do not have this "guidance" molecule, the veins enter a different part of the heart – the coronary sinus. Understanding how these molecules work during embryonic development could help physicians prevent certain forms of heart failure.

## NEUROSCIENCE: IT'S ALL IN THE MIND

I believe we are in a "golden age" in the field of neuroscience. New technologies and molecular and genetic approaches are converging, allowing us to do things we could never do before. **We need to get these tools in the hands of basic scientists** so they can understand the brain in a way that's unprecedented. There is no boundary of where neuroscience can reach, from bioengineering to surgery and psychiatry, and Penn is the place where those exciting connections can be made.

– John A. Dani, Ph.D.
*Chair, Department of Neuroscience*
*Director, Mahoney Institute for Neurosciences*



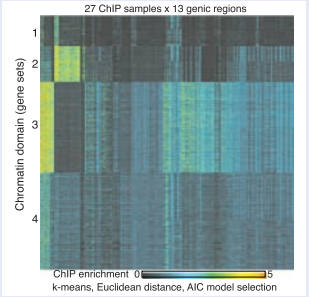

Dr. Dani has long studied how people become addicted to cigarettes and what causes the symptoms of nicotine withdrawal. A paper in *The Journal of Neuroscience* explains how nicotine works on the cellular level to produce those symptoms.

The diagram shows shows where researchers injected drugs – which would block specific types of receptors – into the brain regions of mice either dosed with nicotine (red dots) or a placebo (known as a "vehicle," in yellow). The appearance of symptoms of withdrawal in the nicotine-dosed mice helped confirm the brain signaling systems involved.

## EPIGENETICS: THE MASTER CONTROL OF OUR DNA

Until recently, scientists believed that mutations in DNA – hence, genetics – were the only genomic source of human diseases. But it turns out that simple disease-causing mutations are relatively rare. We now believe that epigenetics – the layer of regulation over our DNA that turns genes on and off – is key to aging, infertility, cancer, immunity, and how our bodies respond to stress, and will be able to teach us much more about human health and disease. I was lucky to be working on the right proteins when the age of epigenetics began in 1995, and I feel proud that we have built a program that has become among the nation's best in a very short time. I don't think there's an area of biology and medicine that epigenetics does not touch, so **we need to keep building on that investment.**

– Shelley L. Berger, Ph.D.
*Daniel S. Och University Professor*
*Director, Penn Epigenetics Program*




Why do female carpenter ants that are genetically the same end up as either queens or workers with very distinct physical appearances and roles? This square is a visualization of the 9,861 protein-coding genes sequenced for a study to learn how epigenetics may play a role in determining ants' social caste and behavior.

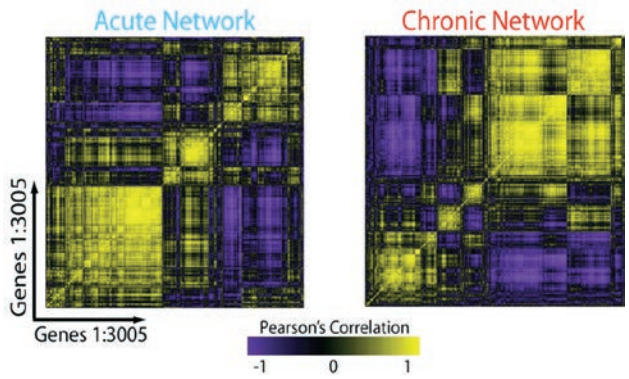
The four different horizontal bands mark differences in the expression of the DNA and proteins in a cell's nucleus, also known as chromatin. These epigenetic clues helped Dr. Berger's team identify which modifications were responsible for the social division of ants.

# Development Matters

## IMMUNOLOGY: TEACHING THE BODY TO HEAL ITSELF

As a basic scientist, it has been thrilling to witness Penn Medicine make groundbreaking strides, applying our findings to clinically translatable approaches. Penn's commitment to multi-disciplinary collaboration means our work in viral immunity and immune regulation can have a significant impact on the treatment of cancer, transplantation, and infection. The promise has never been greater – as well as the need for new hope for our patients and their families. **Philanthropy will be crucial in rapidly expanding the scope of our work**, providing the resources we need for basic research to touch even more lives.

– E. John Wherry, Ph.D.
*Associate Professor, Department of Microbiology*
*Director, Penn Institute for Immunology*




As part of his renowned work in immune system T cells, Dr. Wherry and his team examined how T cells may become "exhausted" – no longer able to destroy infections. By comparing which genes turn "on" and "off" when a certain kind of T cell, CD8+, either functions properly or becomes exhausted, researchers can begin to identify targets for keeping these immune cells working hard in chronic infections and cancer.

These "heat maps" depict networks of genes – defined by strong correlations in yellow – and identify pathways and genes that can be studied further for improving immune responses to infections and tumors.

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### JOIN THE RIDE TO CONQUER CANCER, OCT. 11-12

Philadelphia's first annual Ride to Conquer Cancer® will take place October 11-12, 2014. This ride isn't just for cyclists or athletes. It's for anyone who wants to strive for the life-changing goal of defeating cancer.

The 150+ mile cycling adventure through the picturesque landscapes around Philadelphia is designed with more casual riders in mind, and organized training activities are available to help you prepare. Hundreds of survivors, family members, students, alumni, faculty, and friends are expected to participate.


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The spaces shown here, and more, are available to be named. For information, contact Brett Davidson, Executive Director of Development & Alumni Relations, at (215) 898-9175 or Brett2@upenn.edu

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# AMERICA'S FIRST MEDICAL SCHOOL IS TURNING 250!

**Please join us on campus and around the U.S. to celebrate.**

**Monday, September 8, 2014**

250th Kick-Off Celebration Cake Party
4:00 – 5:00 p.m.
College Green, Penn campus

**Monday, November 3, 2014**

Penn to You Boston
The Fairmont Copley Plaza
Boston

**Sunday, November 9, 2014**

AAMC Annual Meeting
Hyatt Regency Chicago
and Swissotel Chicago

**Friday, May 15, 2015**

All classes welcome to reunion dinner and other activities

**Saturday, May 16, 2015**

Ribbon Cutting of the
Henry A. Jordan M'62
Medical Education Center
10:30 a.m. – 12 noon

250th Celebration Black-tie Gala
7 – 11 p.m.
at the Philadelphia Museum of Art
All Proceeds will benefit the
250th Celebration Fund

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**WWW.PENNMEDICINE.ORG/250TH**

## SPECIAL GRADUATION CONGRATULATIONS TO THREE PENN MEDICINE TRUSTEES

To **Ray Perelman, W '40, HON '14**, and **George Weiss, WG '65, HON '14**, for receiving Penn's Honorary Doctor of Laws Degree

To **Ray Welsh, W '53**, and his wife **Joanne, CW '52**, upon the graduation of their granddaughter **Christina** from the Perelman School of Medicine

With sincere appreciation for all you do for Penn Medicine.

Ray Perelman, W '40, HON '14, (seated) and George Weiss, WG '65, HON '14 (second from right) received honorary degrees from the University on May 19.

## Progress Notes

*Send your progress notes to:*
Donor Relations
*Penn Medicine Development and Alumni Relations*
*3535 Market Street, Suite 750*
*Philadelphia, PA 19104-3309*

# '60s

**Daniel M. Albert**, M.D. '62, G.M.E. '66, has been appointed "distinguished senior editor" of *Ophthalmology*, official journal of the American Academy of Ophthalmology. He joins the editorial board after serving 20 years as editor-in-chief of *JAMA Ophthalmology*. Albert is the Frederick Allison Davis Professor of Ophthalmology and Visual Sciences and director of the Eye Pathology Laboratory at the University of Wisconsin School of Medicine and Public Health. He was named founding director of the McPherson Eye Research Institute and appointed to its advisory board in 2012.

**David C. Rilling**, M.D., G.M.E. '67, Sellersville, Pa., a member of Pennridge Surgical Associates, gave a presentation at the Sellersville Theater in April 2013, sponsored by the West Rockhill Historical Society. It was about one of the most prominent milestones at Grand View Hospital – reattaching the severed arm of Jesse Masarjian on June 9, 1977. Masarjian, 19 years old at the time, accidentally severed his arm at the shoulder while using an electric circular saw at a furniture factory. He was near death when the ambulance brought him to the hospital, where he was operated on by Rilling, Dennis L. Moyer, M.D., and David C. Rising, M.D. Together, they worked seven hours to reattach the bone, veins, nerves, arteries, muscles, and skin of Masarjian's arm. As a surgeon in the Vietnam War, Rilling had experience repairing muscles; Rising had experience repairing bone using implanted plates and reattaching severed nerves. The operation was a dramatic success, and the surgical team and Masarjian himself gathered again, 35 years later.

**Marvin J. Lipschutz**, M.D. '68, was named senior vice president of Greenwich Hospital. He joined the hospital in 2007 and most recently served as chief medical officer and chief quality officer, with a focus on clinical quality, performance improvement, and patient safety. Previously he was senior vice president of medical affairs at South Shore Hospital in Massachusetts.

**Elaine S. Jaffe**, M.D. '69, received the 2013 Henry M. Stratton Medal from the American Society of Hematology for her outstanding accomplishments in the fields of lymphoma and iron homeostasis and erythropoiesis. Jaffe is head of the hematopathology section of the Laboratory of Pathology in the intramural program of the National Cancer Institute. Jaffe joined the National Cancer Institute as a resident in anatomic pathology and has remained there for more than 40 years.

# '70s

**Jack A. Elias**, M.D. '76, G.M.E. '82, former chair of medicine at the Yale School of Medicine, became Brown University's seventh dean of medicine and biological sciences in September. Elias has cared for patients with a wide variety of lung ailments and injuries. He also has conducted research on the effects of smoking and conditions including asthma, chronic obstructive pulmonary disease, pneumonia, and pulmonary fibrosis. With consistent support from the National Institutes of Health, Elias has trained scores of young researchers and published more than 200 original peer-reviewed research papers. He holds several patents and has frequently earned funding from industry and private foundations. He served as chair of medicine and physician-in-chief at Yale-New Haven hospital beginning in 2006.

**Robert J. Spiegel**, M.D. '75, was elected to the board of directors of Edge Therapeutics. Spiegel spent more than 25 years at Schering-Plough, where he was deeply involved in clinical development. He retired from the firm in 2009 as chief medical officer and senior vice president of its pharmaceutical research arm.

**Ronald L. Arenson**, M.D., G.M.E. '79, was named president-elect of the board of the directors of the Radiological Society of North America. He is the Alexander R. Margulis Distinguished Professor and Chairman of the Department of Radiology and Biomedical Imaging at the University of California, San Francisco, where he has been since 1992. Arenson began his academic career in 1976 at the University of Pennsylvania after serving in the U.S. Navy at the National Naval Medical Center. During his tenure at Penn, Arenson was associate chairman of clinical services in radiology, director of administrative services, and interim vice provost for information systems and computing for the campus.

# '80s

**Gary A. Koretzky**, M.D. '84, Ph.D., has been named dean of the Weill Cornell Graduate School of Medical Sciences and senior associate dean for research at Weill Cornell Medical College. Koretzky was the Francis C. Wood Professor of Medicine at the Perelman School of Medicine, where he also served as the department's vice chair for research and chief scientific officer. A former associate director of Penn's M.D.-Ph.D. Combined Degree program, he served on the executive committees for the graduate programs in immunology and in cellular and molecular biology. He also was the co-leader of the immunology program at the Abramson Cancer Center.

# '90s

**Christina A. Bandera**, M.D., G.M.E. '98, has been appointed chief of obstetrics and gynecology at Rhode Island Hospital and The Miriam Hospital. She is board-certified in both obstetrics and gynecology, as well as gynecologic oncology, and her clinical and research interests include the treatment and prevention of gynecologic cancers. In addition, Bandera leads the Center for Gynecologic Cancers at the Women's Medicine Collaborative, Rhode Island's largest multidisciplinary center dedicated to the unique health needs of women.

# '00s

**Adam David Simmons**, M.D. '00, now heads the Parkinson's Disease and Movement Center at the Hospital for Special Care in New Britain, Conn. Certified by the American Board of Psychiatry and Neurology as well as the American Board of Integrative Holistic Medicine, Simmons completed his residency and received a fellowship in movement disorders at Beth Israel Deaconess Medical Center. Previously, he was a neurologist and acupuncturist at Springfield Neurology Associates.

**John H. Leaman**, M.D. '01, M.B.A., was appointed to the executive leadership team of Medgenics, Inc., developer of a novel technology for the sustained production and delivery of therapeutic proteins in patients using their own tissue. Leaman was most recently the vice president of commercial assessment at Shire PLC, with responsibility for the strategic assessment of licensing and M&A opportunities. He received his M.B.A. degree from the Wharton School. While completing a Rhodes scholarship at Oriel College, University of Oxford, he received a degree in psychology, philosophy, and physiology.

**Jay R. Venkatesan**, M.D. '02, M.B.A., has been appointed to the board of directors of Genesis Biopharma, Inc., now part of Lion Biotech, which is focused on developing and commercializing novel cancer immunotherapies. Venkatesan is the founder, portfolio manager, and managing director of Ayer Capital Management, a global health-care long/short equity fund.

**Randy C. Robinson**, M.D., G.M.E. '04, was named chief medical officer of R-Health, a recently launched provider of direct primary care, based in Philadelphia. R-Health aims to bring the doctor-patient relationship back to the forefront of primary-care medicine in order to improve quality and reduce costs. Robinson

is also one of the founders of the start-up, which takes a membership-based approach and uncouples primary care from insurance. Previously, he was CEO of Independence Pain Associates. From 2004 to 2012, Robinson was also a staff physician at Holy Redeemer Hospital.

**Ali Behbahani**, M.D. '07, M.B.A., has been promoted to partner in New Enterprise Associates, Inc., a global venture capital firm. Behbahani, who joined NEA in 2007, specializes in investments in the biopharmaceutical and medical device sectors. Earlier, he was a consultant in business development at The Medicines Company, a specialty pharmaceutical company developing acute-care cardiovascular products. He previously held positions at Morgan Stanley Venture Partners and at Lehman Brothers. He also conducted basic science research in the fields of viral fusion inhibition and structural proteomics at the National Institutes of Health and at Duke University. He received his M.B.A. degree from the Wharton School.

## OBITUARIES

# '30s

**Francis Schumann**, M.D. '39. G.M.E. '46, Machias, Maine, a retired surgeon; December 18, 2013. He completed a general surgery residency at Philadelphia General Hospital, followed by a fellowship at the Lahey Clinic. He then joined the Army Air Force during World War II and served as a flight surgeon in the European Theater. After the war, Schumann practiced general surgery at Chestnut Hill and Roxborough Memorial hospitals for 35 years. An active member of the medical school Class of 1939 alumni, he led the effort to establish the first class scholarship there. In 2002, he received the Alumni Service Award for his efforts. In retirement he was active in local causes in Maine, particularly conservation and the renovation of the Porter Memorial Library in Machias.

**Norman M. Wall**, M.D. '39, Orlando, Fla., a retired cardiologist; September 3, 2013. As a medical officer in the Army during World War II, he helped establish medical facilities in Palestine, one of which later became Israel's largest hospital and research center. Wall became a commanding officer of the 367th Station Hospital Middle East Theatre, with the rank of lieutenant colonel. In 1950, he joined the Good Samaritan Hospital and eventually became the hospital's chief of staff, chief of medicine and cardiology, and director of medical education. A former president of the Pennsylvania Heart Association, he was also a Fellow of the American College of Cardiology.

# '40s

**Sidney N. Franklin**, M.D. '42, G.M.E. '46, Los Lunas, N.M., former professor of medicine at Penn; July 7, 2013. He served three years as a captain in the U.S. Army Medical Corps, where he took part in the Battle of the Bulge and the liberation of Buchenwald. He worked at Penn's School of Medicine from 1948 to 1982. For several years, he was also a staff physician at the Veterans Administration Outpatient Clinic. In 1977, he was honored with a Meritorious Award by the American Legion for his early recognition of an epidemic of Legionnaires Disease at the Bellevue Stratford Hotel in Philadelphia during the American Legion convention. He moved to Orange County in 1982, where he received an appointment as assistant professor of clinical medicine at the University of California, Irvine, and as an attending physician at the Diabetes Clinic at the University of California Medical Center. He was appointed the Orange County medical consultant to the State Medical Board of California in 1984.

**Frederick D. Dove Jr.**, M.D. '44, Williamsport, Md.; September 20, 2013. He served in the U.S. Army during World War II. He practiced 42 years as an obstetrician and gynecologist, and served as chief of staff at Washington County Hospital.

**Ray W. Collins Jr.**, M.D. '46, Middlebury, Vt., a retired surgeon; September 14, 2013. He served in the U.S. Army as a surgeon from 1942 to 1945 in the Atlantic and Pacific theaters. He moved to Middlebury in 1952, where he became the town's first full-time surgeon. While working at Porter Hospital, he raised funds for the American Cancer Fund, the American Heart Fund, and the University of Vermont College of Medicine (UVM). His services were recognized with a variety of awards, including the State Medical Society Robins Award for Outstanding Community Service by a Physician in 1980 and the UVM Physician of the Year in 1983.

**David P. McCallie**, M.D. '46, G.M.E. '50, Chattanooga, Tenn., a retired internist; October 7, 2013. He served in the U.S. Navy in California. In 1952 he returned to Chattanooga to practice internal medicine. He helped form the McCallie Medical Group, which ultimately became one of the founding practices of Beacon Health Alliance. He served as chief of the medical staff for both Erlanger and Memorial hospitals, and in 1969 he was president of the Chattanooga-Hamilton County Medical Society. In that position, he spearheaded the passage of state legislation to establish the Chattanooga Hamilton County Hospital Authority in 1976 and served as its first board chairman. He also helped to create the Siskin Hospital for Physical Rehabilitation, serving as its first chairman from 1987 to 1992. His honors include the Tennessee Medical Association's Outstanding Physician of the Year in 1981 and the Tennessee Hospital Association's Distinguished Community Service Award in 1976.

**John T. Tidd**, M.D. '46, G.M.E. '50, Louisville, Ky., a retired physician; July 31, 2013. He served on the medical staff at Sacred Heart Hospital in Yankton from 1951 until his retirement.

**James N. Dill Jr.**, M.D., G.M. '49, Pittsburgh; May 21, 2013. He served in the Medical Corps at the National Naval Medical Center at Bethesda, Md., and was a medical officer aboard a troop transport in the Pacific and at the United States Naval Hospital at Quantico, Va. He practiced medicine for 45 years at McKeesport Hospital, where he served as president of the medical staff and as clinical chief of staff in obstetrics and gynecology.

**Robert W. Meyers**, M.D. '49, G.M.E '53, Clayton, Mo., a retired psychoanalyst and professor of psychiatry; January 22, 2014. He served as a naval officer and neurologist at Camp LeJeune, N.C., during the Korean War. In 1968 he was one of five founding members of the St. Louis Psychoanalytic Institute, where he became a training and supervising psychoanalyst and director.

**Paul M. Norris**, M.D. '49, Peoria, Ill., a retired surgeon; August 6, 2013. A veteran of World War II, he re-enlisted at the onset of the Korean War and was chief medical officer in Leghorn, Italy, until 1954. He practiced in Jacksonville, Ill., and in Peoria, Ill., until he retired in 1990. He served on the faculty of the University of Illinois College of Medicine at Peoria. He was president of the Peoria Medical Society, delegate to the Illinois Medical Society, and a member of the Illinois College of Surgeons..

**Arnold J. Rawson**, M.D., G.M.E. '49, Sarasota, Fla., former professor of pathology at Penn; January 28, 2014. He joined the U.S. Public Health Service in World War II and was assigned to the U.S. Coast Guard. In this capacity he was medical officer for a flotilla of twelve Landing Craft Infantry ships and took part in the Battle of Okinawa. In 1950 he accepted a position as chief of laboratories in Norfolk General Hospital, Va. He returned to Penn's School of Medicine as an assistant professor of pathology and eventually was promoted to full professor. Before his retirement, he served as acting chair of the department. Author of some 100 scientific papers dealing chiefly with cancer and rheumatoid arthritis, he was honored with the University's Lindback Foundation Award for Distinguished Teaching.

**George F. Tibbens**, M.D., G.M. '49, Washington, Pa., a retired physician; September 16, 2013. He joined the U.S. Air Force in the Korean War and was stationed in Japan and the Philippines. After his discharge as a captain in 1953, he began to practice medicine in 1954 and was on the staff of Washington Hospital.

**Roland F. Wear Jr.**, M.D. '49, G.M.E. '53, Gainesville, Ga., an internist who retired as corporate medical director of Campbell Soup Company; May 27, 2013. He had been a member of the board of directors of the American Occupational Medical Association. In 1984, he received the Health Achievement in Occupational Medicine Award from the American College of Occupational and Environmental Medicine.

## '50s

**Homer C. Curtis**, M.D., G.M.E. '50, Gladwyne, Pa., a retired psychoanalyst; June 4, 2013. As a young man, he went on a Mormon mission to Germany for two years just before the start of World War II. During the war, he served in the U.S. Army Medical Corps in the States. He graduated from the University of Utah Medical School in 1944 and began his psychiatric training as a lieutenant in the Army Reserve. He completed his residency at the former Institute of Pennsylvania Hospital, where he later became senior attending psychiatrist. He held positions as professor of psychiatry at Hahnemann Medical College and as adjunct professor of psychiatry at the University of Pennsylvania Medical School. He was a training and supervising analyst at the Institute of the Philadelphia Association for Psychoanalysis and, later, at the Psychoanalytic Center of Philadelphia. A recipient of the Lifetime Achievement Award from the Philadelphia Psychiatric Society, he had served as president of the Philadelphia Association for Psychoanalysis and of the American Psychoanalytic Association.

**Adele Kynette Friedman**, M.D. '50, G.M. '58, Philadelphia, a retired associate professor of radiology at the Perelman School of Medicine; December 27, 2012. She was the second woman to complete her residency in the school's Department of Radiology. An early specialist in mammography, she also taught the radiographic anatomy section of gross anatomy for first-year medical students, introducing thousands of students to x-rays. She was active in Women in Medicine groups for medical students and trainees. Her late husband, **Sidney Friedman**, M.D. '43, was a professor of pediatrics and pediatric cardiologist in the Children's Hospital of Philadelphia and the Perelman School of Medicine. One of her sons is **David Friedman**, M.D. '84, clinical assistant professor of pediatrics in the Perelman School of Medicine and associate director of the transfusion service at CHOP.

**William H. Spencer Jr.**, M.D. '50, G.M.E. '55, Boise, Idaho; October 7, 2013. He retired as chief of anesthesiology at Newton Memorial Hospital in New Jersey and took part in various volunteer organizations in Boise. He had served as a lieutenant at Naval Base Coronado in California.

**John A. Buesseler**, M.D., G.M.E. '51, Lubbock, Tex., former dean of the medical school of Texas Tech Health Sciences University; March 7, 2013. He served in World War II as a first lieutenant in the Medical Corps and as battalion surgeon. He also served during the Korean War on active duty with the Pennsylvania Air National Guard and in the Vietnam War as an army senior flight surgeon and special forces colonel. He practiced ophthalmology in Madison, Wis., for six years before being appointed founding chief of ophthalmology at the University of Missouri Medical Center in Columbia in 1959. In 1970, he moved to Lubbock, where he was appointed founding dean of the school of medicine, founding vice president for health affairs, founding vice president for health sciences of the Texas Tech Health Sciences University, and founding chief executive officer of the Texas Tech Health Sciences University and Center. In 1973, he was named university professor by the university's board of regents. In 1973 and 1987, the State of Texas House of Representatives awarded him with citations for his contributions in medicine, civic leadership, and service to community, state, and nation.

**Abraham A. Lurie**, M.D. '52, G.M. '56, Bryn Mawr, Pa., a retired anesthesiologist at Lankenau Hospital; January 31, 2013. He had collaborated with Christian J. Lambertsen, M.D. '43, in research on respiratory and cerebral circulatory control and had been on the faculty of Tufts University and the University of Rochester.

**Howard E. Lessner**, M.D. '53, Miami, emeritus professor of oncology at the University of Miami; April 18, 2012. He had published in *Annals of Internal Medicine, Archives of Surgery,* and *The New England Journal of Medicine*.

**James L. Fawcett**, M.D. '55, Cleveland, a retired urologist; June 23, 2013. He served in the U.S. Army with the rank of major and was honored by the Allegheny County Medical Society for his 50 years of medical service.

**James P. Sommerfeld**, M.D., G.M. '55, New Castle, Pa., a retired pediatrician; June 28, 2013. He served in the U.S. Navy during World War II and was a medical doctor in the Air Force during the Korean War. In that role, he received the Korean Service Medal, the United Nations Service Medal, and the National Defense Service Medal. A former president of the medical staff of Jameson Hospital and of St. Francis Hospital, he was a board member of the Pennsylvania Rehabilitation Council. He had been a Fellow of the American Academy of Pediatrics.

**Charles E. Connant**, M.D., G.M. '56, Short Hills, N.J.; April 13, 2013. He had been a fellow in cervical dysplasia and pathology at Brookdale Medical Center in Brooklyn. He spent most of his career at the Margaret Hague Maternity Hospital and at Christ Hospital in Jersey City, where he was assistant director of obstetrics and gynecology. In 1977 he became a clinical professor of obstetrics and gynecology at University of Medicine and Dentistry of New Jersey. A Fellow of the American College of Surgeons and of the American College of Obstetricians and Gynecologists, he was co-author of *Minimal Access Gynaecology* (1995).

**Burton Zweiman**, M.D. '56, G.M.E. '60, emeritus professor of medicine and neurology in the Perelman School of Medicine; December 24, 2013. After completing a residency in internal medicine at Bellevue Hospital Center, he became a fellow in immunology at NYU Medical Center. He completed his training in allergy and immunology at HUP. After service in the U.S. Navy, he was appointed to the Penn faculty in 1968. He became a full professor in 1975 and served as chair of the division of allergy and immunology from 1974 until he became emeritus in 1998. Zweiman helped establish HUP's renal transplant program and developed its first clinical immunology service laboratory. He was editor of the *Journal of Allergy and Clinical Immunology* and chair of the American Board of Allergy and Immunology. A former president of the American Academy of Allergy, Asthma, and Immunology, he was honored by the academy with its Distinguished Service Award; it also established the Burton Zweiman Lectureship. He had also received the University's Lindback Award for Distinguished Teaching.

**Robert L. Klaus**, M.D. '57, Bryan, Tex., formerly a urologist in Philadelphia and Delaware; October 25, 2013. He was a resident in both surgery and urology at the University of Kansas Medical Center before joining Einstein Medical Center. There, he was senior attending physician from 1981 to 1984 and later served as the center's chief of urology, a position his father, Irving Goncer Klaus, had held previously. Earlier, Klaus was chief of surgery and urology at the Philadelphia Geriatric Center. From 1990 to 2010, he also was on the staff at Milford Memorial Hospital in Milford, Del., where he had a private practice as well. A former president of the Philadelphia Urologic Society, Klaus was a Fellow of the American College of Surgeons and a member of the American Board of Urology and the Philadelphia College of Physicians.

**Albert M. Dickson Jr.**, M.D. '58, Virginia Beach, Va.; October 1, 2013. He had served in the U.S. Navy and was retired from family practice.

**Chester Barton Martin Jr.**, M.D. '58, Middleton, Wis., May 26, 2013. In 1977, he joined the faculty of the Obstetrics and Gynecology Department at the Catholic University and St. Radboud Hospital in Nijmegen, Netherlands, where he taught and researched fetal physiology and behavior and ran a clinical obstetrics practice. He also served on the Committee on Perinatal Monitoring of the Commission of European Communities (1979-84) and as chairman of the Working Group on Description and Evaluation of Cardiotocograms of the European Communities (1979-84). He was a founding member and chairman of the Dutch Perinatal Biology Study Group. An emeritus professor at the University of Wisconsin-Madison, he published 85 articles in peer-reviewed journals and chapters in 10 books. In recognition of his commitment to medical education and research, the University of Wisconsin has established the Chester B. Martin, M.D., Training Program Award.

**Wallace T. Miller Sr.**, M.D., G.M. '58, emeritus professor of radiology; June 23, 2013. He received a medical degree from Jefferson Medical School and took an internship at Akron City Hospital. He then came to HUP with a fellowship in radiology and joined the faculty of the School of Medicine as assistant instructor of radiology in 1957. A former chief of the diagnostic section in HUP's radiology department, he practiced until his retirement in 2012. Miller received many teaching honors, including the first I. S. Ravdin Master Clinician Award from Penn's School of Medicine; the Medical Student Government Teaching Award; and the University's Lindback Award for Distinguished Teaching. He also was the recipient the Gold Medal Award from the Radiological Society of North America and the Philadelphia Roentgen Ray Society Outstanding Educator Award. Miller had been editor of *Seminars in Radiology*, wrote three medical textbooks, and published several articles that are considered seminal works in diagnostic radiology.

The Wallace T. Miller Sr. Endowed Chair of Radiologic Education was established in his honor in 2001 and the Wallace T. Miller Scholarship Fund in 1996.

One of Dr. Miller's sons, Wallace T. Miller Jr., M.D. '86, is associate professor of radiology in the Perelman School of Medicine.

**Bernardo Moreno**, M.D., G.M. '58, Fort Lauderdale, Fla.; July 8, 2013. He was a professor of surgery and dean of the Medical School at Javeriana University in Colombia. He was also executive director of the Colombian Association of Medical Schools and director of the Colombian Institute of Family Welfare. After moving to Florida in 1971, he earned surgical privileges at local hospitals, including Holy Cross Hospital, and later became president of its medical staff and a member of its board of trustees. He was a Fellow of the Colombian College of Surgeons and of the American College of Surgeons. In 1998, he was named "Doctor of the Year" by the Caducean Society of Greater Fort Lauderdale.

**Harold Nichols Burnham Jr.**, M.D. '59, Raymond, Maine; July 31, 2013. Before attending medical school, he taught at Scattergood Friends School in Iowa. As a Quaker, he served nine months in prison as a conscientious objector. As a young doctor, he made house calls, delivered babies, and offered hypnotherapy and other alternative services. After retiring from private practice in 1986, he worked for the chemical dependency program of Mercy Hospital.

## '60s

**Fredric L. Hildebrand Sr.**, M.D. '60, Neenah, Wis.; January 4, 2014. He completed his training at the Mayo Graduate School of Medicine. After more than 40 years, he retired after practicing in the field of internal medicine and pulmonary disease. He was a Fellow of the American College of Chest Physicians and of the American Thoracic Society. During a period of rapid growth, Hildebrand oversaw the merger of several small clinics into what is now a regional medical group, Affinity Medical Group, with more than 200 staff members. After retiring, he volunteered at a local free clinic.

**Dorothea D. Glass**, M.D., G.M. '61, Palm City, Fla., former chief of physical medicine and rehabilitation at the Miami Veterans Affairs Hospital; April 20, 2013. She had also been a clinical professor of orthopaedics at the University of Miami and was an emeritus professor of rehabilitation medicine at Temple University. Glass was a recipient of the Frank H. Krusen, M.D., Lifetime Achievement Award, presented by the American Academy of Physical Medicine and Rehabilitation.

**Walter G. Bishop**, M.D. '63, Greenwood, S.C., a retired physician; June 20, 2013. He served in the United States Army for two years at Fort Jackson. He practiced medicine for 42 years.

**Patrick M. Growney**, M.D., G.M.E. '64, Villanova, Pa., a retired Main Line hematologist who helped start the Bryn Mawr Medical Specialists Association; December 8, 2013. After earning his medical degree at Georgetown University, he was a resident in internal medicine at HUP and completed a fellowship in hematology. In 1964, he joined the staff of Bryn Mawr Hospital, where he was chief of hematology for 34 years. He served a term as president of the hospital's staff and was a trustee for four years. Growney was also instrumental in providing medical coverage for the Rush Hospital for Consumption and Allied Diseases in Malvern, which later merged with Bryn Mawr Hospital to become Bryn Mawr Rehabilitation Hospital.

**John Cathcart Jr.**, M.D., G.M.E. '65, Greenwood, S.C.; August 25, 2013. He served as a lieutenant in the U.S. Army. He practiced obstetrics and gynecology for 35 years. After retiring from his practice, he served as chairman of the Cherokee County Health Policy and Planning Council and the Cherokee County Chapter of the American Red Cross.

**Alexander Fasulo**, M.D., G.M. '65, Long Beach Island, N.J., a retired orthopaedic surgeon; June 27, 2013. As a young man in Italy during World War II, he served as a translator for the British Army. He earned his medical degree from the University of Naples in 1946. He later worked as a company physician for NJM Insurance Company in New Jersey before helping form the Trenton Orthopaedic Group. He also worked as an attending physician at St. Francis Hospital and Hamilton Hospital and served as chairman of orthopaedics at both hospitals for several years.

**James E. Fulton Jr.**, M.D., Ph.D., G.M.E.'66, Miami, a dermatologist; July 4, 2013. He earned his doctorate in biochemistry at the University of Miami. He opened the Acne Research Institute and developed and manufactured a line of patented skin care products. In 1990, he founded JEF Medical Group, a cosmetic surgery and dermatology practice where he pioneered fat transfer techniques and laser surgery. The author of *Acne Rx*, he published more than 300 medical articles on cosmetic surgery and dermatological procedures. He was a member of several professional groups, including the Dermatology Foundation's Leader Society. A Fellow of the American Academy of Cosmetic Surgery and the American Academy of Dermatology, he worked at Penn with Albert Kligman, M.D. '47, Ph.D., in developing tretinoin (Retin-A).

## '70s

**John F. McClellan**, M.D. '75, Marshfield, Mass.; September 11, 2013. He was medical director of Plymouth Medical Group, chairman of an overseeing committee at Harvard Pilgrim Health Care, and chief of internal medicine at Jordan Hospital.

**Philip A. O'Dowd**, M.D. '77, Barrington, R.I., former hematologist, residency director, and professor emeritus at Brown University; February 13, 2013. He had also been chief of staff at Roger Williams Medical Center.

**Andrew I. Weinstock**, M.D. '79, Ph.D., Philadelphia, a surgeon who was also a designer of medical software designer and programmer; October 7, 2013. His doctorate from the University of Michigan was in experimental psychology. Previously, he had had an office in Oberlin, Ohio.

## FACULTY DEATHS

**Lewis A. Barness**, M.D., Tampa, Fla., former professor of pediatrics; November 18, 2013. He entered Harvard College at the age of 16; earned his medical degree from Harvard Medical School; and did his residency and research fellowship at Boston Children's Hospital. During World War II, he served as a captain in the U.S. Army. He joined Penn's faculty in 1950. In 1972, he became the founding chairman of the Department of Pediatrics at the University of South Florida College of Medicine, a position he held until 1988. He continued his work at the University of Wisconsin School of Medicine and then returned to USF until his retirement in 2007. He made pioneering research contributions to the field of infant nutrition and metabolism. Among his honors was the John Howland Metal, presented by the American Pediatric Society.

**Homer C. Curtis**. See Class of '70

**Sidney N. Franklin**. See Class of '42.

**Adele Kynette Friedman**, M.D. See Class of 1950.

**James E. Fulton Jr.** See Class of '66.

**Nicholas A. Kefalides**, M.D., Ph.D., emeritus professor of medicine; December 6, 2013. Born and raised in Greece, he lived through the invasion and occupation of Greece by German and Italian armies and survived a period in a concentration camp. After emigrating to the United States in 1947, he went on to earn his medical degree from the University of Illinois. In 1957, Kefalides was drafted into the U.S. Public Health Service, for which he directed a research project in Lima, Peru, on the treatment of burn patients. He worked as an academic physician and scientist at the University of Chicago before coming to Penn in 1970. He was a pioneer in the study of the extracellular matrix – components of the body that fill the space between structured cells. He identified three novel components of the matrix.

With the closing of Philadelphia General Hospital in 1977, Kefalides moved his research labs to the University City Science Center. He was director of the Center's Connective Tissue Research Institute and a principal investigator. He also helped launch an interdisciplinary lecture series, "Lunch for Hungry Minds" and had been a member of Penn's institutional review board.

Kefalides became a professor emeritus in 1996. A member of the board of the Association of Senior and Emeritus Faculty, he also served as its president. In retirement, he wrote two memoirs – *Echoes From the Cobblestones* and *Finding Aesculapius Across the Atlantic*. He was a Fellow of the American Association for the Advancement of Science and a elected member of the American Society for Clinical Investigation. In 1987, he received an honorary degree from the University of Reims, France.

**Kenneth L. Kershbaum**, M.D., former clinical associate professor of medicine in the Perelman School of Medicine; March 19, 2013. After earning his medical degree from Thomas Jefferson Medical College in 1967, he practiced internal medicine and cardiology for more than 40 years at Pennsylvania Hospital. There he served twice on its executive committee and was on the board of the hospital's Cardiology Foundation for more than 20 years. In 1974, he was appointed assistant clinical professor of medicine in Penn's School of Medicine and promoted to clinical associate professor of medicine in the associated faculty in 2005. In 1986, he was awarded Pennsylvania Hospital's Viner Teaching Award.

**Wallace T. Miller Sr.** See Class of '58

**Arnold J. Rawson.** See Class of '49.

**Burton Zweiman.** See Class of '56.

LEGACY GIVING

# Compassionate Care of the Patient and Physician

*Physician, heal thyself.*

*Sharon Youcha, M.D., G.M.E. '88, believes physicians need to take the saying literally.*

*After almost two decades in obstetrics and gynecology, Dr. Youcha left her Philadelphia-area practice for advanced training in psychiatry. As she began, she read a list of burnout symptoms – exhaustion, ennui – and instantly saw herself.*

*"I was on the verge of burning out, and I didn't even recognize it," she says. "Being compassionate is part of being an excellent physician and healer, but it can be sustained long-term only when we as physicians take care of ourselves."*

*She began a crusade to help physicians guard against burnout, conducting weekend retreats and lecturing on the dangers. She helped conduct a survey for the American College of Obstetrics and Gynecology that found more than half of Ob/Gyn specialists suffered from at least one symptom of burnout. Today, she teaches empathy, compassion, and the importance of well-being to medical students as an adjunct associate professor of gynecology at Drexel University College of Medicine.*

*According to Dr. Youcha, "Pressures in the current medical system may not support the well-being of physicians or protect the time for the physician-patient relationship."*

*She considered ways to support young physicians and decided to take the unusual step of endowing an award to honor Ob/Gyn residents at Penn for excellent, compassionate patient care and to encourage them to use the funds to take "compassionate care of themselves." Through a bequest, she will add to the endowment.*

*The Department of Obstetrics and Gynecology will award the first Sharon Youcha, M.D., Compassionate Patient Care Award this year.*

*"I want the recipients to understand that they are being recognized for both their excellence in medicine and for who they are as people," she says. "I hope they will use the award for something that brings them joy."*

*Dr. Youcha chose one of a multitude of creative gift opportunities that benefit both Penn Medicine and donors. The Office of Planned Giving is ready to assist in developing an appropriate strategy to incorporate your charitable objectives. Contact Christine S. Ewan, J.D., executive director of planned giving, at (215) 898-9486 or cewan@upenn.edu. For more information, please visit www.plannedgiving.med.upenn.edu.*

## Passing Wisdom On

Penn's medical students encounter great teaching, but attending classes is not the only way they learn what they need to know. Through the Penn Pearls Teaching Awards Ceremony, the students honor those who have served as mentors outside the classroom. Those honored teach through explicit instruction and counsel or through example. They are particularly useful when imparting "the hidden curriculum" – those things students don't learn from books, lectures, and videos but that are valuable nonetheless.

Elsewhere in this issue, you can read about a new Penn Medicine program that honors "master clinicians" selected by their peers (pp. 29-31). In contrast, the Penn Pearls recipients are selected exclusively by the students, with some organizational help from the Office of Student Affairs.

I first became aware of Penn Pearls in 1998, when I assigned my assistant editor to cover the event. We knew the dean would be attending, which gave the ceremony some automatic gravitas. That year was its eighth year of existence, and, as in the years to follow, the students had singled out both attending physicians and residents. (Fellows were added in more recent years.) In return, those being honored would offer "pearls of wisdom" to the students. The pearls, as might be expected, varied widely.

For example, there was Peter Argenta, M.D., G.M.E. '99, today a gynecologic oncologist at the University of Minnesota. "Don't ever refuse a breath mint," he said. But he also emphasized the importance of making time for family and friends, even within the students' busy schedules. He also noted that the best doctors are those who can read between the lines when caring for patients.

Lisa Forman, M.D. '95, G.M.E. '98, now at the University of Colorado in Denver, was honored at the same ceremony. She passed on a lesson that she said she had learned the hard way: "If a patient is itching, wear gloves!"

### How to Treat Your Patient

In more recent years, Roger Band, M.D., assistant professor of emergency medicine at Penn Medicine, advised the students to consider how you'd want physicians to treat your own family – and to try to act that way in your own career. Along those same lines, Lauge Sokol-Hessner, M.D. '07, G.M.E. '10, an internist who recently joined Beth Israel Deaconess Medical Center, advised the students to "be present" for your patient; don't look at the clock; and "treat her as you'd treat your mother."

One of this year's recipients is Nadia L. Bennett, M.D., assistant professor of clinical medicine and associate director of the Internal Medicine Clerkship. Her pearl was about taking charge of one's own learning. An important part comes from asking questions – of attending physicians, nurse, patients, and colleagues. "You become a much stronger physician when you take a little extra time to actively engage in learning from those around you."

It's clear that the award recipients are very appreciative of this kind of recognition from the medical students. A couple of years ago, Vera Fridman, M.D., G.M.E. '10, now at Mass General, said, "there actually isn't an award more meaningful" and called it one of the most gratifying experiences in her life. Noel Williams, M.D., professor of clinical surgery and director of the Penn Metabolic & Bariatric Surgery Program, told the students "how important this award is to me." It was, he said, his first award for teaching after 18 years at Penn Medicine.

Receiving a Penn Pearls teaching award is often an indication of future success. Many of the house staff, fellows, and attending physicians who receive them go on to receive other teaching honors, not only from the Perelman School of Medicine and the University, but also from the institutions where they currently work. In many cases, the Penn Pearls are listed among their other honors in their CVs and biosketches.

### Pearls from the Past

While the Penn Pearls Awards program has been around officially for nearly 30 years, the yearbooks of the past often had dedications or salutes to clinical teachers. In its edition of *Scope*, for example, the Class of 1954 included these items under the heading of "Informals." The first two are:

1. Always remember that patients are people.
2. Consider the patient as a whole.

One of the medical school's former instructors, the late Louis R. Dinon, M.D. '49, a clinical professor of medicine, received the University's Lindback Award for Distinguished Teaching in 1982. His clinical teaching was so appreciated that an award was later established in his honor. One *Scope* from the 1990s included a page listing of what were described as "Dinon's Dictums." Among them:

- You don't take a history from a patient; the patient gives you the history.
- More is missed by not looking than by not knowing.
- Doctors need both a headlight and a heartlight.

These "Informals" and "Dictums" are very much in the tradition of "pearls of wisdom." All could very well be on a mental checklist that every physician carries in his or her head when dealing with a patient. ●

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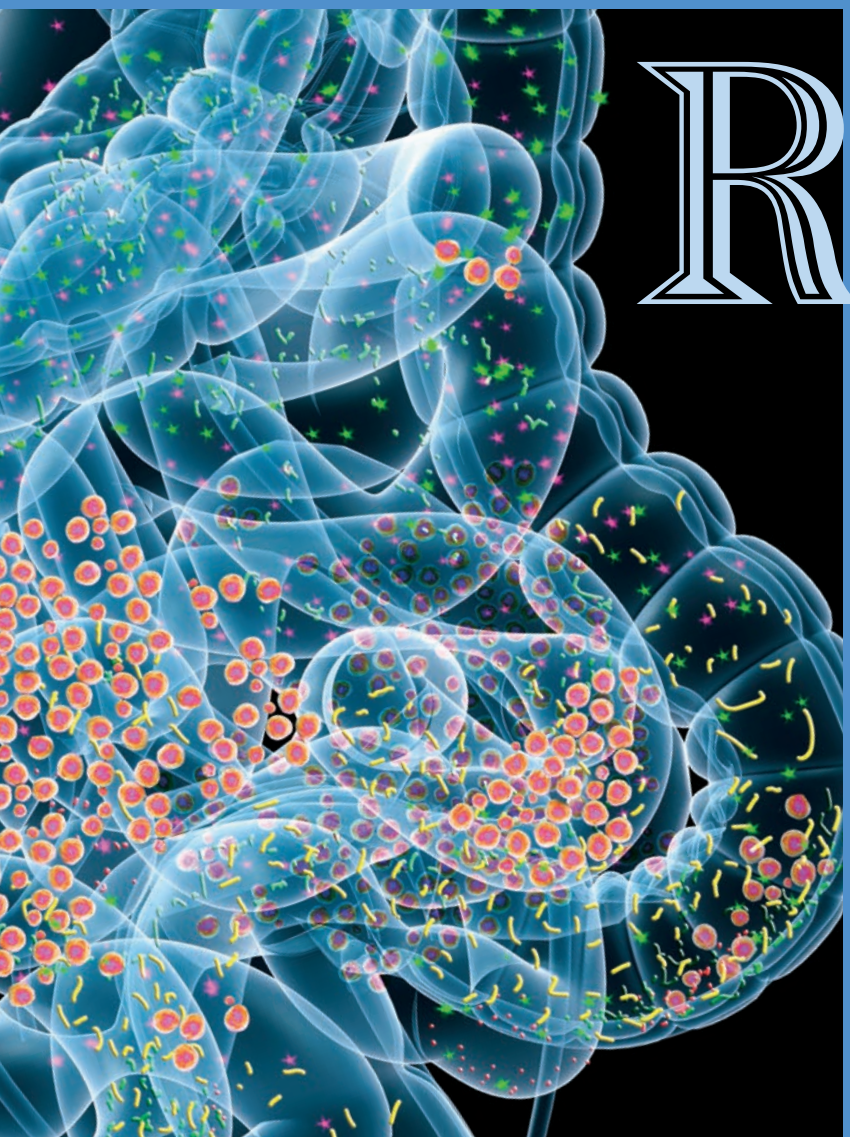

Researchers in the rapidly expanding research field of microbiomics have shown that the human body is home to an entire ecosystem of bacteria, viruses, fungi, and other microbes. What's more, these microbes play an important role in regulating many of our physiological processes.