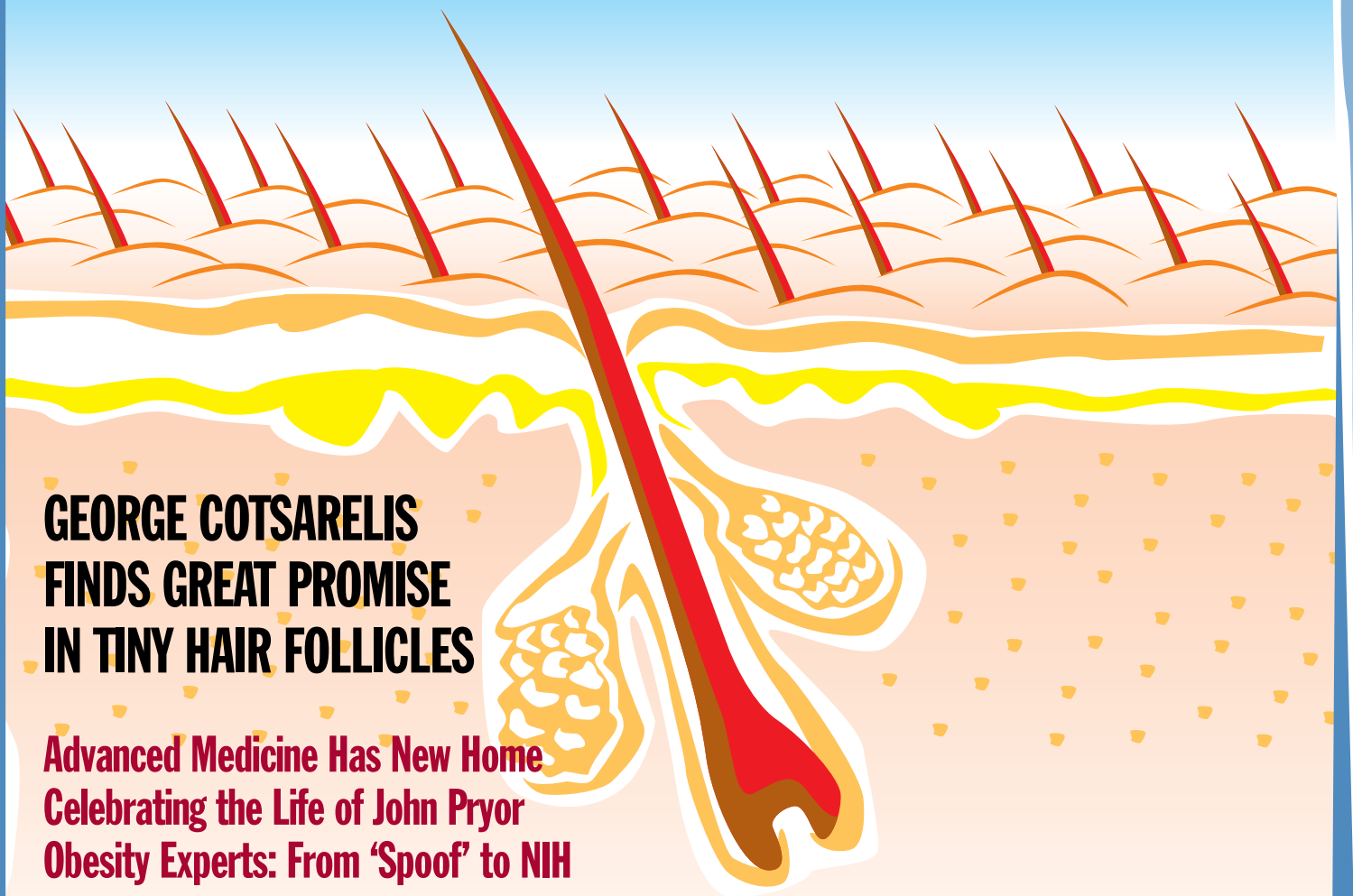


PENN Medicine

WINTER 2008/09



GEORGE COTSARELIS FINDS GREAT PROMISE IN TINY HAIR FOLLICLES

Advanced Medicine Has New Home
Celebrating the Life of John Pryor
Obesity Experts: From 'Spoof' to NIH

Good News from Botswana

Seven years after the University of Pennsylvania School of Medicine sent its first representatives to Botswana, the nation's former president visited the Penn campus. Early in 2008, Festus Mogae stepped down after completing his second five-year term. Now 69 years old, Mogae studied economics at English universities. After returning to Botswana, he joined the International Monetary Fund. In 1992, he became vice president of Botswana.

Mogae's ten years at the helm have been widely celebrated. In March, he received the Grand Cross of the Légion d'Honneur from Nicolas Sarkozy, president of France, who praised his "exemplary leadership." About two weeks after his visit to Penn, Mogae was presented the 2008 Mo Ibrahim Prize for Achievement in African Leadership, which comes with a large cash prize. At the Ibrahim ceremony, he was cited for "outstanding leadership" that has "ensured Botswana's continued stability and prosperity in the face of an HIV/AIDS pandemic which threatened the future of his country and people."

HIV/AIDS was Mogae's topic when he spoke at Penn in October. He was introduced by Harvey M. Friedman, M.D., professor of medicine and chief of the Division of Infectious Diseases, who directs the Botswana UPenn Partnership. Friedman emphasized that Mogae understood the danger facing his nation early on in his presidency and was determined to confront HIV directly. Ten years ago, nearly 40 percent of the people of Botswana were infected with the AIDS virus. Today, that number has dropped to about 4 percent. Antiretroviral drugs are now reaching some 95,000 of 100,000 needy people.

"I am honored to be standing here in front of you," said Mogae. With a touch of exaggeration, he confessed that he did not want to tell the people in the auditorium of the Biomedical Research Building what they already knew, because "so many of you have been to Botswana." What he decided to do was provide some historical context.

The first case of AIDS was in 1985. "We were all puzzled by it." With its rapid spread and without medicine to fight the disease, "there was a lot of fear and ignorance . . . and also, ultimately, stigma." Botswana's health facilities were overwhelmed. When the necessary medications were identified, "prices were way above what we could afford." The government began negotiations with pharmaceutical companies and indeed was given discounts up to 95 percent. Merck, the Gates Foundation, and the U.S. Government provided testing kits for HIV. But Botswana's doctors did not know how to treat their patients. "That's where Penn comes in," said Mogae. "You, here, in the University of Pennsylvania, with Harvard." He also thanked Baylor College of Medicine for providing pediatric care. What Botswana wanted was "more of your services and more of your expertise."

Today, things are much better. Mogae noted that some people with HIV "who would have died" have now lived for 10 years. But there is still stigma, and the current top priority is "a new campaign focused on behavioral change." The government must also fight against complacency.

Mogae acknowledged that President George Bush was "not at the highest of his popularity" at the time of his Penn visit. On the other hand, in Africa Bush was popular because of the U.S. President's Emergency Plan for AIDS Relief (PEPFAR). A member of the audience

asked about possible constraints on the PEPFAR funding, citing its emphasis on abstinence. "We don't look a gift horse in the mouth," replied Mogae.

Two weeks after Mogae's campus visit, the University announced that the Botswana UPenn Partnership had received a \$2 million grant from the Tiffany & Co. Foundation, the philanthropic branch of the international jewelry company. Part of the donation will help support the building of a facility for treating HIV/AIDS on the grounds of the Princess Marina Hospital in Gaborone, Botswana's capital. Penn and the Botswana Ministry of Health are also contributing to build the facility. The rest of the Tiffany grant will support Penn's health-care initiatives in clinical care, education, and research. The Botswana UPenn Partnership is also helping to establish a curriculum for internship and residency training at Botswana's new medical school.

After his prepared remarks, Mogae noted the shortage of physicians and other health-care workers in Botswana. That's why the planned medical school will be invaluable. The school, said Mogae, "will depend on the good will of men and women like you."

Although those men and women came originally from the School of Medicine's Division of Infectious Diseases, the Partnership has broadened considerably and now includes many from Penn's other schools. In fact, on the day of his talk, Mogae met with nursing students who had been in Botswana during the summer. Both Penn's president and provost have also visited the country. At a campus meeting this fall, President Amy Gutmann said, "Our program in Botswana is a model."

As Harvey Friedman put it, "Much has been accomplished. Much more has to be done." ♥

John Shea



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HAIR BRAINED *By Martha Ledger*

George Cotsarelis, M.D. '87, G.M.E. '92, is a dermatologist specializing in scalp and hair disorders and a basic scientist who studies the mini-organ hair follicle. His team's recent scientific papers offer hope for people with hair loss – and shed new light on the road that stem cells travel toward differentiation, which is crucial in the regenerative process.

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A DAY OF RED RIBBONS

By Sally Sapega and John Shea

The Ruth and Raymond Perelman Center for Advanced Medicine – built at a cost of \$302 million, comprising 500,000 square feet – will offer an unprecedented level of outpatient care and advanced therapies, bringing together physicians in new ways that will lead to closer collaboration among specialists.

A VERY RARE GEM

By Sally Sapega and John Shea

John P. Pryor, M.D., G.M.E. '01, director of HUP's trauma program, was on his second tour of duty in Iraq when he was killed by an enemy mortar round. His death has saddened many at Penn and far beyond. But his life and example of service and dedication are being celebrated as well.

ENGINEERED T CELLS GAIN A WEAPON AGAINST AN ELUSIVE ENEMY: HIV

By Karen Kreeger

HIV is well known for being able to evade the body's defenses. Now, researchers at Penn and the United Kingdom have engineered T cells that are able to recognize HIV-1 strains that have evaded the immune system. The T cells also respond to the virus much more vigorously.

A POPULATION IN NEED OF BETTER SLEEP

By Nan Myers

Insufficient sleep has been linked not only to fatigue but also to diabetes, cardiovascular disease, obesity, depression, and increased mortality. One of the major difficulties has been making people more aware of the seriousness of the problem.

TWO IN TUNE *By Rita Rooney*

Obesity research is not the only interest shared by Jack A. Yanovski, M.D. '86, Ph.D. '89, and Susan Zelitch Yanovski, M.D. '85, both widely known experts at the National Institutes of Health. It was music that first brought them together.

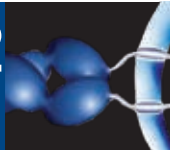
THE IMPORTANCE OF LISTENING *By John Shea*

According to Benjamin Natelson, M.D. '67, some doctors are not well prepared to help patients with chronic fatigue or pain – especially when the doctors fail to come up with a diagnosis. Natelson has published a book to help such patients. He has suggestions for physicians, too.

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Keeping the Focus on Vision

Less than a year ago, two widely publicized studies reported improvements in the vision of patients with Leber's congenital amaurosis (LCA) through gene therapy. One of the research teams was led by Jean Bennett, M.D., Ph.D., professor of ophthalmology at Penn. (See *Penn Medicine*, Summer 2008.) Now another team with Penn faculty members has reported additional encouraging results in treating the same disease, which eventually causes total blindness because of retinal degeneration.

Three young adults with this inherited form of blindness showed evidence of improved day and night vision and no adverse effects following a specialized gene transfer procedure in a Phase I clinical trial funded by the National Eye Institute. These findings were reported online in the September 22 issue of *Proceedings of the National Academy of*

Sciences and in the September 7 issue of *Human Gene Therapy*.

This study is the first to show that gene therapy can improve both day and night vision in patients with LCA. For two of the three patients, the improvements were dramatic: day vision was improved by 50-fold and night vision by 63,000-fold compared to the levels before treatment. The patients had a specific form of LCA caused by mutations in the RPE65 gene. In such cases, retinal neurons called photoreceptor cells fail to respond to light because the defective RPE65 proteins cannot produce sufficient vitamin A molecules. Patients in the study received a subretinal injection in one eye to replace the gene that was not functioning.

"The converging results from three independent and contemporaneous clinical trials are remarkably encouraging for patients and for scientists and clinicians who have worked tirelessly for decades in

the field of retinal degenerative disease," said Samuel G. Jacobson, M.D., Ph.D., professor of ophthalmology at Penn and principal investigator of the trial. Still, he added, "There are many next steps needed to be taken and soon."

According to Artur V. Cideciyan, Ph.D., research associate professor of ophthalmology at Penn, one of the discoveries involved the speed at which the patients' eyes adjusted from bright to dim environments. The speed of day vision was close to normal, but night vision took more than eight hours to adjust to darkness as compared to one hour in normal eyes. Said Cideciyan, "The first clues came while interviewing patients about their visual experiences after treatment, and we immediately altered our testing strategies appropriately."

The clinical trial was funded by the National Eye Institute. Research was conducted at Penn and at the University of Florida at Gainesville.

New Class Welcomed with White Coats

At this fall's White Coat Ceremony, 155 members of the Class of 2012 gathered in the University's Zellerbach Theatre to mark the official beginning of their medical studies. One by one, they came onstage to receive their symbolic white coats from Gail Morrison, M.D. '71, G.M.E. '77, vice dean for education, and Stanley Goldfarb, M.D., associate dean for curriculum. Then, as a group, they recited the Hippocratic Oath in front of family and friends.

Among the new students was Kathryn Cunningham Hall, who comes to Penn with a significant accomplishment on her record. During a visit to the West African nation of Gambia, Cunningham Hall became deeply concerned about the

difficulty of delivering proper health care without electricity and running water. As a result, she started Power Up Gambia!

and has raised \$300,000 to install solar panels that will provide clean water and constant electricity to a Gambian hospital.



Above: Karen Blumenthal is helped into her white coat by Gail Morrison, M.D., vice dean for education, and Stanley Goldfarb, M.D., associate dean for curriculum.

Right: Kathryn Cunningham Hall and Michael Hall, her husband, also a member of the Class of 2012.



Penn Presby Is Among the Tops

Penn Presbyterian Medical Center, one of the three hospitals in the University of Pennsylvania Health System, was again named among the “100 Top Hospitals for Cardiovascular Care” by the health-care business of Thomson Reuters. Now in its tenth year, the annual study identifies the 100 U.S. hospitals that are setting the nation’s benchmarks for cardiovascular care by analyzing clinical outcomes for patients diagnosed with heart failure and heart attacks and for those who received coronary bypass surgery and angioplasties. Penn Presbyterian was among the 30 winners in the category of teaching hospitals with cardiovascular residency programs.

Honors & Awards

David A. Asch, M.D., M.B.A., the Robert D. Eilers Professor of Medicine and Health-Care Management and Economics at the School of Medicine and the Wharton School, received the 2008 VA Under Secretary’s Award for Health Services Research. The highest honor for Veterans Affairs health-services researchers, it recognizes a VA researcher whose work has led to major improvements in the quality of veterans’ health care, has made key contributions through excellence in training and mentorship, and has enhanced the visibility and reputation of VA research through national leadership. Asch is executive director of the Leonard Davis Institute of Health Economics.

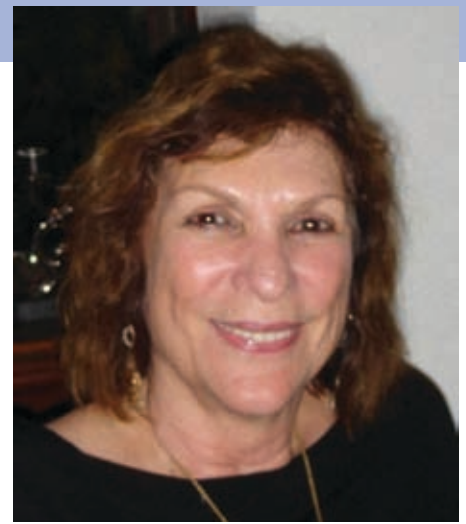
Arthur L. Caplan, Ph.D., director of the Center for Bioethics and chair of the Department of Medical Ethics, was among “The 50 Most Important, Influential, and Promising People in Science,” as selected this fall by *Discover* Magazine. Caplan was included among the 10 “Most Influential People” in science, described by the magazine as “the operators who control so

much of the agenda for science, often from behind the scenes.” Other “Influentials” included the founders of Google, Larry Page and Sergey Brin; Bill Gates, founder of Microsoft; Harold Varmus, former director of the National Institutes of Health; and U.S. Senator Barbara Mikulski.

According to *Discover*: “Caplan has sorted through the ethical traps of science for the United Nations, the National Institutes of Health, the president of the United States, and the Olympics and has written or edited more than 30 books and 500 articles on ethics in biomedicine. . . . Although he sometimes loses battles against politicians, he often succeeds in swaying public opinion, which in the end may be his proudest achievement. . . . As a champion of accountable government regulation, universal health care, and individual liberty, he has applied the values of the Enlightenment to the 21st century.”

Britton Chance, Ph.D. ’40, Sc.D., the Eldridge Reeves Johnson Emeritus University Professor of Biophysics, Physical Chemistry, and Radiologic Physics, received a 2008 Friendship Award, the highest honor the Chinese Government gives to foreigners who have made outstanding contributions to China’s economic and social progress. Chance works for several months a year in Singapore and frequently visits China for his research to develop imaging systems to detect breast tumors and to improve optical diagnostics in general. This year, 50 foreigners from 19 different countries accepted the Friendship Award.

Edna B. Foa, Ph.D., professor of clinical psychology in psychiatry, delivered the keynote address at the annual convention of the Connecticut Psychology Association. Her topic was “The Phenomenology, Theory, and Treatment of Post-traumatic Stress Disorder.” She made use of concepts from emotional processing theory to



Foa

suggest why some traumatized individuals recover while others go on to develop chronic disturbances, notably post-traumatic stress disorders. Foa, who is director of Penn’s Center for the Treatment and Study of Anxiety, received the association’s Outstanding Lifetime Contribution to Psychology Award as well.

William James, M.D., vice chairman and program director of the Department of Dermatology, has been elected president-elect for 2009 and president for 2010 of the American Academy of Dermatology. The academy is the largest dermatologic organization in the United States, with more than 14,000 members. James, who is the Paul Gross Professor of Dermatology, has special interest in allergic contact dermatitis, acne, and rosacea.

Carl June, M.D., professor of pathology and laboratory medicine and director of translational research at the Abramson Cancer Center of the University of Pennsylvania, will receive \$1 million over the next three years from the Alliance for Cancer Gene Therapy, Inc., to harness the immune system to fight the worst cases of ovarian cancer.

June plans to use the grant to carry out a Phase 1 clinical trial to test whether the immune cells his laboratory has designed to withstand the toxic effects of ovarian tumors are able to mediate tumor regression in patients with advanced cancer that

has not regressed after chemotherapy. In preliminary studies, June's group has developed genetically engineered T cells to augment traditional treatments.

Mitchell A. Lazar, M.D., Ph.D., the Sylvan H. Eisman Professor of Medicine & Genetics, was elected to the American Academy of Arts and Sciences. Members are recognized as leaders in science, arts and humanities, business, public affairs, and the nonprofit sector. Lazar heads the division of Endocrinology, Diabetes, & Metabolism and is director of the Institute for Diabetes, Obesity, and Metabolism.

Frank T. Leone, M.D., G.M.E. '98, a pulmonologist and associate professor of medicine at Penn Presbyterian Medical Center, took part in a pro bono educational program on tobacco treatment, prevention, and policy earlier this year in Bucharest, Rumania. The event was sponsored by the American College of Chest Physicians. Leone is on the Treating Tobacco Dependence: ACCP Tool Kit Committee.



Moreno

Jonathan Moreno, Ph.D., the David and Lyn Silfen University Professor of Ethics and professor of Medical Ethics and of the History and Sociology of Science at the University of Pennsylvania, was named to one of the review teams for the incoming Obama-Biden administration. The mission of the teams was to make a thorough review of select departments, agencies, and commissions of the United States government, as well as the White

House, to provide the president-elect, the vice President-elect, and their advisors with information needed to make strategic policy, budgetary, and personnel decisions before the inauguration. Moreno was appointed to lead a review of the President's Council on Bioethics.

Earlier, Moreno was named a Benjamin Rush Scholar at the College of William & Mary, an honor presented to those who have distinguished themselves with written scholarship in health or bioethics law. Each spring, the honoree is invited to present a symposium of his or her work at the College. Moreno is a Penn Integrates Knowledge professor, which means he has an appointment in two different schools in the University. He is a member of the Institute of Medicine of the National Academy of Sciences.

Stephen C. Rubin, M.D. '76, the Franklin Payne Professor of Gynecologic Oncology in the Department of Obstetrics and Gynecology and chief of the Division of Gynecologic Oncology for the Health System, was appointed to the executive committee of the American Board of Obstetrics and Gynecology. He also serves the board as a director, as chair of its Division of Gynecologic Oncology, and as chair of the Subspecialties Committee.

C. William Schwab, M.D., received the Surgeons' Award for Service to Safety, presented in October by the American College of Surgeons, the Association for the Advancement of Surgical Trauma, and the National Safety Council. Professor of surgery and chief of the Division of Trauma & Surgical Critical Care, Schwab was honored for his "visionary leadership and steadfast commitment" to preventing firearm injury and his "distinguished surgical career marked by excellence in clinical care, prodigious research, and inspirational mentorship and training of young surgeons." In 1997, Schwab founded the



Schwab

Firearm & Injury Center at Penn (FICAP) with Therese Richmond, Ph.D., C.R.N.P., of Penn's School of Nursing. In the face of the public health epidemic of firearm violence, "Dr. Schwab has built FICAP as a resource to policymakers, health and service providers, researcher, and community members."

Preventing Suicide

Gregory K. Brown, Ph.D., research associate professor of clinical psychology in psychiatry, and **Thomas R. Ten Have, Ph.D.**, professor of biostatistics and director of the Biostatistics Analysis Center, were appointed to a nine-member experts panel that will make recommendations on ways the Department of Veterans Affairs can improve its programs in suicide prevention, suicide research, and suicide education. Their charge is to provide professional opinion, interpretation, and conclusions on information and data to the work group.

Brown, who serves as co-principal investigator of Penn's Center for the Treatment and Prevention of Suicide, has published on borderline personality disorder and on using cognitive therapy to help people who have attempted suicide.

Ten Have is collaborating on trials involving the prevention of suicide in elderly primary-care patients; the use of estrogen to treat post-menopausal women for depression; the treatment of substance abuse, anxiety, and depression in elderly



Bennett



Epstein



Koretzky



Muller



McCauley



Schwartz

veterans; and disparities of screening and treatment for mental health disorders in participants of color. He is associate editor of *Biometrics* and of the *Journal of the Royal Statistical Society, Series C*.

IOM Elects Six from Penn

One year after four members of Penn's medical faculty were elected to the Institute of Medicine of the National Academy of Sciences, the Institute has elected four School of Medicine professors, a professor in the School of Nursing, and the chief executive officer of Penn's Health System. That brings Penn's total to 68 in what is widely considered one of the nation's most prestigious institutions. In addition to honoring professional achievement in the health sciences, the IOM provides independent analysis and recommendations on issues related to medicine, biomedical sciences, and health.

The new Penn IOM members are:

* **Jean Bennett, M.D., Ph.D.**, the F. M. Kirby Professor of Ophthalmology and Cell and Developmental Biology. Vice chair for research in Ophthalmology, she also serves as senior investigator at the F. M. Kirby Center for Molecular Ophthalmology

at Penn's Scheie Eye Institute. Bennett studies the molecular genetics of inherited retinal degenerations in order to develop approaches for treating these diseases. Her laboratory reported the first gene therapy success in slowing the disease process in an animal model of inherited retinal degeneration. Earlier this year, her team's successful preclinical studies on an inherited blinding disease, Leber's congenital amaurosis, led to human clinical trials for this disease.

* **Jonathan A. Epstein, M.D.**, the William Wikoff Smith Professor of Medicine. He is chair of the Department of Cell and Developmental Biology and scientific director of the Penn Cardiovascular Institute. A founding co-director of the Penn Institute for Regenerative Medicine, Epstein studies the molecular mechanisms of cardiac development in order to understand adult and congenital cardiovascular disease and to develop therapies. He is president-elect of the American Society for Clinical Investigation.

* **Gary A. Koretzky, M.D. '84, Ph.D. '84**, the Leonard Jarett Professor of Pathology and Laboratory Medicine and vice chair for research and chief

scientific officer of the Department of Medicine. He also serves as director of the Signal Transduction Program at the Abramson Family Cancer Research Institute, where he is an investigator. Koretzky's laboratory focuses on understanding the regulation of signaling events, which lead to hematopoietic cell development and function. Editor-in-chief of *Immunological Reviews*, he is a former president of the American Society of Clinical Investigation.

* **Ralph W. Muller, M.A.**, CEO of the University of Pennsylvania Health System. From 1985 to 2001, he was president and CEO of the University of Chicago Hospitals and Health System. A Fellow of the American Association for the Advancement of Science, Muller is a director of the National Committee for Quality Assurance and a commissioner of The Joint Commission.

* **Linda A. McCauley, Ph.D., R.N.**, the Nightingale Professor in Nursing and associate dean for nursing research in the School of Nursing. She has conducted large community-based participatory research projects that seek to reduce exposures to pesticides among minority farm workers. McCauley is course director of the undergraduate community health nursing course and is program director of the Occupational Health Option for both master's degree and doctoral students.

* **J. Sanford Schwartz, M.D.**, the Leon Hess Professor in Internal Medicine in the School of Medicine and professor of health-care management in the Wharton School. He is a senior fellow of the Leonard Davis Institute of Health Economics, where he served several years as executive director. Schwartz's research focuses on the assessment of medical technologies and practices (including cost-quality tradeoffs); adoption and diffusion of

medical innovation; and medical decision-making. He is a former president of the Society for Medical Decision Making and of the American Federation for Clinical Research.

Urology Center Awarded \$6.11 Million Grant

Researchers in the Division of Urology have concluded their third successful competitive renewal for the George M. O'Brien Center for Urologic Research. The National Institute of Diabetes and Digestive and Kidney Diseases has awarded the center \$6.11 million over five years. Penn's program is directed by Samuel K. Chacko, D.V.M., Ph.D., professor of pathology in the School of Veterinary Medicine and director of basic urology research in the School of Medicine's Department of Surgery.

The NIDDK established the George O'Brien Urology Research Centers (there are five in the nation) to create a research community for major urologic diseases and syndromes. According to Chacko, the O'Brien award "will help provide an environment for investigators to apply state-of-the-art tools in cell and molecular biology to research related to the pathogenesis of diseases in the lower urinary tract." The new grant is focused on bladder wall remodeling in Lower Urinary Tract Symptoms (LUTS). The prevalence of LUTS is believed to be as high as 90 percent in men 50-80 years old. Such conditions, which can lead to bladder dysfunction and urinary incontinence in adults, cost Americans nearly \$11 billion a year, according to a new report from the National Institutes of Health.

The center is composed of faculty in the schools of Medicine, Veterinary Medicine, and Dental Medicine, as well as investigators in the divisions of Neuroscience and Pediatric Urology at The Children's Hospital of Philadelphia.

Penn Researchers Receive NIH Director's Awards

James Eberwine, Ph.D., the Elmer Holmes Bobst Professor of Pharmacology and co-director of the Penn Genome Frontiers Institute, has been awarded the Director's Pioneer Award by the National Institutes of Health. The award provides \$2.5 million over the next five years.

Aaron D. Gitler, Ph.D., assistant professor of cell and developmental biology, has been awarded the Director's New Innovator Award, which provides \$1.5 million, also over five years. According to Elias A. Zerhouni, M.D., director of the NIH, "These programs are central elements of NIH efforts to encourage and fund especially novel investigator-initiated research, even if it might carry a greater-than-usual degree of risk of not succeeding."

Eberwine, who is co-director of the Penn Genome Frontiers Institute, already holds a MERIT award from the NIH. The research efforts of his laboratory have been directed towards understanding the molecular basis of neuronal functioning. Eberwine has led the field of single-cell genomic analysis and plans to use his award to understand how RNA populations encode a cellular memory that helps to control the development and maintenance of cellular identity.

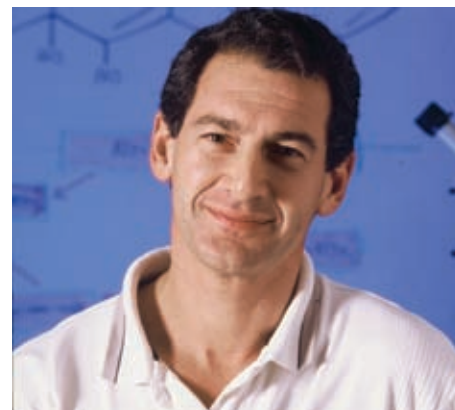
Gitler studies the mechanisms that cause proteins to misfold and aggregate. He does so by identifying genes and cellular pathways that are affected by misfolded human disease proteins. By harnessing baker's yeast as a model system to study the mechanisms underpinning protein-misfolding diseases such as Alzheimer's and Parkinson's, the Gitler laboratory aims to perform high-throughput, genome-wide screens to elucidate the basic cellular mechanisms of toxicity. These yeast models will provide the Gitler lab with a unique opportunity to observe and understand protein folding and misfolding in

real time as it occurs in a living cell. The innovative aspect of Gitler's approach is not only that they are working in yeast, but that they are using this system as a tool to discover new drug targets.

Gitler has received two other major honors this year. He was named a 2008 Pew Scholar in Biomedical Sciences. The Pew program supports scientists in early or mid career, giving each of the 20 scholars a four-year, \$240,000 award to help support their work. He was also recognized as one of seven 2008 Rita Allen Foundation Scholars. He will receive \$300,000 over three years to further his research on neurofibromatosis.

Appointments & Transitions

Lewis A. Chodosh, M.D., Ph.D., was appointed chair of the Department of Cancer Biology, effective September 1.



Chodosh

He has pioneered novel approaches to understanding fundamental mechanisms relevant to clinical outcomes in breast cancer patients, using genetically engineered mouse models, genomics, computational biology, and non-invasive imaging. Chodosh directs one of three sites of the National Cancer Institute's Mouse Models for Human Cancers Consortium focused on breast cancer, and in 2005 he was named director of a Congressionally

Directed Breast Cancer Center of Excellence at the University of Pennsylvania. Chodosh also serves as an advisor to the Harvard Nurses' Health Studies I and II and is editor in chief of *Breast Cancer Research*. A member of the American Society for Clinical Investigation, Chodosh was elected to the American Association of Physicians earlier this year.

Chodosh holds secondary appointments in the Department of Cell & Developmental Biology and in the Department of Medicine in the Division of Endocrinology, Diabetes, and Metabolism. He joined the Penn faculty in 1994, was appointed vice chair of the Department of Cancer Biology in 2002, and served as interim chair of the department since 2007. An investigator in the Abramson Family Cancer Research Institute, Chodosh became director of its Cancer Genetics program in 2005. He also serves as associate director for basic science at the Abramson Cancer Center and leads its Breast Cancer Research Program.

Chodosh earned his M.D. degree from Harvard Medical School and his Ph.D. degree in biochemistry from the Massachusetts Institute of Technology.

Arnold I. Levinson, M.D., professor of medicine and neurology, was named associate dean for research in the School of Medicine. As associate dean, he is responsible for establishing and enhancing Penn's programmatic relationships with federal and state agencies and with pharmaceutical companies; chairing the Limited Applications Committee; directing the annual grant-writing seminar; overseeing the research portion of the Awards of Excellence process; and chairing the School of Medicine Space Committee.

Levinson joined Penn's faculty as an assistant professor of medicine in 1978. His research has largely focused on the cellular and molecular basis of human autoimmune disease, particularly relating

to the role of the thymus in the pathogenesis of myasthenia gravis. A member of several editorial boards, Levinson has served as chief of the allergy and immunology section of the pulmonary, allergy, and critical-care division in Penn's Department of Medicine. He also has served as director of the Penn Center for Clinical Immunology. Outside of Penn, Levinson has been chair of the American Board of Allergy and Immunology and president of the Clinical Immunology Society.

Kenric Michael Murayama, M.D., is the new chief of surgery of Penn Presbyterian Medical Center. He joins PENN Medicine from the University of Hawaii John A. Burns School of Medicine in Honolulu, where he was professor of



Murayama

surgery and chief of general surgery. Murayama was director of the Center for Minimally Invasive Surgery at The Queen's Medical Center in Honolulu. He also served as associate chair for Robotics & Emerging Technologies and director of the Minimally Invasive Surgery Program at the Burns School of Medicine. Murayama received his medical degree from the University of Hawaii and completed

his surgical residency at the Northwestern University Medical School. He was selected as the Teacher of the Year for three consecutive years while instructing surgical residents at St. Louis University and Northwestern University.

Mark L. Tykocinski, M.D., has stepped down as chair of the Department of Pathology and Laboratory Medicine to become dean of Jefferson Medical College and senior vice president of Thomas Jefferson University. He will also serve as president of Jefferson University Physicians. Tykocinski came to Penn 1998 from Case Western Reserve University, where he had been director of its Gene Therapy Facility. His research interests included the design of novel recombinant proteins with immunotherapeutic potential. A member and former chairman of the N.I.H. Pathology B Study Section, he has also chaired the N.I.H. Fellowship Review Committee. Under Tykocinski's leadership, Penn's department attained the top ranking in funding from the N.I.H.; created new divisions; featured cytopathology as a showcase academic-clinical service; and enhanced pediatric pathology. The more recent projects include a new blood bank, a new histology processing center, and a new automated laboratory.

John Tomaszewski, M.D. '77, G.M.E. '83, has been named interim chair of the department. He served as director of surgical pathology at HUP from 1995-2005 and is currently vice-chair for anatomic pathology-hospital services. Tomaszewski, recognized as an expert in diagnostic genitourinary pathology, was named several times as a "Top Doctor" in regional and national surveys. His numerous teaching awards include the Peter Nowell Teaching Award and the Dean's Award for Excellence in Basic Science Teaching.

A search for a permanent chair will begin soon.

Paul Root Wolpe, Ph.D., was appointed director of Emory University's Center for Ethics, effective August 1. Wolpe was a professor of sociology in the School of Medicine's Department of Psychiatry, with secondary appointments in the Department of Medical Ethics and the Department of Sociology

in the School of Arts and Sciences. According to Emory's provost, Earl Lewis, "Wolpe is an internationally recognized scholar, a bridge builder, and one committed to charting new possibilities for the role of ethics on campus and in the broader community." The immediate past president of the American Society

for Bioethics and Humanities, Wolpe serves as the first chief of bioethics for the National Aeronautics and Space Administration. Wolpe is a co-author of the textbook *Sexuality and Gender in Society* and is the first national bioethics advisor for the Planned Parenthood Federation of America.

LETTERS

Impressionable and Unskeptical

I wasn't surprised to see the acupuncture article in the Spring 2008 issue of *Penn Medicine*. I did however think that the aborted, almost disastrous relationship with Tai Sophia, an acupuncture mecca, might have caused the School of Medicine to be more cautious about its lax approach to such forms of alternative medicine. Certainly a couple lectures on acupuncture as part of a course on the history of therapies or the use of placebos in medicine would appear reasonable. However, I am almost certain that young, impressionable, and often unskeptical medical students are not properly prepared prior to their exposure to these alternative, unscientific treatments.

My fear is that these young physicians will go on to attempt to cure real diseases with these therapies, delaying effective therapies – that's what we are seeing out there in the real world.

I feel that Penn's acupuncture elective would be academically deficient if students were not required to read *Snake Oil Science* by biostatistician R. Barker Bausell (Oxford University Press, 2007) prior to embarking on such mystical adventures.

Carl E. Bartecchi, M.D. '64
Distinguished Clinical Professor of Medicine,
University of Colorado School of Medicine

Acupuncture: No Business Being Taught

Keep up the good work! Generally, it's a fine publication.

Just a passing observation on your piece on acupuncture. This material has utterly no business, in my view, being taught at the University of Pennsylvania School of Medicine. Most distressing were the photos of the young Penn medical students "lapping it up." As elders, mentors, and teachers, we owe them every chance to acquire a solid, physiologically based curriculum. They have vastly more important things to learn and accomplish in their coming, complicated lives than to spend any of it chasing "Qi."

Lee A. Bricker, M.D.
Kalamazoo, Michigan

Dr. Mao responds: I appreciate the concerns raised by Drs. Bartecchi and Bricker but disagree respectfully with their view on teaching acupuncture to medical students. Acupuncture is currently being used by two million adults in the United States, and it is offered in over half of the hospitals according to a recent national survey. Medical students need to learn about acupuncture so that they can provide informed discussion with their patients. Additionally, research in acupuncture – including that conducted

at Penn – has demonstrated the physiological effect of acupuncture on CNS neuropeptides as well as on the limbic system of brain. These findings help us understand the potential mechanism of acupuncture and provide the physiological basis of chronic pain and its maladaptive behavior.

Furthermore, medical education recently emphasized the value of cultural competence: the acupuncture elective in China aims at helping students see how culture shapes medical beliefs and

practices. This understanding contributes to learners developing awareness that patients' world views about illness and health may differ from the biomedical perspective or their own. Consequently, this perception may decrease cultural miscommunication and lead to patient-centered clinical care.

Jun J. Mao, M.D., M.S.C.E.
Assistant Professor of Family Medicine
and Community Health, University of
Pennsylvania School of Medicine

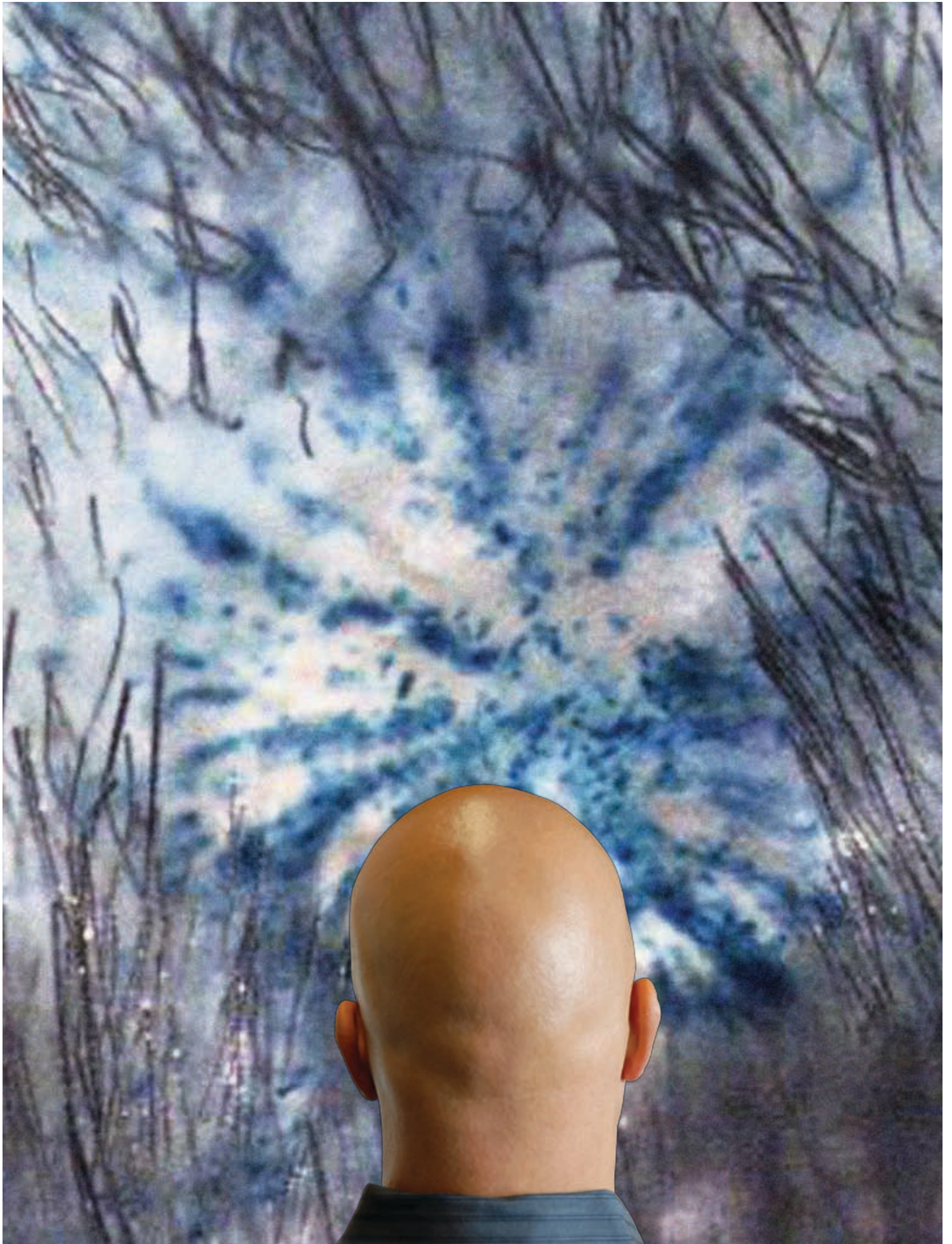


MEDICAL ALUMNI WEEKEND



RETURN
RENEW
REUNITE

May 15-17, 2009



Hair Brained

By Martha Ledger

George Cotsarelis might cure baldness, but his discoveries are even more far-reaching.

In March 2004, Diane Sawyer's people woke George Cotsarelis, M.D. '87, G.M.E. '92, at 4:30 a.m. Would he agree to be on *Good Morning America* that morning? Could he get to ABC's studio in Philadelphia by 7?

Cotsarelis, a PENN Medicine dermatologist specializing in scalp and hair disorders and a basic scientist who studies the mini-organ hair follicle, was about to report findings in *Nature Biotechnology*, and a pre-publication press release was attracting attention outside the scientific community. His team had generated new hair follicles by isolating adult stem cells from murine hair follicles and implanting them in immunodeficient mice – and the new follicles had produced hair.

To people with less hair than they would like, this was big news. It suggested a future therapy in which stem cells could be harvested from a person's remaining hair follicles, multiplied *in vitro*, and injected back into that person's bald spots.

"The week the paper came out was insane," recalls Cotsarelis, a totally unpretentious, upbeat, and articulate man (picture Jimmy Stewart with the scrubbed face and talking ability of Brian Williams). "I'd never experienced anything like it." Throughout the month, he appeared on TV and radio and was interviewed for dozens of newspaper articles in this country and around the world.

The off-site interview with Sawyer was what one would expect. Cotsarelis endured bright lights in his eyes and wore an earphone and Sawyer asked him questions, which he answered. But it was a pre-interview detail that Cotsarelis still chuckles about. Before going on-air, he heard a producer on Sawyer's end ask via speakerphone, "Hey Joe, does the doctor have hair? Is he bald?" Would baldness have explained the motivation for Cotsarelis's

research? Would it have convinced viewers that a therapy was really not yet available? For the record, Cotsarelis, 47, still has a good head of hair with maybe a slightly receding hairline.

Cotsarelis had his 15 minutes of fame, but, not long afterward, he had 15 minutes more. In May 2007, his lab was back in the spotlight because people really care about hair. Publishing in *Nature* this time, his team reported that after mice had had a full-thickness patch of skin removed from their backs, new hair follicles had formed in the healing skin. The press went wild. They reported that Cotsarelis had co-founded a start-up biomedical company dedicated to hair regeneration and implied that it wouldn't be too long before a treatment was available – one that would work for everyone. People began e-mailing Cotsarelis, offering themselves for clinical trials.

Both scientific papers do offer hope for people with hair loss, and there are many such people. Five of every 10 men and three of every 10 women suffer a significant degree of age-related baldness by age 50. In addition, there are disorders that cause people to lose scalp hair and sometimes all body hair. And as director of PENN Medicine's Scalp and Hair Clinic – which has a very long waiting list of patients – Cotsarelis is acutely aware of their angst.

Nonetheless, Cotsarelis, the Albert M. Kligman Associate Professor of Dermatology, is not mounting a frontal attack on baldness. His discoveries may lead to a cure for it, but they break ground in other significant areas as well. The *Nature* paper documents the first successful regeneration of a mammalian organ. The experiments it describes shed new light on the road that stem cells travel toward differentiation, which is crucial in the regenerative process.



George Cotsarelis, M.D., examines the scalp of Steve Wlodarczyk.

I recently asked Gerald Lazarus, M.D., former chairman of PENN Medicine's Department of Dermatology, about the scientific significance of this work. "On a scale of one to 10," he said, "I think it's somewhere between eight and nine. Ten," he quickly added, "is relativity."

* * *

A variety of things led Cotsarelis into dermatology. The first was growing up with a brother who had a really bad case of acne. "He'd come back from the doctor," Cotsarelis recalls, "with these terrible marks on his face where pimples had been cut open and expressed. And I was like, boy, I hope I never have to go through that."

Fortunately, he didn't, but his brother's experience made an impression on him. So much so that as a high-school student in central Pennsylvania, Cotsarelis did a report on acne, researching it in the library of the Milton S. Hershey Medical Center. It was there, in the stacks, that Cotsarelis first encountered Albert M. Kligman, M.D., Ph.D., Penn professor of dermatology – his name, anyway, and his writing style. "The best articles, the ones

written so well that even a high-school student could understand them," Cotsarelis says, "were written by Albert Kligman. It was a great thrill when I actually met him, when I became a Penn student."

But it was Brian Jegasothy, M.D., then

"When George started working, he didn't have an enormous vested interest in what the result was going to be. He expected Y to happen. Y didn't happen. But Z did. George was really good at dealing with Z, asking 'what do these results mean?'"

vice chairman of dermatology at Penn and Cotsarelis's first-year medical advisor, who made the field seem especially appealing. "He was a very nice man who seemed quite satisfied with his life," Cotsarelis recalls, "so I considered it." By his third year, he had decided. He dropped into the lab of Robert Lavker, Ph.D., then associate professor of dermatology, and asked if he could do some work there.

"Medical students," Lavker explains, "would – and still do – come in for two or three months hoping for a letter of recommendation for their residency application and something interesting to talk about in their interviews." He's not sure that Cotsarelis's motivation was any different, only

that he turned out to be the real thing.

Lavker and his collaborator Tung-Tien Sun, Ph.D., were looking for the stem cells that maintain the cornea, and they set Cotsarelis to work on a variety of experiments to find them. He used a tech-

nique based on the slow-cycling nature of stem cells. Since these cells rarely divide, they retain a radioactive label much longer than normal cells that divide frequently and halve their marker with each division. After a period of time, the slow-cyclers can be detected through autoradiography. Cotsarelis also devised his own experiments to monitor corneal repair, "very creatively developing his own ointments to stimulate the eye," according to Lavker, who is now professor of dermatology at Northwestern University.

Cotsarelis was able to show that all of the stem-cell-like activity was coming from the peripheral cornea, or limbus, where the white of the eye meets the

pigment. These findings led to a first-author paper in *Cell* and, not long after, a change in the way corneal transplants were done. At that time, ophthalmologists normally grafted only the central part of the cornea, and if the patient had suffered a full-thickness burn, the graft lasted only about six months. When surgeons began incorporating limbal cells in the transplant, these grafts lasted as long as the patient did.

Cotsarelis was hooked on research. Lavker explains: “Once you get findings like these . . . you just can’t get enough of it.” Plus, the laboratory was fun. “We laughed a lot. It wasn’t at all dictatorial, and there was freedom to do what you wanted.”

It was so good that Cotsarelis considered postponing graduation and spending another year in the lab. Lavker, for one, argued strenuously against it. “I was looking at it solely as a parent would,” he says.

In the end, Cotsarelis decided to finish his medical degree on schedule. He interned in medicine at Geisinger Medical Center, and in 1988, before he started his residency at Penn, he returned to Lavker’s lab as a research fellow. It was then that he started studying the hair follicle.

* * *

“The reason the hair follicle is so fascinating is its cycling,” Cotsarelis explains with enthusiasm. “A hair grows, falls out, and another grows in its place. It’s the body’s only organ in which there’s a total loss of [hair-generating] cells and then a total regrowth of those cells. And this cycling goes on throughout your lifetime.

“The cells that make a hair are some of the most rapidly proliferating in the body – and quite suddenly, they shut down and die. The follicle’s stem cells are very quiescent – and quite suddenly, they awaken and set regrowth in motion. How do cells know when to do these things?

What signals are they responding to?” says Cotsarelis. “These are fundamentally important questions relevant to treating cancer and wounds, where you want to turn off or turn on cells.

“An understanding of the follicle may lead to a treatment for hair loss,” he says, but adds that he hopes studies like his “will lead to a lot of other advances as well.”

In the lab, Cotsarelis started looking for the stem cells that control the follicle’s cycling process. The hypothesis was that stem cells would be in the bulb, the rapidly growing bottom part of the follicle. Cotsarelis didn’t find any slow-cycling cells there, but he did find them in another part of the lower follicle, in a shallow pocket that had no name. “You must be doing something wrong,” Lavker and Sun said. “Go back and do it again.” Says Cotsarelis: “I kept doing it and kept getting the same results.”

Cotsarelis continued the work into his residency. While researching the follicle to make a Rounds presentation, he consulted a 1956 book by biologist William Montagna, Ph.D., that described

the work of P. G. Unna, a 19th-century German scientist. In 1876, Unna had noted the presence of the follicle’s wulst [bulge], which he said seemed prominent during fetal development but whose function was unknown. Looking through his microscope, Unna also noted that he rarely saw cell division occurring there. Cotsarelis realized at once that this bulge area was exactly where he was seeing slow-cycling cells. He had indeed found the follicle’s stem cells, as well as the name for the structure that housed them. In 1990, still a resident, Cotsarelis had another first-author paper in *Cell*.

To Lazarus, who is currently director of the Center for Wound Healing at Johns Hopkins Bayview Medical Center, Cotsarelis has the right attitude to do great science. “A lot of scientists have an end in mind – a hypothesis that they’ve got to prove so they can write papers about it. When George started working, he didn’t have an enormous vested interest in what the result was going to be. He expected Y to happen. Y didn’t happen. But Z did. George was really good at dealing with



Mayumi Ito, Ph.D., left, who worked in the Cotsarelis lab as a postdoc, consults with Zaixin Yang, M.D., a research specialist.

Z, asking ‘what do these results mean?’ This kind of maturity is very unusual, and George had it from the very beginning.”

Lavker notes that Cotsarelis also had “the trick of writing, of presenting your stuff in an appealing and understandable way.” What he didn’t have upon completion of his residency, however, was training in molecular biology or experience with anything beyond the most basic, labor-intensive investigative tools. Supported by a Howard Hughes Medical Institute Postdoctoral Research Fellowship, he acquired the background he needed.

Still, Cotsarelis initially made less progress than he had hoped. He was trying to find genes specifically activated in the bulge area, but after four years he had identified only a few, and they were also activated elsewhere. One day, he talked with Stephen Lyle, M.D., Ph.D., a pathology resident at Penn, who was studying melanoma. Lyle told Cotsarelis that a part of the hair follicle was routinely being stained by a protein-seeking antibody he was using. The marked area turned out to be the bulge, and Lyle soon identified the tagged protein as keratin 15 (K15).

* * *

This was the turning point for Cotsarelis. He identified the section of DNA that controls K15 expression and began using it to target the bulge cells with genes that produced a fluorescent protein. Soon after, he was able to isolate the bulge stem cells and show that they are multipotent – that is, they generate all the different types of epithelial cells in the lower hair follicle and shaft.

Cotsarelis had expected follicle stem cells to contribute to maintaining the epidermis as well. But this turned out not to be the case. To prove the independence of the epidermis, his research team created a transgenic mouse with a “suicide gene” in its follicle stem cells. They

“The dogma was that you were born with the total number of hair follicles that you were ever going to have. Their loss was considered permanent.” So where were these new follicles coming from?

grafted a piece of its skin onto an immunosuppressed mouse and then activated the gene, which destroyed the follicle. The hair on the graft fell out, but the epidermis survived. This result explains why cosmetic removal of unwanted hair is at least theoretically safe.

If the *skin* is wounded, however, follicle stem cells do participate in repairing the epidermis. Using transgenic mice whose follicle stem-cell progeny could be tracked, Cotsarelis’s researchers demonstrated that cells migrated from the bulge to the area of skin rebuilding, eventually making up 25 percent of the healing wound. There, they began acting like epidermal cells, expressing epidermal rather than follicle stem-cell genes. This display of plasticity was both remarkable and temporary. As the wound healed more thoroughly, these cells disappeared. The findings have therapeutic implications: Once scientists understand the signals that summon bulge cells to a wound, they will be able to augment their presence and more successfully treat wounds and aging disorders like epidermal atrophy.

In the course of his research, Cotsarelis took advantage of newly emerging technologies for molecular studies. He ticks off the arsenal: transgenic mice; rapid gene-sequencing techniques “that let you do in a day or two what took years before”; micro-array chips, “where you can look at 30,000 genes at once instead of just five or 10”; and fluorescent-activating cell sorting. “The last is an incredible technology. You separate skin cells using an enzyme, add an antibody with a fluorescent tag to a cell’s surface protein, and then shoot the cells through a machine where a laser hits each one. If the cell fluoresces, it gets separated out from the rest of the batch. That’s how we ended



up sorting out the stem cells – because we could make them fluoresce.”

During the wounding studies, Mayumi Ito, Ph.D., a postdoc from Japan, who had come to the United States in 2003 to work with Cotsarelis, noticed structures very similar to embryonic hair germs forming in the healed wound.

This fact was unexpected. “The dogma,” says Cotsarelis, “was that you were born with the total number of hair follicles that you were ever going to have. Their loss was considered permanent.” Moreover, he explains, mammals don’t normally regenerate their tissues. Instead, they’ve evolved to repair themselves. They form scar tissue, which has thick collagen bundles that lack hair follicles and sebaceous glands.

So the question was, where were these new follicles coming from?

Ito searched the literature and found three articles from the 1950s that discussed the growth of new hair after wounding. Two of the papers dealt with wounded rabbits. The third, by Albert

Kligman, noted the phenomenon in biopsies done on dermabraded patients. The possibility of regeneration was debated for about 10 years after these papers, but, in 1967, researcher William Straile published a review article arguing that established follicles had simply migrated in from the wound's edge.

Cotsarelis's team would have to disprove Straile's conclusions. To eliminate the possibility of migrating follicles, Ito created a wound that was large enough (1/2-inch by 1/2-inch) to still leave an area open for examination after the wound contracted. She also removed the full thickness of skin, so there could be no existing follicles.

In a few weeks, new skin formed in the wound, and a few weeks after that, hair began to grow from its center. "I was so excited to see the result, I cut a section by myself," she says.

"We knew what we had," Cotsarelis explains, "because we studied the skin at several time intervals after wounding and saw under the microscope that hair follicles were developing. They looked identical to embryonic follicles. We just had to prove they were the same molecularly."

Which the lab did. As they reported in the 2007 *Nature* paper, hair-follicle differentiation markers were notably absent from the epidermis for several days after wound closure, but these markers reappeared when hair germs started to develop. The regenerated follicles also expressed the same proteins and enzymes (KRT17, Lef1, alkaline phosphatase, Wnt10b, and Shh) that are present during embryonic follicle development. The researchers showed, too, that Wnt proteins played a major role in the regenerative process: When Wnts were blocked, no follicles formed; whereas excess Wnts doubled the production of follicles.

Through genetic-lineage analysis, the researchers also demonstrated that there was a negligible number of bulge-cell

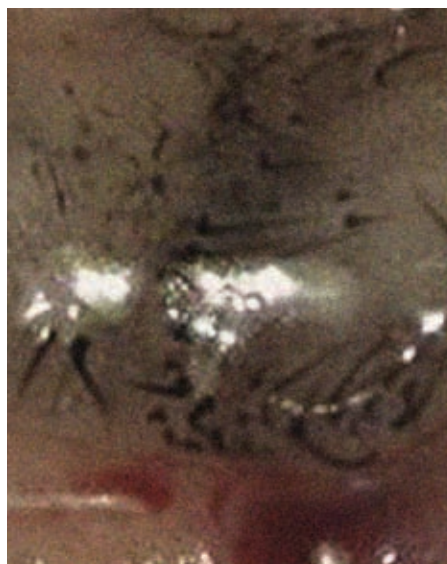
offspring in the new follicles, which took care of William Straile's explanation once and for all.

Most importantly, the researchers demonstrated that the new follicles arose from epidermal cells. That discovery suggests that wounding makes significant remodeling possible: epidermal cells turning into follicle cells and, as the earlier wounding experiment showed, follicle cells turning into epidermal ones.

"When cells move in to close a wound," Cotsarelis explains, "they are trying to make a decision: Should I make epidermis or should I make a hair? If there is a lot of Wnt around, they choose to become hair follicles.

"Maybe – and we're not sure yet – what's going on is de-differentiation," says Cotsarelis, "where cells that are usually committed to one lineage actually revert back to a state where they can become something else."

If this proves to be the case, a window of opportunity exists in which to manipulate cells. In terms of treating hair loss, this regeneration model suggests a different kind of therapy from stem-cell implants, one that might combine dermabrasion with a topical application of something containing Wnts or other factors.



Hair follicle stem cells isolated from an adult mouse generate new hair follicles when injected into another mouse. Each black line is a newly generated hair.

But the patch of new hair on a mouse's back might be a more far-reaching breakthrough, one that opens a door to organ replacement, a kind of science-fiction idea that at least some people think is the future of medicine. Some scientists are definitely moving in this direction.

In 2007, two research teams elsewhere were able to turn an adult cell into a pluripotent cell (one with unlimited differentiation possibilities) by inserting four genes. But, as Ito notes, "even though the cells have the capacity to differentiate into many types of cells, it's still very difficult for them to make a whole organ. In order to make an organ, cells must know how to collaborate with each other. In our model, the entire process of organ generation can be induced and studied at the molecular level." And at present, this is the only model scientists have for the complete regeneration of a mammalian organ.

"These are important and seminal observations," Lazarus says. They were possible, he adds, because Cotsarelis has been totally focused throughout his career. "One thing built upon another, and the applicability of his initial observations keeps broadening."

Ito, who recently established her own lab at New York University, has an additional idea about why the Cotsarelis lab has been so productive. "George gives freedom. If he wanted us to look only at hair-follicle bulge cells, this regeneration project would not have happened. Some of us work on his hypotheses. Some of us work on our own interests. He identifies questions. We identify questions, too. He gives us a chance and room to think from zero. And then he is very patient. He can wait. He can leave us alone to get the results of our ideas.

"So the lab never narrows," Ito says. "And that's a good thing for science." ♥

A Day of Red Ribbons



As Ralph Muller, Amy Gutmann, and Arthur Rubenstein cheer them on, Raymond and Ruth Perelman cut the ribbon to the new center.



Perelman Center for Advanced Medicine

The atmosphere was festive for the dedication of the Ruth and Raymond Perelman Center for Advanced Medicine on October 2. Not only were brightly costumed mimmers strumming away at the front entrance, but one of the first things people saw upon entering the five-story glass atrium was the gigantic red ribbon circling the second floor. Quite appropriate for a red-letter day. A miniature version of the new center – a carefully detailed white cake – also bore a red ribbon, done in icing. Hundreds of guests, along with the occasional representative of the local news media, chat-

ted and admired the new surroundings. Then they took the long escalator to the second floor, where scores of chairs were laid out facing a podium, lectern, and screen. And here, too, was yet another a red ribbon of more conventional size, waiting to be cut a little later in the program by the guests of honor.

A little less than three years ago, many of the same people had gathered on campus for the symbolic ground-breaking of the center. Now, the Perelman Center – built at a cost of \$302 million, containing 500,000 square feet – was taking a place of pride across the street and a few yards

south of the main entrance of the Hospital of the University of Pennsylvania.

"In the life of a great academic medical center, there are certain defining moments that move it to the next level of excellence," said one of the speakers at the event, Arthur H. Rubenstein, M.B.,B.Ch., executive vice president of the University of Pennsylvania for the Health System and dean of the School of Medicine. "For PENN Medicine, the Perelman Center for Advanced Medicine is one of those moments."

The center will offer an unprecedented level of patient care and advanced therapies, bringing together physicians in new ways that will lead to closer collaboration among specialists. For example, a thoracic surgeon uploads a patient's high-resolution CT scans to an imaging center and confers with an expert chest radiologist, crafting a personalized treatment plan for the patient. The care team quickly relays the plans to the patient, paving the way for quick access to a team of other specialists – such as nutritionists and social workers – without leaving the department. If the patient requires more studies, they're only a short escalator ride away from the appropriate testing areas. Similar outpatient services will be available for patients with cancer, cardiovascular diseases, diabetes, and other complex conditions.

"It was a bold, simple, and timely idea," said Raymond G. Perelman, a businessman and philanthropist who graduated from the Wharton School in 1940. "It reflects Penn's unwavering commitment to patient-centered care."

By early 2009, the center will be home to 12 clinical specialties. All services of Penn's Abramson Cancer Center will be located there, as will heart, lung, vascular, and digestive diseases services. Other specialties will include endocrinology, rheumatology, dermatology, plastic surgery, and executive health. When all of

the Perelman Center's practices open, 300,000 patients are expected to visit each year. In addition, by integrating doctors and scientists throughout the building, the Perelman Center also advances PENN Medicine's broader mission to revolutionize translational research and pioneer innovative clinical trials.

"The future of medicine is here," said Ralph W. Muller, CEO of the Health System. "The Perelman Center sets a new standard for accurate and timely patient care, based on collaboration, consultation, and cutting-edge research."

An Environment of Comfort and Healing

The Perelman Center is the largest capital project in the history of the Health System. It includes 225 exam rooms, 84 private chemotherapy infusion bays, and an outpatient surgical pavilion with eight state-of-the-art operating rooms of 600 square feet. Designed by Perkins Eastman/Rafael Viñoly Architects, a joint venture, the Perelman Center was built to create a comfortable and easy-to-navigate environment for patients and their families. The soaring glass atrium aims to create a welcoming central area adjacent to café and retail space. Exam rooms are a spacious 110 square feet, providing ample room for family members and friends. Special consultation rooms throughout the facility bring doctors, nurses, and other medical professionals directly to patients and their families, eliminating the need for visits to different offices around the medical campus.

Additional waiting rooms offer a comfortable retreat for family caregivers during appointments, supporting research that found social interaction helps patients with cancer live longer. Among other comforts are valet parking that puts patients within steps of their clinics and free wireless Internet access throughout the facility.

Much of the Perelman Center was constructed with recycled local materials

and wood from sustainable forests. It will be 15 percent more efficient than older buildings and is expected to be among only a few U.S. hospitals to earn the prestigious LEED certification as a "green" building. A green housekeeping program uses non-toxic chemicals to clean, and the building stocks only recycled paper cleaning products. Energy-saving components include motion sensor lights and 21 stations in the underground garage for charging electric cars.

In 2005, Raymond Perelman and his wife Ruth pledged \$25 million toward creating the Perelman Center for Advanced Medicine. "The facility is a powerful symbol of hope to patients and their families," said Amy Gutmann, Ph.D., president of the University of Pennsylvania, who introduced Raymond Perelman. "It is a fitting tribute to the compassion and generosity of Ruth and Ray Perelman and their loyal and steadfast support for Penn." Gutmann, Rubenstein, and Muller stayed close by on the podium as the Perelmans cut the red ribbon. Then it was time to sample the ceremonial cake.

In addition to the Perelmans, numerous faculty members, trustees, patients, and School of Medicine alumni contributed generously to make the Perelman Center possible.

Adjacent to the Perelman Center – and currently under construction – are the Jerome and Ann Fisher Translational Research Center (scheduled to open in 2010) and the Roberts Proton Therapy Center (opening later this year). Together, they will further align medical research and care and allow Penn to offer the most advanced treatments.

As Rubenstein asserted, "These buildings will make Penn the destination of choice for patients, students, and researchers." ■

– Sally Sapega and John Shea

A Very Rare Gem



John P. Pryor, M.D., aboard a military plane in Iraq, December 2008.

The Death and Life of John Pryor

By Sally Sapega and John Shea

It was only two years ago that John P. Pryor, M.D., G.M.E. '01, a trauma surgeon at HUP and an assistant professor of surgery in the School of Medicine, returned from a tour of duty in Iraq. Pryor was also a major in the United States Army Reserve Medical Corps, having volunteered in 2004. As he recounted in the Fall 2006 issue of *Penn Medicine*, he spent three months with the 344th Combat Support Hospital in Abu Ghraib, operating on wounded soldiers. Some did not make it. In his account, Pryor wrote: "There was – and always is – a palpable grief that comes over the entire staff when we lose an American soldier. Everyone is affected, and everyone deals with it in a different way. For me, this is not an objective, depressing thing; it is very, very personal. I was the surgeon who couldn't save him. For me the grief is intolerable."

Today, Pryor's colleagues at Penn are trying to deal with the same kind of grief. On Christmas Day, back in Iraq for a second tour of duty, John Pryor was killed by an enemy mortar round that exploded nearby. Deployed on December 6, he was on location near Mosul with a forward surgical team of the U.S. Army's 1st Medical Detachment. He was 42, married to Carmela V. Calvo, M.D., and father of three young children.

Raised in Upstate New York, Pryor showed an inclination to help others from an early age. He became certified in CPR when he was 14, joined the Clifton Park-Halfmoon Ambulance Corps at 17, and became a New York State EMT at 18. He completed his medical degree at the State University of New York at Buffalo, where he also became chief resident in general surgery. In 1999, he arrived at Penn for a fellowship in trauma and surgical critical care.

C. William Schwab, M.D., chief of the Division of Trauma and Surgical Critical Care, met Pryor for the first time in the

fall of 1998, when he interviewed the young surgeon for the fellowship. "It was obvious from the start that he was extremely focused on service and devotion and the welfare of others," said Schwab. "At his core were many great values, but his passion was for service to others." When Pryor completed his fellowship, Schwab offered him a spot on the Trauma and Surgical Critical Care faculty "with not a moment's hesitation. I wanted him to become a trainer, a mentor, . . . and he outperformed all of my expectations."

Even before Pryor left on his first tour of duty in Iraq, he had demonstrated his acute sense of service. When the two towers of the World Trade Center were destroyed by the terrorists on September 11, 2001, Pryor traveled from HUP to New York City, ready to offer his skills. He was told to remain in a room with other doctors until he was called to do something. He chose not to wait. Instead, "he did what he thought he should do," said Rev. Damian McElroy, pastor of Pryor's church, Our Lady of Good Counsel, in Moorestown, N.J. As he put it while delivering Pryor's eulogy, "He went outside, flagged down an ambulance, went to Ground Zero, and worked through the night."

In moving between West Philadelphia and the Army hospital in Iraq, Pryor sometimes found himself comparing his experiences. In one of his messages from Iraq in May 2006, which he called "I Know Death," he personalized death as a devious adversary. "When I decided to be a trauma surgeon, it became an all-out war between him and I. We meet every night in the trauma bay. Some nights it is routine stuff, hemorrhage, pulmonary failure, shock – he knows not to mess with me with this easy stuff." Other times, Death wins some of the rounds. The intensity changed in Iraq: "As a war surgeon, I have seen a level of destruction that even I thought was not possible. . . .



Photo: David Warren, Philadelphia Daily News

I fear him for the first time: he is not the same beast I foil with in Philadelphia. Any control or balance I had with him back at home is lost here; I feel totally defeated."

In an op-ed piece he wrote the following year, published in *The Washington Post*, he again compared the two settings. In "The War in West Philadelphia" (August 5, 2007), he described a day when the victims of a shooting at a crack house were rushed to HUP: "As the gurney rolled in, I saw a lifeless young man with more gunshot wounds than I could count. I was poised to start a resuscitation effort when a voice behind me announced that three more were coming in. As the team started CPR and checked for cardiac activity, the second and third victims were wheeled in." One of them was a young girl, who had suffered a gunshot wound to the abdomen "that made her writhe in pain."

"In the swirl of screams and moving figures, my mind drifted to my recent experience in Iraq as an Army surgeon. . . . As nine or 10 patients from a firetruck rolled in, I sometimes caught myself saying 'just like another Friday night in West Philadelphia.'

"The wounds and nationalities of the patients are different, but the feelings of helplessness, despair, and loss are the same. In Iraq, soldiers die for freedom, for honor, for their country, and for their

buddies. Here in Philadelphia, they die without honor, without purpose, for no country, for no one.”

Pryor grieved for these victims as much as for the soldiers fighting in Iraq – and he urged the nation to pay attention to them as well. “There is a war at home raging every day, filling our trauma centers with so many wounded children that it sometimes makes Baghdad seem like a quiet city in Iowa.” This war on the streets, as he put it, “continues unabated” because of a lack of “compassion and empathy.” Where, he asked rhetorically, is the outrage? Where are the Senate hearings to end this war at home?

Nicknamed “JP,” Pryor was recognized at HUP not only as an excellent surgeon but as a gifted teacher. Daniel Holena, M.D., a fellow in Trauma and Surgical Critical Care, said, “There’s sometimes a tendency in medicine to look down on someone who doesn’t know something, but Dr. Pryor used these times as an opportunity to educate, to help us learn.”

Pryor had an open-door policy. He never hesitated to tell people to contact him if there was a problem. “The first time I took call as a fellow, a guy came in with multiple gunshot wounds and was bleeding to death,” Holena recalled. “I called Dr. Pryor, and he told me what to do – gave me a plan – to get the patient out of trouble. It was only later that I learned that he was in Hawaii when we talked.”

It wasn’t only fellows who benefited from Pryor’s approachable teaching style. According to Holena, “He took anyone interested in learning under his wing.” Indeed, Pryor became a mentor to nurse practitioners, defining their role in trauma and giving lectures for a trauma course for nurses. He also allowed students from the School of Medicine and the Wharton School to shadow him.

Douglas Tansey, for example, met Pryor shortly after beginning med school. As



Pryor enjoys a rare break with one of his mentors at HUP, C. William Schwab, M.D.

Tansey put it, it was the start of a relationship that “played a huge part in my life.”

Pryor invited Tansey to do research with him during the summer. In his second year, Tansey shadowed Pryor, taking on the same shifts. “I had no clinical experience, but he was so patient. He always took the time to explain what he was doing.”

To expose other medical students to these types of experiences, Pryor and Tansey established the Penn Association for the Surgery of Trauma in September 2007. The goal was to promote Trauma and Surgical Critical Care through a variety of initiatives, including workshops, sessions in the simulation lab, and lectures. Said Tansey, “Dr. Pryor not only designed all these scenarios in the simulation lab, he also ran a bunch of simulation training sessions. He always told me, ‘Book learning is important, but you have to practice.’ And he always took a few minutes to give me encouraging advice. He was a huge source of support for me.”

Before Pryor left for Iraq, he and Tansey worked together to create a Trauma Evaluation and Management Program for medical students across the city, based on the Advanced Trauma Life

Support program for surgical residents. They had planned to move ahead with the program in the spring, when Pryor returned home from his second tour.

In the days after his death, many colleagues spoke of Pryor’s compassionate side. “JP really connected with patients,” said Kate Fitzpatrick, R.N., C.R.N.P., M.S.N., clinical director of Nursing Operations. “He was very empathetic – he’d cry with them, he’d laugh with them. He’d visit longer-term patients on the unit just to say hello.”

His compassion and caring extended to coworkers as well. “Everyone had equal standing with John,” said Fitzpatrick. “He always made you feel important.”

Chris Brown, a second-year pastoral care resident, recalled talking to Pryor while on call in the ED. “I had moved from Atlanta 16 months before to get training with doctors and was overwhelmed with grief. I wasn’t accustomed to see so much violence with African Americans, and I told Dr. Pryor I was ready to quit.”

Pryor talked quietly with Brown for 45 minutes. “He took off his ‘doctor’ hat and ministered to me. He said ‘You are a gift to

us. This is war and you were brought here to serve. We need more African American chaplains up north. I can heal patients and send them out, but they see someone different when you talk with them.”

Outside of work, Fitzpatrick spent time with Pryor, his wife Carmella (a pediatrician at St. Christopher's Hospital for Children), and their three children (Danielle, Francis, and John Jr.). Fitzpatrick spoke of going to dinner at their house with other members of a group who had participated in the first Penn Advanced Trauma Operative Management program.

“After dinner, John, his older kids, and I went down to his basement for a



Photo: Alejandro Alvarez, The Philadelphia Inquirer

Pryor's casket is carried into Philadelphia's Cathedral Basilica of Saints Peter and Paul.

jam session. John was on guitar and his son played the drums. It's a really great memory of the kind of dad he was – spontaneous and fun.”

Pryor also had a great sense of humor, which did not fail him even after he became director of the Trauma Program in September 2006. “He took kidding and could dish it out,” said Holena. “He loved verbal sparring – but he was often the butt of his own jokes. He didn't take himself too seriously.”

Some Fridays after work, the trauma team would head over to the nearby New Deck Tavern to relax and talk. They also

used the time together to quarterback events of the past week. “We'd brainstorm about how to make the trauma unit better,” said Corinna Sicoutris, M.S.N., C.R.N.P., C.C.R.N., a critical care nurse practitioner on Rhoads 5 and clinical administrator for the Penn Trauma Network. “John would write ideas on a napkin. . . . He was a leader, innovative and brilliant.”

Anne-Marie Podgorski, R.N., M.B.A., had a similar experience. Pryor, she said, “was constantly drawing diagrams to explain things. He'd hand me a paper with lots of blocks and connecting lines and arrows to help put things in perspective.”

Podgorski came to Penn as manager of the Trauma Program in 2007. “John was my boss but we were like left and right arms.”

In addition to being her mentor, Pryor was also her introduction to the world of food trucks outside of the hospital. “I was always trying to get him to eat healthier foods, but he loved his cheese steak and would tell me, ‘No greens!’”

The impact of Pryor's death has been felt far beyond his family, his friends, and his coworkers, and media coverage has extended far beyond Philadelphia. “John touched so many lives in such a positive manner – at HUP, across the region, and around the world,” said Garry Scheib, chief operating officer of Penn's Health

System and executive director of HUP. “His dedication and commitment to his patients and his profession established standards which we all strive to achieve.”

The Department of Emergency Medicine has received more than 1,000 e-mails, including from places like Norway, Taiwan, and South Africa. Podgorski herself has received calls and e-mail messages from trauma centers throughout the country. “I've been flooded with calls from patients and their families,” she said, “even from people who didn't know John.”

A blog on the *Times Union*, of Albany, N.Y., a newspaper near Pryor's hometown, has more than 25 pages filled with heartfelt messages. (A link can be found on www.drjohnpryor.com, a web site created by his family to share thoughts and memories of him.) On the day of his funeral, flags flew at half mast at state government buildings in New York and New Jersey.

Because of the outpouring of grief after Pryor death, his funeral mass was moved from the community church closer to his home in Moorestown to the Cathedral Basilica of Saints Peter and Paul in Philadelphia. The cathedral was packed to capacity – more than 1,300 people paid their last respects. “He never waited for others to do what he could do,” Father McElroy, Pryor's pastor, told those attending the service. “He found it impossible to rest on his laurels. He always wanted to do more – be an example, personally and professionally, be a better doctor, a better father.”

Pryor's mentor, William Schwab, came to much the same conclusion. “At Penn, we have a constant flow of beautiful gems who come to learn trauma and critical care management,” he said. “Then comes along a very rare gem – someone with phenomenal intellect, tremendous skills, as well as goodness, devotion, and a constant concern about other people.

“John was the best of the best.” ♥

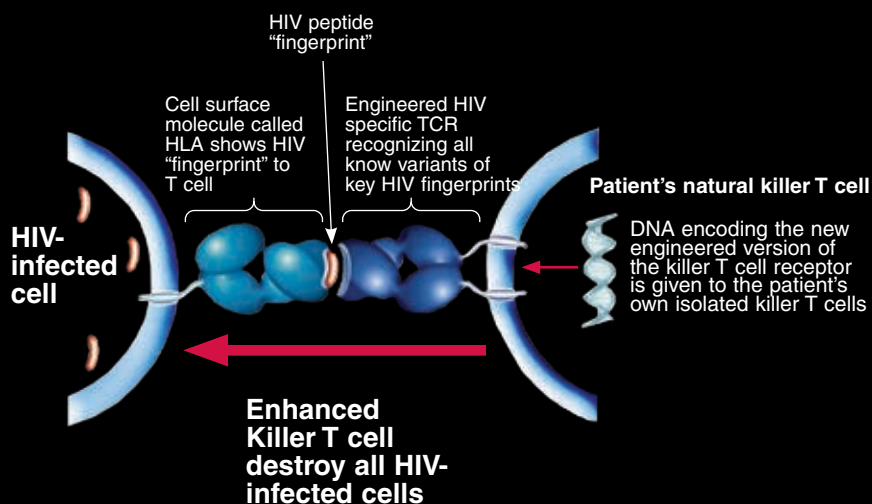
A Fund for Dr. John Pryor has been established to help his wife and their three children. Donations can be made to:

***UPHS – Dr. John Pryor Fund
Suite 750
3535 Market Street
Philadelphia, PA 19104***

Engineered T Cells Gain a Weapon Against an Elusive Enemy:

HIV

By Karen Kreeger



Scientists have long noted the exceptional ability of HIV to evade the body's immune system. Compared to other viruses, HIV-1 has been a much more challenging foe.

Viruses that enter the body hijack the machinery of host cells to replicate and spread infection. When the body's cells are infected with a virus, they expose small parts of the virus on their surface. That exposure offers a molecular "fingerprint" (called an epitope) for killer T cells from the immune system to see. The immune system responds, sending the killer T cells to eliminate the virus and any cells involved in its production. But HIV has the ability to mutate quickly, swiftly disguising its fingerprints to allow it to hide from killer T-cells.

Until now. Researchers at the University of Pennsylvania School of Medicine and colleagues in the United Kingdom have engineered T cells that are able to recognize HIV-1 strains that have evaded the immune system. Their findings, published online in *Nature Medicine* (9 November 2008), have important implications for developing new treatments for HIV, especially for patients with chronic infection who fail to respond to antiretroviral regimens.

Natural T cells recognize their targets through weak molecular interactions me-

diated by the T cell receptor. Through a clever molecular process, the investigators were able to isolate a group of T-cell-receptor encoding genes that bind to HIV-1 about 450-fold more strongly. According to James Riley, Ph.D., research associate professor of pathology and laboratory medicine at Penn and senior co-author of the study, "Not only could T cells engineered to express the strongly binding T cell receptor see HIV strains that had escaped detection by natural T cells, but the engineered T cells responded in a much more vigorous fashion so that far fewer T cells were required to control infection."

Angel Varela-Rohena, Ph.D., the study's first author, points out another benefit: "With the present availability of potent systems to replicate and deliver high-affinity HIV-1 specific T-cell receptors, billions of these anti-HIV-1 warriors can be generated in two weeks." Varela-Rohena recently completed these studies as part of his doctoral dissertation at Penn.

"We knew there would never be a conventional vaccine for HIV," explains Professor Andrew K. Sewell from Cardiff University, United Kingdom, co-senior author of the study. "In the face of our engineered assassin cells, the virus will either die or be forced to change its disguises again, weakening itself along the way. We'd prefer the first option but I

suspect we'll see the latter."

Carl June, M.D., professor of pathology and laboratory medicine at Penn, describes the next steps: "We hope to begin clinical trials using the engineered T cells in patients with advanced HIV infection next year, a group for whom many drug regimens have stopped working." June, who is also director of translational research at the Abramson Family Cancer Research Institute at Penn, is co-author of the *Nature Medicine* study. "If the therapy in that group proves successful, we will treat patients with early-stage, well-controlled HIV infection. The goal of these studies is to establish whether the engineered killer T cells are safe and to identify a range of doses of the cells that can be safely administered."

The engineered receptor, says Bent Jakobsen, Ph.D., co-lead author of the study, "is able to detect HIV's key fingerprints and is able to clear HIV infection in the laboratory. If we can translate those results in the clinic, we could at last have a very powerful therapy on our hands." Jakobsen is chief scientific officer at Adaptimmune Ltd., a company based in the United Kingdom that owns the rights to the technology.

The study was funded in part by the National Institute of Allergy and Immune Diseases and Wellcome Trust in the U.K. ♥

A

Population in Need of Better Sleep

By Nan Myers

“For a price, everyone wants to help us sleep.” So said Nirav Patel, M.B.,B.S., assistant professor of clinical medicine in Penn’s Division of Sleep Medicine. He spoke at a recent symposium on “Population Sleep,” sponsored by Penn’s Center for Sleep and Respiratory Neurobiology. Examples are plentiful: drugs like Lunesta (“A great tomorrow starts tonight”), even

cular disease, obesity, depression, and increased mortality. It also goes without saying – fatigue.”

There are many reasons that people of all ages don’t sleep well. Most presenters agreed that our driven society plays a part – hectic schedules, shift work, disruptive noise, the always-available Internet, and round-the-clock television.

Patel and his team are conducting research in West Philadelphia to be able to tailor messages about the importance of sleep and to create interventions. “We have to let people know in a way they will understand.” In another study, Patel’s group will look at individual households to understand generational differences in the attitudes and perceptions among

A theme of the symposium:
“We have to put sleep deprivation on the same level as smoking in the minds of the public.”

a good old Serta mattress. As Patel put it, “A good night’s sleep is an overlooked pillar of healthy living. It is a crucial health behavior that is biologically driven, but undoubtedly socially constructed.”

Madison Avenue *knows* that insufficient sleep is a problem. Experts in the field agree that most adults need seven to nine hours of sleep to be fully rested. So why do so many fail to get a good night’s sleep regularly? That was one of the questions posed at the symposium, which included sleep researchers, physicians, nurses, public health officials, social workers, and others. The main message was that insufficient sleep, although a widespread problem, is not well recognized among the public, the medical community, or the business community.

“We have to put sleep deprivation on the same level as smoking in the minds of the public,” said Allan Pack, M.B.,Ch.B., Ph.D., director of the sponsoring center.

According to Wayne H. Giles, M.D., from the Centers for Disease Control and Prevention, “insufficient sleep is linked to such problems as diabetes, cardiovas-

Always connected means always stimulated. Stress can be a major factor.

Lauren Hale, Ph.D., associate professor of preventive medicine at the State University of New York at Stony Brook, takes a less obvious approach, looking at household environments. For example, how does sharing a bedroom, especially among people who live in lower-economic urban environments, affect sleep habits? Hale presented recent data showing that if mothers have poor bedtime routines, the behavior may trickle down to their children; in turn, they don’t learn good bedtime routines and can begin a lifetime cycle of poor sleep.

“Sleep patterns and sleep disorders vary by race and ethnicity in the United States,” Hale reported. “The relationships tend to be tied to socioeconomic factors such as education, unemployment, neighborhood, and obesity, and probably begin early in life. As a result, these racial and ethnic differences in sleep patterns may contribute to disparities in educational attainment, economic productivity, and health.”

their members. “We might interview a 40-year-old with poor health habits. How does his lifestyle affect his sleep and the sleep of the people who live with him – his parent and his child?”

Patel also discussed the popularity of over-the-counter sleep aids. “These products are being promoted as a cure for sleep issues.” Although some drugs may help with insomnia, “we don’t know their long-term effect.” At Penn, a psychologist is available to work with people “who feel they must have a sleeping pill and who don’t have any underlying psychological or medical problem. The psychologist helps patients to restructure their sleep behavior.”

“We have so much more to learn,” said Giles of the CDC. “For instance, if we treat a person’s sleep apnea, will it affect their diabetes?” Or, as Allan Pack asked, “Can you transform someone who sleeps five hours a night into someone who sleeps seven hours a night and also improve their health?”

Such questions need answers, and there’s really no time to sleep on it. ♥

TWO IN

*From Music to
Obesity*



As Jack A. Yanovski, M.D., Ph.D., monitors the readings, Laura Wolkoff, B.A., sits inside the Bod Pod. The machine measures body composition (fat mass and fat-free mass) non-invasively.

TUNE

Photographs by Addison Geary

by Rita M. Rooney

The three Yanovski children share a love of music with Jack and Susan. Here, daughter Rachel and son Andrew enjoy a family jam session.



Research

Circa 1982: Onstage in Dunlop Auditorium, the annual Penn Med “Spoof” presents a medically satirized collection of Gilbert and Sullivan songs under the title *The Medikado*. To the tune of “I Am the Very Model of a Modern Major General,” a male voice intones with comic emphasis:

I am the very sample of a simple surgeon general.

I know which anesthetics are long lasting or ephemeral.

I’ve taken out a thousand extra tonsils and appendices

And aided millions by removing hemorrhoidal varices.

This satire, or rather the music that inspired it, was the impetus for bringing together Jack A. Yanovski, M.D. ’86, Ph.D. ’89, and Susan Zelitch Yanovski, M.D. ’85. They met when she organized and directed a medical school choir, and he became her star baritone. They performed in spoofs and shows, including *Guys and Dolls*, in which Jack played the gambler Nicely-Nicely Johnson, and Susan the Salvation Army general. Both wrote lyrics for several of the medical students’ Spoofs. Among Susan’s compositions was one on the joys of being accepted to Penn Med, crafted to the tune of *West Side Story*’s “Somewhere,” and another called “Anatomy Rag,” set to the music of Tom Lehrer’s “Vatican Rag.” She is quick to claim, however, that Jack was the more prolific of the two, and that *The Medikado* undoubtedly was his crowning achievement.

Years later, following a school production of *Annie*, in which their son, Andrew, played the villainous Rooster Hannigan, someone approached the couple, asking how they could have three children who were all such talented actors and musicians. “I thought you are both doctors,” the man pointed out.

Susan laughs today remembering the incident and their explanation that they were actors and

musicians before they were doctors. As she puts it, “Penn Med just reinforced our belief that music and medicine go hand in hand.”

Today, the Yanovskis share not only a long involvement in music but parallel medical careers in which they have become internationally recognized authorities on obesity, particularly the escalating problem of childhood obesity. Some of their joint pieces for professional journals include a review of recent advances in basic obesity research in *The Journal of the American Medical Association* (October 27, 1999); a review of drug therapy to treat obesity in *The New England Journal of Medicine* (February 21, 2002); and an editorial in *JAMA* on the treatment of pediatric and adolescent obesity (April 9, 2003).

They have often been cited in the popular press as well. For example, both were quoted in *The Washington Post* on the challenge of getting through the holiday season without gaining weight. (Thomas Wadden, Ph.D., director of Penn’s Weight and Eating Disorders Program, was quoted in the same article.) Susan Yanovski was one of only two experts cited in a 2002 editorial in *The New York Times* called “America’s Epidemic of Youth Obesity.” And last September, Susan was quoted in *The Washington Post* on the question of whether food should be considered addictive. She expressed doubt that food addiction “is a real phenomenon” and pointed out one of the possible complicating factors – that abstinence, the standard treatment for drug and alcohol addiction, would not work with food.

“You can be totally abstinent in using drugs or alcohol,” she wrote, “but you can’t be abstinent with eating.”

Until now, Jack Yanovski explains, drug treatments for pediatric obesity have been ineffective because they haven't targeted the multiple root causes of increased body weight. He adds that there is still no approved medication for the treatment of obese children, and only one, which is relatively unsuccessful, is approved for adolescents. All that, however, may be changing.

"The personalization of medicine has allowed us to move forward and make important strides in our obesity research," he says. "This is an exciting time for scientists in the field, as we move closer to understanding cause and effect and to finding new forms of treatment."

A widely known expert in the endocrinology and genetics of pediatric obesity, Jack heads the Unit on Growth and Obesity at the Eunice Kennedy Shriver National Institute of Child Health and Human Development, one of the National Institutes of Health (NIH).

Susan is director of the Obesity and Eating Disorders Program and co-director of the Office of Obesity Research, both at the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). A pioneer in the earliest studies of binge eating in adults, she now is involved primarily in the study of children who binge eat – and it is in this area that the Yanovskis' work comes together.

In addition to conducting her own clinical research, Susan coordinates clinical obesity studies funded by NIDDK. She helps determine the areas of obesity to be funded, pinpointing gaps and opportunities for study. She also is responsible for nurturing young investigators. Jack covers everything from basic science – working with animal models and cell research – to clinical trials, and conducts lab work involving genetic differences. In addition to their individual publications, together they have published papers on children who binge eat or demonstrate loss of control in their eating habits.

Beyond their published work and grasp of obesity research on a variety of aspects, both pediatric and adult, the Yanovskis have earned the unqualified regard of colleagues. According to Kelly D. Brownell, Ph.D., a professor of psychology, epidemiology, and public health at Yale University and director of the Rudd Center for Food Policy and Obesity, "Susan and Jack are top-rate researchers who were studying the problems of over-nutrition and obesity long before those issues became the coin of the realm."

Brownell, a professor in the Department of Psychiatry at Penn from 1977 to 1990, says, "The Yanovskis are important and visible figures in the field, not only by virtue of their research, but because of their insights, leadership, and positions in government."

Discussing her recent work, Susan reports, "We're now looking at children in a laboratory setting in which they are presented with an array of foods. Some of these children are as young as six years old, and they include both lean and obese children, some of whom report loss-of-control eating. We're finding interesting differences in eating patterns that may help us develop more targeted interventions to help prevent weight gain in kids at risk."

This and other studies have shown that, when parents and children are asked separately about eating habits, one often recognizes a problem and the other doesn't; that's why the researchers decided to study eating behavior in a laboratory setting rather than relying on reports by the study participants. In addition, there is evidence that, when parents think there is a need to restrict a child's food intake, and even when parents try to cut back on portions, the child nevertheless is at very high risk for putting on extra pounds. It remains unclear, however, whether the weight gain is a response



Gathered for a discussion on obesity are, left to right, Abena Akomeah, B.S., Susan Z. Yanovski, M.D., Jack Yanovski, M.D., Ph.D., David M. Savastano, Ph.D., and Marian Tanofsky-Kraff, Ph.D.

to the attempt to restrict food or because of a genetic susceptibility to over-eating.

Susan contends that it's difficult to conclude whether a child's obesity is caused by environmental factors or genetics when the child's parents are obese and they have obese children. To distinguish among some of the environmental factors and genetic differences that may lead to over-eating, the Yanovskis are collaborating with Myles Faith, Ph.D., assistant professor of psychology in psychiatry at Penn's Center for Weight and Eating Disorders.

"For years, Sue and Jack Yanovski have been driving forces in the field of pediatric obesity, including its onset and treatment," says Faith. "Their current work, for example, is providing important insights into eating patterns that may lead to childhood obesity and how these behaviors may have a genetic component. Here at Penn, we're fortunate to be collaborating with them on some of this work."



Susan Yanovski outside her NIDDK suite.

The Yanovskis published a paper in the April 2006 issue of *Pediatrics*, the journal of the American Academy of Pediatrics, citing evidence that children who binge eat are more likely to become obese adults. (Jack was senior author, and there were six other authors in addition to Susan.) The study showed that these children gained more body fat than those who did not binge over an average of four years. As Susan puts it, “That leads us to hope that, if we can address binge eating before youngsters become very overweight, we may be able to prevent adult obesity in these kids.”

Previous research shows that a variety of weight-reduction programs have succeeded in getting people to lose 5-10 percent of body weight, which is sufficient to produce significant health benefits. The NIH conducted a study on diabetes prevention in which overweight people at high risk for diabetes lost about seven percent of body weight. That loss

was enough to cut their risk of type 2 diabetes in half. Among most scientists studying the ramifications of obesity, the question has become how to prevent undue weight gain in the first place.

That’s exactly what Jack Yanovski is investigating. Since 1996, his laboratory has been working on identifying both the physiological and genetic factors that predispose children to obesity.

In 1994, scientists at Rockefeller University cloned leptin, a protein made by fat cells that regulates energy balance, leading to a quantum leap in understanding the pathology of obesity. It was a first step in elucidating the cascade of proteins that work in the hypothalamus and elsewhere in the brain to control eating behavior and metabolism.

“It is true that, when obese people who can’t make leptin are given leptin, they greatly decrease their food intake and develop a more normal body weight,” says Jack. “However, almost all overweight people have high leptin levels, leading to the conclusion that there are many genes other than leptin involved in obesity that may function downstream of leptin.”

Recently, the Yanovski lab has been looking beyond the leptin receptor, focusing on two different genes, *MC3R* and *BDNF*, both of which work downstream of leptin. The lab discovered a pair of polymorphisms of the *MC3R* gene that are highly linked with pediatric obesity and are more prevalent in African American children. They now are attempting to understand the mechanisms by which these mutations alter *MC3R* signaling.

According to Jack, “We are just starting to characterize two strains of mice which we have engineered to replace the mouse *MC3R* gene with either the normal human *MC3R* gene or the mutant human *MC3R* gene we found in some children with obesity.” He adds that the effects of leptin and the leptin receptor

may have the same impact on children and adults, but he believes there are a number of genes that act differently at different ages. For that reason, some of his laboratory studies have been designed to look longitudinally in order to understand the actions of genes during development as well as in adulthood.

“It may be possible to identify important factors in adults that are different from those that have an early impact,” he says. “It may be, too, that the stronger genetic effects manifest themselves early. That’s one reason we emphasize the importance of pediatric research.”

Still another, he says, is the need to learn how to treat obesity in young children because being overweight as a child predisposes one to an increased risk for heart disease and colon cancer later in life – whether the person remains obese as an adult.

As Jack points out, the challenge of prevention and treatment is a difficult one, complicated by the interaction of environment and genes. “It’s pretty clear that a child’s genetic predispositions towards obesity can be affected by prenatal, family, and cultural environments in ways that may mitigate or exacerbate risk.”

That explains why the Yanovski laboratory pursues a multi-pronged approach that looks at genetic factors as well as the environment to examine how genes and environment interact. Ideally, researchers want to determine which children are most at risk and why, so that they can develop the precise prevention strategies. The Yanovskis say they want to know why some children tend to eat when they aren’t hungry, why others get hungry more often, or have a preference for high-fat foods, or engage in low levels of physical activity. Pinpointing who is at risk and why, they believe, will hasten the availability of effective treatments.

When they’re not at work, the Yanovskis put family first, followed by music. But

their two interests, it turns out, often overlap. The parents have instilled an appreciation of science and music in all three of their children. Josh, the oldest, is studying computer science and mathematics at the University of Chicago, where he plays jazz guitar. Rachel, a high-school senior, studies voice, jazz dance, and acting, and 14-year old Andrew studies jazz piano and saxophone. The three are as likely to be seen with their parents having a jam session at home or enjoying an Andre Watts performance with the Baltimore Symphony Orchestra as they are collaborating in the family sport of writing parodies. Dinnertime often includes discussion of developments in Susan or Jack's work or a recent scientific paper one of them has read.

As for parodies, the whole family got together to write one for a recent Passover Seder in which they created a musical version of the story of the Exodus, using the melody of the Beatles' "I Saw Her Standing There."

For Susan, this kind of creative sidebar to medicine is one of the aspects they enjoyed in medical school. "One of the things Jack and I loved about Penn Med was the fact that, in spite of the academic demands, so many students had talents and interests beyond medicine. I think it is a tribute to the admissions process that it goes beyond looking at GPA and MCAT scores to find students who will not only make good physicians but who will contribute to the fabric of the community."

Jack agrees, remembering that medical school gave them the opportunity to mix with people who were not focused on a single interest. Both Yanovskis served on the admissions committee for students while at Penn. Jack recalls there were many students who had other careers first and brought the richness of those experiences to the medical scene.

"I believe such experience often leads to the making of more compassionate physicians," he says.

Compassion and the ability to understand the emotional as well as the physiological ramifications of childhood obesity are important qualities for obesity researchers – and the people they have worked with find these qualities in both Yanovskis.

Marian Tanofsky-Kraff, Ph.D., assistant professor at the Uniformed Services University of the Health Sciences, was a fellow in Jack's laboratory and worked with Susan as well, specifically in the area of binge eating. (She was an author of the *Pediatrics* study.) Although the Yanovskis credit her for much of the important work being done in the field, she deflects the compliment and cites the couple's intrinsic generosity.

"Few people are as brilliant as they are, or have contributed as much to the study of obesity," says Tanofsky-Kraff. "They have a masterful talent for balance and understanding the issues involved. Susan did some of the first really thorough assessments of binge eating and obesity. I'm constantly impressed by Jack and Susan's clear thinking, not only by how quickly they come up with ideas, but how open they are to the ideas of others."

Jack Yanovski's persistent search for genetic clues to the prevention of childhood obesity recently produced some exciting findings that may eventually lead to a new form of treatment. He is senior author of a study, published in the August 28, 2008, issue of *The New England Journal of Medicine* and reported that day in *USA Today*, that points to another effector system downstream of leptin. Called brain-derived neurotrophic factor (BDNF), it appears to have an important impact on food intake. When the investigators increased the amount of BDNF in animals, they tended to eat less, suggesting that a deficiency of BDNF might lead

to obesity. More than one model bears this out.

"We were part of a team that described a severely obese and hyperphagic child with a chromosomal inversion that, by our measurements in serum, seemed to induce low BDNF," Jack reports. "There also is a more general phenomenon – that some obese children have very low serum BDNF concentrations." Speak-



Jessica Heavin, M.S., and Jack Yanovski observe as Caroline A. Roza, B.S., performs exercise tests on a stationary bicycle. The tests measure fitness, a crucial factor in determining health in overweight and obese people.

ing about the *NEJM* study, he says, “We recently characterized a group of individuals with chromosomal defects that delete one copy of the *BDNF* gene. These patients had early onset of obesity before age 10.

“If we can replace BDNF in the brain of these individuals, we believe we might very well have a new treatment for at least some people with obesity.”



A “Perspective” by two English scientists in that issue of the *Journal* asserted that the study provided “elegant evidence that the gene encoding brain-derived neurotrophic factor (*BDNF*) is also involved in obesity. . . . When the researchers compared patients whose *BDNF* gene was included in the deletion with those with an intact gene, the situation was clear: whereas 20% of patients with an intact gene were obese (not very different from the national average), every single one of the patients with a *BDNF* deletion had a body-mass index above the 95th percentile.”

No surprise that this potential treatment excites Jack Yanovski, who points out that treating pediatric obesity has been ineffective because science has not been treating its root causes. “Treatments so far have consisted of attempts to restrict food or increase activity, or efforts to work through final common pathway neuro-transmitters, as appetite suppressants do,” Jack explains. “But these are non-specific approaches for most children because we don’t know the multiple genetic and environmental factors that contribute to obesity in those children. There are many redundant systems that maintain body weight, so treatments affecting only one weight-regulating pathway seem unlikely to succeed for everyone.”

Therefore, the idea – which is likely to seem as heady to the entire medical community as it does to Yanovski – is to design specific treatments for specific etiologies. It goes to the core of understanding the phenotypic expression in children that maps to their genetic differences. Jack Yanovski concludes that once that such mapping is done, it will be possible to address the causes of childhood obesity much more effectively.

Susan adds that childhood obesity has become a major priority at the NIH. Part of her work extends to interacting with obesity experts from many NIH institutes to develop research initiatives that

will address pediatric obesity at multiple levels. These approaches include studies of the intrauterine environment, observational research, clinical trials, community-based studies, and studies that examine the impact of policy change. Recently, the NIH issued a request for research that helps develop interventions for preventing or treating childhood obesity in primary-care settings.

“Traditionally, there has been a problem in getting physicians to recognize that kids are overweight,” says Susan. “There often is a hesitancy to address the problem for fear of hurting feelings. It’s important for doctors to assess family history, obesity-related risk factors, and carefully track a child’s BMI over time. However, many physicians don’t know how to intervene effectively to help overweight kids and their families. Our job is to provide them with the evidence base to help them better deal with the issues of prevention and treatment in the real world of medical practice.”

When it comes to childhood obesity and binge eating, the Yanovskis have probed everything from genes to behavior. Susan’s work encompasses not only her own research but the NIH’s support for relevant studies undertaken in academic centers throughout the country. Jack’s *BDNF* research has pointed to promising treatments for childhood obesity in the not-too-distant future. That possibility, he concludes, has been aided by recent scientific discoveries in how body weight is regulated.

To suggest what the future may bring, Jack uses an analogy from one of Gilbert and Sullivan’s enduring operettas. “The Mikado of Japan ordered that the punishment should fit the crime. The principles of personalized medicine, in which specific techniques can be applied to individual genetic differences, hopefully will make it possible for us to let the treatment fit the cause.” ♥

The Importance

For Benjamin H. Natelson, M.D. '67, the timing couldn't be better. Or worse? Recently, he published a book for patients who suffer from pain, fibromyalgia, or chronic fatigue. Then an article in *The New York Times* appeared (January 14, 2008), questioning the very existence of his general topic. The article reported the doubts of some medical experts that fibromyalgia is real. At the same time, however, the *Times* did present the other side of the issue, and the article provided Natelson and some like-minded readers an opportunity to express their own views to a wide audience.

The starting point for the *Times* article was a new television campaign for a drug (Lyrica) meant to help treat fibromyalgia. Although the more positive views of advocacy groups and some doctors were included for balance, the article noted that no biological tests exist to diagnose fibromyalgia. Nevertheless, worldwide sales of Lyrica reached \$1.8 billion last year. The *Times* also cited skeptics who characterize the condition as "vague complaints about chronic pain" rather than a real disease. In fact, one expert asserted that "The diagnosis of fibromyalgia itself worsens the condition by encouraging people to think of themselves as sick and catalog their pain."

Natelson, who recently became director of the Pain and Fatigue Center at Beth Israel Medical Center in New York City, responded promptly. He was not alone. The *Times* ran seven responses as letters to the editor on January 17. Natelson was one of two physicians whose letters were printed. The president and founder of the National Fibromyalgia Association also responded.

Benjamin Natelson is concerned that some doctors fail to do all they can to help patients with chronic fatigue or pain.



In his letter, Natelson criticized what he termed "medical materialism," in which "doctors tell patients nothing's wrong, if no abnormality can be found." For Natelson, the pain felt by his patients is more than just a physical response to everyday pressures. That view, he asserted, ignores "published medical literature showing brain abnormalities in fibromyalgia and drugs that clearly improve patient health." He also cautioned that patients who cannot be diagnosed by "classic medicine" may turn to alternative medicine.

The timing of the *Times* article was fortuitous, because in some ways it provided a context for Natelson's book, *Your Symptoms Are Real: What to Do When Your Doctor Says Nothing Is Wrong* (Wiley, 2008). In it, Natelson suggests what he calls "a comprehensive, practical, and new approach to getting well." That approach involves providing "a road map of what your doctor is thinking" while he or she evaluates patients and their symptoms, including "how to interact with your doctor so that your communication can, indeed, improve." Part two of the book discusses depression, which Natelson argues is "an illness that makes

all symptoms worse and can produce fatigue and pain by itself." Other topics are stress, sleep problems, and the benefits of exercise. The last part looks at some complementary approaches to becoming well and some "promising cutting-edge research"—much of its examining the immune system—and promising treatments.

Although Natelson discusses what he calls "The Doctor-Patient Disconnect," he does not recommend a flight from "classic medicine" to alternative treatments. He describes his Six Week Rule: "I give a treatment six weeks to show that it helps. If after six weeks, the person isn't sure whether the treatment worked, I stop it." And that applies to alternative therapies as well. In fact, one of his chapters is called "From Complementary Medicine to Quackery." He describes several complementary products on the market. For instance, Natelson ran a double-blind, placebo-controlled trial of a "nutraceutical" called Ambrotose, which is an extract of the aloe plant. He found no evidence that it relieved symptoms of fatigue, poor sleep, and pain any better than placebos. As Natelson says in general about similar products and the heartfelt testimonials

of Listening

By John Shea

that accompany them, “If this promise were real, I would have no patients. But I have all too many.”

This fall, as it turned out, an advertisement appeared in *The Philadelphia Inquirer* with the headline “Fibromyalgia? The Doctors Were Right . . . Fibromyalgia IS All in Your Head!” It went on to cite a “local doctor” who has developed “a simple and easy screening to determine if there is a problem in the part of your brain that controls all your muscles as well as your balance.” No concrete details are given about the “brain-based” program that can “finally fix your fibromyalgia,” but readers were invited to call or go to its web site.

Natelson raised some of the same issues discussed in his book in an opinion piece in *The Washington Post*, “Lost in a System Where Doctors Don’t Want to Listen” (August 3, 2008): “Learning how to make a diagnosis is a critical part of medical education. . . . But what happens when your symptoms don’t add up to a clear-cut diagnosis? Studies have shown that in more than 50 percent of cases, patient complaints don’t have any diagnosable medical cause that can be determined by careful laboratory testing. Pain, fatigue, dizziness, and trouble sleeping are among the most common symptoms, and doctors have problems with these because they don’t point to any particular diagnosis.”

In *Your Symptoms Are Real*, Natelson supports his contentions with some historical perspective. One example is Somatization Disorder (SD), in which the symptoms include overattention to one’s bodily sensations or a set of health concerns that have no medical cause. According to the traditional view, SD “amounts

to a chronic form of worrying. . . . One problem with the diagnosis of SD is that it attributes a psychiatric cause to medically unexplained symptoms; it ignores past examples, like torsion dystonia, where medicine made the wrong assumptions about the cause of the disease and where the physical (not psychiatric) cause was very real. . . . Furthermore, once the SD diagnosis is made, the patient is often blamed for being ill.”

Unlike the anonymous advertisement that ran in *The Philadelphia Inquirer*, Natelson does not promise wonder cures. As he put it in his op-ed essay, the treatment of a symptom-based illness is usually “a slow process that unfortunately doesn’t end in a cure but often leads to improvement.”

In an e-mail message, Natelson says



he views himself less as an advocate “but more of an educator. I try to teach med students more appropriate ways” of coping with the lack of knowledge when they attempt to treat patients with conditions that elude ready diagnosis. In addition, he believes that the new emphasis on learning communications skills in medical school “would certainly lead to better doctors.”

Still, the advocacy side came out enough in his *Washington Post* piece to provoke two published letters to the editor and 20 Web comments. They were sent by both doctors and lay persons, and the responses ranged from fairly unfavorable to wildly enthusiastic. (One writer, in fact, wrote: “Dear Dr. Natelson, Will you marry me?” before noting that he is fortunate “to have a doctor very much like you” who has made his life “manageable.”) Two writers reported years of pain and discomfort without a diagnosis. One eventually took matters into his own hands, did some research, and began to suspect he had celiac disease. “I consulted my gastroenterologist and a simple blood test and a follow-up biopsy confirmed that I had celiac.” The other, whose 20 years of chronic fatigue were dismissed as “just imagination,” eventually found a doctor who did “proper testing. . . . He discovered that I have both borrelia (Lyme) and cryptosporidium (microscopic lung worms).”

As his book makes clear, Natelson’s goal is to have patients and doctors working together from the start. “I don’t want you to act as your own doctor, but I do want you to be informed.” A healthy patient-doctor relationship promises the best results. ■



Development Matters

A NEW “FRONT DOOR” FOR THE SCHOOL



The new education space will reinforce the identity of the School of Medicine on the University's campus, creating a “front door” for medical education.

The excitement has been building on PENN Medicine's campus: in June, the first patients started to receive treatment at the new Ruth and Raymond Perelman Center for Advanced Medicine. The massive cyclotron that will be housed in the Roberts Proton Therapy Center arrived early in 2008. And with the naming gift from Wharton graduate and PENN Medicine board member Jerome Fisher and his wife, the new Anne and Jerome Fisher Translational Research Center will soon be added to the West Philadelphia skyline.

And yet this grand picture of medical innovation remains incomplete. While the School of Medicine has introduced and refined its pioneering curriculum over the past 10 years, peer institutions have focused instead on enhancing their physical facilities. Now the time has come to improve Penn's education spaces.

“Our curriculum is second to none in training young physicians for a rapidly changing field,” says Arthur H. Rubenstein,

M.B.,B.Ch., executive vice president of the University of Pennsylvania for the Health System and dean of the School of Medicine. “Now, with the opportunity created by the ‘Making History’ campaign, our top priority is to redesign our campus to support new teaching methods that reflect evolving medical practice and to keep pace with our peer schools.”

Indeed, one of the significant goals of the campaign is to make that redesign a reality – financing for this project will rely entirely on philanthropy. Scheduled to be completed in 2012, the new medical learning environment will combine the power of technology with collaborative learning in a media-rich environment. It will create exciting new opportunities for medical education by facilitating evidence- and problem-based learning, as well as team-based approaches to medical education.

It's a need that current students as well as recent graduates have recognized and are excited to offer their support for. “I'm

OF MEDICINE

currently doing my residency at Stanford,” explains Tim Pirolli, M.D. '08, “and I have found that the places that you would expect to have a good reputation and funding typically have good quality spaces for their students to learn, socialize, and relax. That is the major thing that Penn’s School of Medicine is currently missing.”

Another recent graduate, Patty Salmon, M.D. '08, agrees. “I chose Penn because the curriculum was innovative and reflects the continuing advances in medical technology and practice. We need a physical space that can make our curriculum even more effective – and give Penn’s medical students a place of our own.”

Providing group workspaces will allow students to discuss patient cases and present medical problems, collaborate in order to generate and test hypotheses, and develop their findings into reports using state-of-the-art media and technology. The new space will also harness the strong collaborative relationships among PENN Medicine researchers and other members of the University community.

“I’m very excited about these renovations because they will bring more students together,” says Tara Wedin, a second-year medical student, “and the new space will easily facilitate group studying and collaboration, which are mainstays of a Penn School of Medicine education.”



The Changing Face of Medicine

The School of Medicine's curriculum is regarded as state of the art, but it needs improved physical facilities to help fully realize the program’s educational potential.

“There is a changing landscape in medicine today, and we constantly have to think about how to train the next generation of physicians for the world ahead,” says Gail Morrison, M.D. '71, G.M.E. '76, vice dean for education and director of the Office of Academic Programs. “We are designing this innovative medical education space to encourage teamwork and bridge clinical and research experience – skills that will help our students develop broader solutions to health and societal challenges.”

Currently, the school is forced to schedule classes in six different buildings in order to find enough small classrooms to support the curriculum’s team-based learning approach. It is still working with insufficient technological resources; for example, wireless Internet access is available in only one medical campus building. Limited study space in the school sends students to other Penn libraries. And the school's 30 year-old Biomedical Library, built around books and stacks, does not

20th Century	>>	21st Century
Academic Training		
Large lectures in auditoriums	>>	Small group learning
Slides and microscopes	>>	Digital images viewed on-line
Standard, fixed classrooms and labs	>>	Flexible spaces that easily incorporate new technology
Clinical Training		
Observe acutely ill patients in the hospital	>>	Interact with actors trained to behave as patients
Practice procedures on actual patients	>>	Use simulation technology to perfect technique
Information		
Read print textbooks and scholarly journals	>>	View fresh, constantly updated information on the Web
Stacks of books and journals	>>	Technology-rich information commons
Subdued study environment	>>	Conversational “coffee house” environment
Learning		
Learning based in classrooms or the bedside	>>	Learning possible 24/7
Individual accomplishments	>>	Learning as teams
Individual study	>>	Group study

reflect the 21st century's flow of information enriched through digital technology.

How will the new medical education space support the School of Medicine's curriculum? In addition to featuring clustered, flexible classrooms that will facilitate small-group learning, the space will bring all classes back into one building. Every classroom will be furnished with the latest multimedia technology, making viewing of clinical simulations standard teaching procedure.

The vibrant and active common area, based along Hamilton Walk, will reinforce the identity of the School of Medicine on the University's campus – creating a “front door” for medical education at the University of Pennsylvania.

The Biomedical Library will also be transformed into an innovative information commons that will support individual and team-based study. All of these new facilities will be closely integrated with other School of Medicine, School of Nursing, and Health System buildings in order to more fully integrate the entire spectrum of research and clinical experience.



The new space will feature study booths very much like ones found at the David B. Weigle Information Commons, located in the Van Pelt-Dietrich Library Center.



A look north through the connector to Hamilton Walk. All the new facilities will be closely integrated with other health-care buildings, bringing together the spectrum of research and clinical experience.

Taking Medical Education to the Next Level

By creating a learning environment that will enable students to move easily from team to individual study and coupling it with state-of-the-art media and technology, the new space will enable medical students to:

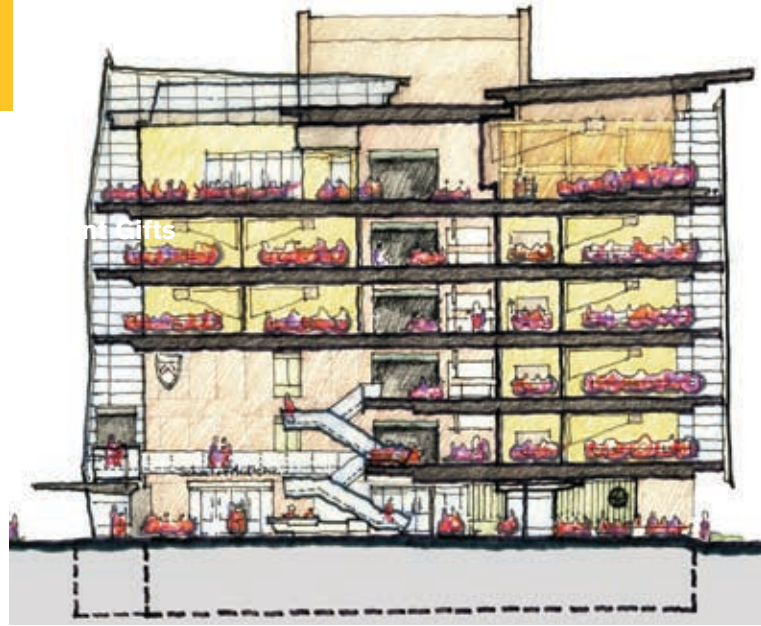
- * Collaborate with fellow Penn students, researchers, or virtually any person in the world using chat, Skype (phone over Internet), and wiki (collaborative on-line encyclopedia) technologies. Videoconferencing over the Internet will facilitate conversations with biomedical experts worldwide.
- * Create mini-documentaries of patients participating in LEAPP (Longitudinal Experience to Appreciate Patient Perspectives) and witness the impact of chronic illness in an entirely new light. Students can also compile and edit audio interviews for easy sharing and presentation.
- * Take differential diagnosis to a new level with interactive multimedia presentations, instant polling technology, and instant access to online resources, including medical journals and texts.
- * Develop, publish, and share case-based presentations and other multimedia creations, and upload them onto the School of Medicine's virtual curriculum for viewing by classmates and faculty.
- * Gather with patient-care teams to review information from electronic medical records, medical imaging, and on-line medical literature.

In addition to the Biomedical Library and information commons, there will be plentiful areas for study and conversation that create an appealing “coffee house” environment to foster interaction and information sharing. Perhaps most important, the new space will enhance and strengthen the School of Medicine's collaborations with other schools at Penn – fully integrating knowledge and developing comprehensive solutions to health and societal challenges.

“This new educational space will rightfully display the University of Pennsylvania School of Medicine as a learning institution with superior facilities that match a high-caliber educational experience,” says Jeffrey Stambough, a second-year medical student. “I'm very excited to see that day.”

We invite you to be part of the next innovation at the University of Pennsylvania School of Medicine. Since its founding in 1765 as the nation's first medical school, Penn's School of Medicine has been one of the leading institutions for the practice of medicine and the training of physicians. Your support of our new education space will ensure that the rich tradition of our landmark buildings will join with the finest technological resources to create a learning environment that continually defines excellence in medical education.

To learn more about how you can make a difference in the future of medical education at PENN Medicine, please contact Vanessa Marinari in the Office of Development and Alumni Relations at (215) 898-5164 or marinari@upenn.edu.



This cut-away view at the connector shows that there will be plentiful study and conversation areas that will create an appealing "coffee house" environment to foster interaction and sharing of information.



Recent Gifts

The estate of **Jean Bellet Green** has continued to support PENN Medicine with gifts totaling \$1.8 million. These funds will support the Jean Bellet Green Cardiology Strategic Fund; the Jean Bellet Green Melanoma Research Fund at the Abramson Cancer Center; and the Samuel Bellet M.D./M.B.E. Scholarship Fund at the Center for Bioethics, created in honor of her late husband's long and distinguished career as a cardiologist at Penn.

The Association Française contre les Myopathies (the French Muscular Dystrophy Association) has continued to support the research of Gideon Dreyfuss, M.D., with a \$2.3 million grant. The funds will further the study of the molecular functions of the Survival of Motor Neurons (SMN) protein complex as well as a search for therapeutics for Spinal Muscular Atrophy.

Philips Respironics, Inc., has generously pledged to provide \$3 million to fund the John L. Miclot Professor of Medicine. The Miclot chair, held by Allan I. Pack, M.B., Ch.B., Ph.D., is the first dedicated to the study of sleep disorders at Penn. It will support Pack's efforts as director of the Center for Sleep and Respiratory Neurobiology. The professorship is named for the company's former president and CEO, who now serves as CEO of Philips Home Healthcare Solutions.

The Robert Wood Johnson Foundation continues to support its Clinical Scholars Program at Penn with a grant of \$1.2 million. Under the direction of Katrina Armstrong, M.D., M.S.C.E, and Joshua Metlay, M.D., Ph.D., the program is designed to provide training in health policy and community-relevant research to outstanding physicians who are committed to improving health care in the United States. The program includes didactic experiences in study design and analysis for community and policy research, as well as training in leadership, communication, bioethics, and multidisciplinary science.

To make a gift to PENN Medicine, or for more information, please contact the **Office of Development and Alumni Relations**, 3535 Market Street, Suite 750, Philadelphia, PA 19104-3309, or call 215-898-8094.

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'60s

David G. Kline, M.D. '60, the Boyd Professor of Neurosurgery and chair of the department at Louisiana State University, was honored by a *festschrift* held at the Neuroscience Center of the L.S.U. Health Sciences Center in New Orleans. More than 80 scientists and clinicians from many parts of the world attended and presented papers in the areas Kline has studied, such as peripheral nerve injuries and repair and the tumors of nerves. The materials are to be published in a neurosurgical journal in 2009. Former president of the Southern Neurological Society, Kline is president-elect of the Society of Neurological Surgeons. His book *Nerve Injuries* (with A. Hudson) is considered a classic reference text.

William Allen Eaton, M.D. '64, Ph.D. '67, was honored with a symposium on "New Challenges in Protein Science," held at the University of Parma, Italy, June 4-6, 2008, on the occasion of his 70th birthday. Since 1986, he has served as chief of the Laboratory of Chemical Physics, the principal laboratory at the National Institutes of Health, carrying out research in the biophysical sciences, and as scientific director of the N.I.H. Intramural AIDS Targeted Anti-viral Program. Eaton is a fellow of the American Physical Society, the Biophysical Society, the American Academy of Arts and Sciences, and is a member of the Association of American Physicians and the National Academy of Sciences.

Richard A. Ratner, M.D. '66, a psychiatrist and clinical professor of psychiatry and behavioral science at George Washington University School of Medicine, reports that he lost his wife of 39 years, Linda, in June. She "was a

great friend of the class of 1966 and will be missed." An adjunct professor of law at Georgetown University, Ratner is a former president of the American Society for Adolescent Psychiatry, which presented him the Schonfeld Award in 2003. He has also been president of the Washington, D.C., Psychiatric Society.

Doris Gorka Bartuska, M.D., G.M.E. '68, is the 2008 recipient of the Pennsylvania Medical Society's Distinguished Service Award. She was described as an endocrinologist who advanced treatments focused on the genetic aspects of endocrine diseases, endocrinology of aging, osteoporosis, and thyroid diseases. Her work stimulated national interest in a woman's health agenda with emphasis on prevention and treatment of osteoporosis and smoking. Her involvement in medical humanities and medical ethics led to her participation in the President's Forum on Physicians and Social Responsibility. An emeritus professor of medicine at Drexel University College of Medicine, Bartuska was the director of the division of endocrinology, diabetes, and metabolism as well as the endocrine fellowship training program at Woman's Medical College-Medical College of Pennsylvania, now Drexel University College of Medicine. She is a former president of the Philadelphia County Medical Society, the medical staff at the Medical College of Pennsylvania, the Philadelphia Endocrine Society, and the American Medical Women's Association.

'70s

Joseph Loscalzo, M.D. '78, Ph.D., the Hersey Professor of the Theory and Practice of Medicine at Harvard Medical School, chair of the Department of Medicine, and physician-in-chief at Brigham and Women's Hospital, is one of the seven editors of the 17th edition of *Harrison's Principles of Internal Medicine* (McGraw-Hill, 2008). The new edition features global health and medicine throughout; has sections on regenerative medicine and stem-cell biology; includes many four-color illustrations and images; and

comes with a DVD that has 39 digital-only chapters on important clinical and curricular issues and 90 state-of-the-art video clips. Loscalzo formerly was the Wade Professor and Chair of Medicine at Boston University. An associate editor of *The New England Journal of Medicine* for nine years, he is currently editor-in-chief of *Circulation*. His honors include the Research Career Development Award from the N.I.H. and the Glaxo Cardiovascular Research Award. He is a member of the Institute of Medicine of the National Academy of Sciences.

'90s

Cecelia Haines Boardman, M.D. '92, associate professor specializing in gynecologic oncology in the Department of Obstetrics and Gynecology at Virginia Commonwealth University Medical Center, has been selected to participate in the 2008-2009 class of the Medical Society of Virginia Foundation's Claude Moore Physician Leadership Institute. The institute helps physicians strengthen their leadership abilities and gain the skills necessary to improve health care in Virginia. The session topics are specifically focused on physicians and include patient safety and quality of care, community health, public policy, and executive management issues. Boardman also serves as secretary-treasurer to the Virginia chapter of the American College of Surgeons and to the Mid-Atlantic Gynecologic Oncology Society. She is married to **N. Douglas Boardman III, M.D.** '92, associate professor of orthopaedic surgery at VCU.

OBITUARIES

B. John Ashley, M.D., G.M.E. '31, Topeka, Kans., a former otolaryngologist and ophthalmologist; October 27, 2001. He established a specialized practice in Topeka in 1932. After he was qualified by the American Board of Ophthalmology, he became the first ophthalmologist in Topeka in 1941. In 1947, he went to India to practice cataract surgery in

an eye hospital in Shirkarpur in what is now Pakistan. A former president of the Shawnee County Medical Society and the Kansas City Society of Ophthalmology and Otolaryngology, he was chairman of the Kansas State Advisory Committee for Selective Service of Physicians and Dentists from 1953 to 1961. He served in the Navy and held the rank of commander when he was discharged in 1946. He received the Balfour Jeffrey Award from the Stormont-Vail Foundation for his many contributions to medical care in northeast Kansas.

Joseph S. Silverberg, M.D., G.M.E. '33, Brooklyn, N.Y., a former otolaryngologist; January 31, 2008.

Theodore Livingston Hartridge, M.D. '34, Madison, Wis., a retired surgeon; February 20, 2008. He took his internship at Philadelphia General Hospital, and was an otorhinolaryngology fellow at Washington University in St. Louis. He had been a professor at Baylor Medical College, where he established an ear, nose, and throat residency program. During World War II, he served in Gen. George Patton's 3rd U.S. Army Medical Corps. He established battle-area hospitals during the Battle of the Bulge, for which he was awarded two Bronze Stars and five battle stars. He was one of the first American medical officers to examine prisoners at the Buchenwald, Cham, and Mauthausen concentration camps. After the war he served at the Brooke Army Hospital in San Antonio. Following his retirement from the Army, he joined the surgical staff of the Jackson Clinic in Madison. He was a fellow of the American Academy of Ophthalmology and Otorhinolaryngology and of the American College of Surgeons.

J. Morton Orman, M.D. '37, Wyncote, Pa., a retired family physician; January 27, 2008. During World War II, he was a flight surgeon in the Army Air Corps at a base in Louisiana. After his discharge, he established a practice in Hatboro, Pa. Throughout his career, he delivered thousands of babies at Abington Memo-

rial Hospital. When he retired in 1999, he had been on the Abington staff longer than any other physician affiliated with the hospital.

Harold Erwin Stauffer, M.D. '37, Lancaster, Pa., a retired family physician; February 6, 2008. He practiced medicine for 58 years, seeing his last patients in nursing homes when he was 85. He was president of the Lancaster City and County Medical Society in 1970. He delivered more than 1,500 babies, many in their homes among the plain and Amish Community.

James M. Flood, M.D., G.M.E. '40, Waverly, N.Y., a former dermatologist; March 23, 2008. After completing his training, he joined the Guthrie Clinic Sayre, where he was associate and chief of dermatology until his retirement in 1981. He was elected to the board of directors of the Guthrie Clinic Ltd. and was its vice president from 1961 to 1975. A fellow of the American Academy of Dermatology, he had served as president of the Philadelphia Dermatological Society, the Pennsylvania Allergy Society Association, and the Pennsylvania Academy of Dermatology.

Camillo T. DeBerardinis, M.D. '41, G.M. '45, Elkins Park, Pa.; March 23, 2008. A physician for 31 years, he served in the Army during World War II, then completed his residency in internal medicine at Jefferson University Hospital. For his entire career he was on staff at Jefferson and Germantown hospitals.

John L. McClenahan, M.D. '41, Richmond, Va., co-founder and former president of the Wissahickon Hospice of Philadelphia; January 1, 2008. He completed a residency in both radiology and academic medicine at the Cornell Medical Center. In 1956, he opened a solo practice in Philadelphia. A former president of the Philadelphia Roentgen Ray Society, he retired from radiology in 1983. He was an editor and contributor to *Transactions and Studies*, a journal about medicine and the history of medicine based at the College of Physicians of Philadelphia. He published some

60 articles on both medical and non-medical topics. He also wrote two books and edited a third.

Richard August Brunner, M.D. '42, G.M. '49, Narberth, Pa., a former psychiatrist; June 7, 2008. As a naval lieutenant, he served in the South Pacific in World War II.

Henry A. Shenkin, M.D., G.M. '42, Haverford, Pa., a retired neurosurgeon; December 8, 2007. He was founding director of the neurosurgical-research laboratory at Episcopal Hospital. A former associate professor of neurosurgery at Penn, he was also a professor at the Medical College of Pennsylvania and at Temple University. After retiring in 1982 he wrote five books, including *Medical Ethics: Evolution, Rights, and the Physician* and *Medical Care Reform: A Guide to Issues and Choices*.

Julius Ammons Howell, M.D. '43, G.M.E. '50, Winston-Salem, N.C., a retired plastic surgeon; March 13, 2008. In 1952, he began his plastic and reconstructive surgery training at the University of Wisconsin Hospital. His training was interrupted by a tour of duty in the U.S. Army, where he served as captain until 1953 and received the Bronze Star. During his military service, he was the personal physician of Syngman Rhee, president of South Korea. When he returned to the U.S., Howell completed his training in plastic surgery at the New York Hospital of Cornell University. In 1957, he became an instructor in plastic and reconstructive surgery at Bowman Gray School of Medicine, only the second plastic surgeon practicing in North Carolina. From 1973 to 1979, he served as chairman of its section on plastic and reconstructive surgery. He chaired the medical-legal committee of the Medical Society of the State of North Carolina and the constitution and bylaws committee for the American Society of Plastic and Reconstructive Surgeons and periodically taught a medical-legal course at Wake Forest University School of Law. In 1995, a chair in surgery was established in his honor at Wake Forest University Baptist Medical Center.

John Keyser Knorr III, M.D., G.M.E. '43, Newton Square, Pa., an obstetrician and gynecologist at Lankenau Hospital for 32 years; November 13, 2007. He helped found Lankenau's Health Education Museum – which featured Pandora, a talking skeleton – and conducted classes for expectant parents. He earned his medical degree from Thomas Jefferson University. During World War II, he served in the Navy Medical Corps in the Philippines. After completing his residency in obstetrics and gynecology at Pennsylvania Hospital, he remained on the staff there for several years.

John B. McDevitt, M.D. '43, New York City, a former psychiatrist; November 19, 2007.

Edith Torgan Penneys, M.D. '43, G.M.E. '47, Merion Station, Pa., a retired psychiatrist; March 10, 2008. She completed her residency in internal medicine at the Mayo Clinic in Rochester, N.Y. While maintaining a practice in internal medicine at her home in Merion Station, she became fascinated with the connection between her patients' physical illnesses and their mental states and decided to change specialties. In the 1960s, she completed a residency in psychiatry at Pennsylvania Hospital. She remained on the hospital's staff and practiced psychiatry from her home until retiring in 2005.

James I. Wendell Jr., M.D. '43, G.M.E. '47, Pottstown, Pa., a retired pediatrician; December 2, 2007. He and his wife, Kathleen, opened the first pediatric practice in Pottstown, which was the first specialist practice of any kind in the town. During World War II, he served in the U.S. Army, retiring as a major.

Robert D. Krudener, M.D. '44, Naples, Fla.; March 3, 2008. A captain in the U.S. Army Medical Corps during World War II, he went on to practice medicine in Ridgefield, N.J., and became president of the Bergen County Board of Health. In 1970, he relocated to Florida and worked in the North Collier Hospital Emergency Room before establishing his own medical practice in Naples. He retired in 1986.

Lester G. Steppacher, Jr., M.D. '44, G.M.E. '48, Philadelphia, a retired surgeon; May 14, 2008. He had a solo practice and was associated with St. Mary Hospital in Langhorne. Active statewide and nationally with the American Cancer Society, he had been a trustee of the J. F. Kapnek Trust, which supports a pediatric AIDS fund for Zimbabwe. In 1995 he received the Alumni Service Award from Penn's School of Medicine in recognition for his years of service as the Class of 1944 class agent.

Joseph Wallace Jr., M.D., G.M.E. '45, York, Pa., a retired otolaryngologist; February 1, 2008. He established a practice in Lansdowne, Pa., in 1945 and served on the staffs of Delaware County Memorial Hospital and Penn's medical school. He taught head and neck anatomy for several years at Penn's Graduate School of Medicine. He retired in 1991.

Albert C. Grunow, M.D. '46, G.M. '49, Tinton Falls, N.J.; February 13, 2008. He was an Army field doctor during the Korean War. Most of his professional life was spent as a medical executive with Prudential Insurance Co. in Newark.

Joseph H. Schaffer, M.D. '46, Chestnut Hill, Mass., former chief of medicine at Somerville Hospital; December 9, 2007. He completed his residency at Boston City Hospital and worked at Beth Israel Deaconess Medical Center. He was a physician at Somerville Hospital until his retirement in 1990.

Hugh J. Tripplehorn, M.D. '46, Helena, Mont., a former surgeon; November 1, 2007.

Samuel J. Fomon, M.D. '47, G.M.E. '51, Iowa City, emeritus professor of pediatrics at the University of Iowa; December 18, 2007. He was in the forefront of pediatric nutrition research, especially on factors that influence food intake and growth. He served as director of the internationally recognized Infant Metabolic Unit, which later evolved into the Division of Nutrition in the Department of Pediatrics. His book *Infant Nutrition* is still



widely used. Following his retirement, the unit was renamed the Samuel J. Fomon Division of Pediatric Nutrition. He was also the director of the University of Iowa Graduate Program in Nutrition.

Max J. Fischer, M.D., G.M. '48, former chief of the ear, nose, and throat division at Children's Hospital, Washington D.C.; December 15, 2007. He was chief resident at Georgetown University Medical Center before taking over the ear, nose, and throat practice of his uncle, Dr. Aubrey Fischer. He worked at Children's Hospital for the next 55 years and retired in Spring 2007. In addition to running its otolaryngology division, he also was director of the speech and hearing department and helped establish the hospital's first school for autistic children. He was an attending physician at Washington Hospital Center and was a clinical assistant professor at George Washington University Hospital.

George W. Moore, M.D. '48, Venice, Fla., a retired urologist; August 1, 2007. He completed tours in the Navy and Marines, attaining the rank of lieutenant, and was honorably discharged from the Navy in 1951. He completed his internship and residency at Geisinger Hospital in Danville, Pa., and joined a urological practice in 1955. A former chief of staff at both the Jameson Hospital in New Castle, Pa., and St. Francis Hospital, he had also been president of the Lawrence County Medical Society.

Irwin L. Peikes, M.D., G.M. '48, Blue Bell, Pa.; December 3, 2007. He maintained an ob-gyn practice in Norristown from 1952 until his retirement in the late 1980s. He delivered more than 9,000 babies. A native of Canada, he earned a bachelor's degree and a medical degree from the University of Toronto. During World War II, he served in the U.S. Army Medical Corps in Europe. For a year after the war, he cared for injured soldiers and displaced persons in Germany. He received the Bronze Star.

Homer R. Rich, M.D., G.M.E. '48, Ogden, Utah, a retired pediatrician;

May 18, 2008. After earning his medical degree from the University of Tennessee, he was a captain in the U.S. Army and served during World War II as a physician to German prisoners. He started his pediatric practice in Ogden in 1948 and saw thousands of patients before retiring in 1999. He also served as chief of staff at Ogden's McKay-Dee Hospital and was an instructor of pediatrics at the University of Utah Medical School. In 2001, he was named Utah Doctor of the Year by the Utah Medical Association. He was also honored as an advocate for children and received the Marty Palmer Service to Children Award from the American Academy of Pediatrics.

William A. Pratt, M.D., G.M. '49, Rutland, Vt.; April 5, 2008. He opened an internal medicine private in Rutland in 1949. Specializing in cardiovascular disease, he founded the Associates in Internal Medicine in 1971. From 1950 to 1971, he was an instructor in clinical medicine at the University of Vermont. As a member of the Rutland Regional Medical Center from 1949 to 1991, he served terms as chief of medicine and president of the hospital staff. He was also co-founder and president of the Vermont State Heart Association. He was a fellow and life member of the American College of Physicians and served on the board of Blue Cross/Blue Shield for New Hampshire/Vermont.

Leland M. Stetser, M.D., G.M. '50, Port St. Lucie, Fla., a retired gynecologist-obstetrician who lived in Medford, Pa., before retiring to Florida; March 22, 2008. He began practicing medicine in the early 1950s and had an office in Cherry Hill, N.J., for more than three decades. During World War II, he served as a flight doctor with the Eighth Army Air Corps and flew out of Africa and England.

Mary Lois Murphy, M.D., G.M. '51, New York, N.Y., a former pediatrician; April 8, 2008. She took two fellowships, one in experimental chemotherapy at the Sloan-Kettering Institute, and the other in medicine at the Memorial Hospital for Cancer and

Allied Diseases. She was one of the few researchers at that time to focus on childhood cancers. In 1958, she became chairman of the Acute Leukemia Group A, later the Children's Cancer Study Group, a national clearinghouse for children's clinical trials. In 1965, she was named chairwoman of pediatrics at the Memorial Sloan-Kettering Cancer Center. She introduced the day hospital in 1968.

Forrest C. Orman, M.D., G.M. '51, Lufkin, Texas, a former surgeon; April 2, 2008. He was a diplomate of the American Board of Surgery and a fellow of the American College of Surgeons. He served in several leadership roles with the Angelina County Medical Society. He had been chief of surgery at Lufkin Memorial Hospital and chief of surgery and chief of staff at Woodland Heights Hospital.

Charlotte T. C. Tan, M.D., G.M.E. '51, Brookline, Mass., a drug researcher and oncologist; March 22, 2008. From 1952 to 1996, she conducted research at what became Memorial Sloan-Kettering Cancer Center in New York, and she was a vice chairman of developmental therapeutics in the Department of Pediatrics. She was a driving force behind the testing of drugs, including 6-mercaptopurine and daunomycin, that proved effective in treating children with leukemia and other cancers. In 1962, she was named an associate professor of pediatrics at Cornell Medical College.

Ronald A. Lukert, M.D. '52, Largo, Fla.; February 29, 2008. Following an internship at Worcester Memorial Hospital, he practiced family medicine in Millford, Mass. After retiring from practice, he served as associate medical director of the Paul Revere Life Insurance Company. He retired to Florida 11 years ago.

George W. Taggart, M.D. '52, G.M.E. '59, Hazelton, Pa., a retired ophthalmologist; April 30, 2008. After completing his ophthalmology residency at Penn, he supervised surgery residents and taught at Penn's Scheie Eye Institute and the Veterans Administration for 17 years.

Raymond Krain, M.D., G.M. '53, Villanova, Pa.; November 7, 2007. For more than 40 years, he was on the staff of Lankenau Hospital, and he headed its dermatology department for more than 20 years. He was also chief of dermatology at Delaware County Memorial Hospital, and for 20 years he cared for patients at the former Valley Forge Army Hospital one day a week.

Richard J. Watkins, M.D. '53, G.M. '56, Wooster, Ohio, a former orthopaedic surgeon; March 30, 2008.

Alfred P. Bukeavich, M.D. '54, Morristown, Tenn., a specialist in obstetrics and gynecology; December 19, 2007. During World War II, he served in the United States Army in the China-Burma-India Theater. He served a one-year internship and a three-year ob/gyn residency at Henry Ford Hospital in Detroit. A fellow of the American College of Obstetricians and Gynecologists, he had been vice president of East Tennessee Ob-Gyn Inc. as well as chief of staff and chief of ob/gyn and surgery at Morristown Hamblen Healthcare Systems.

Richard Matzen, M.D. '54, Pepper Pike, Ohio, founding chairman of the Department of Preventive Medicine at the Cleveland Clinic; February 24, 2008. He also chaired the clinic's executive health program, conducting examinations of regional corporate executives as well as international corporation executives who traveled to the clinic. He wrote many articles for journals on preventative, pulmonary, and aviation medicine. After retiring from the Clinic in 1992, he often worked several days a week in the clinic's Emeritus Office.

Irving J. Olshin, M.D. '54, Philadelphia, a former pediatrician; March 28, 2008. After his residency and internship in pediatrics, he began teaching at Thomas Jefferson Medical College in 1961. In 1967, he became professor of pediatrics there, where he worked for the next 40 years. His students awarded him the Lindback Award for distinguished teaching in 1969. In 1987, he retired from teaching at Jefferson

and was the physician at George School in Newtown, Bucks County, until 1997.

William J. Sohn, M.D., G.M.E. '54, Elkins Park, Pa., pediatrician; March 3, 2008. He had been a member of the staff of Abington Memorial Hospital for 52 years, and he had a private practice in Willow Grove. He received an award from Abington Memorial for his dedication to teaching residents.

Thomas B. Arnold, M.D. '55, Bloomington, Minn., a specialist in internal medicine; April 3, 2008.

Sarle H. Cohen, M.D. '55, Wynnewood, Pa., a retired internist and geriatrician; May 8, 2008. He interned at Graduate Hospital and completed residencies in pathology at Boston City Hospital and in internal medicine at Philadelphia General Hospital. From 1957 to 1959, he served in the Navy and directed the laboratory at the Naval Hospital in Portsmouth, N.H. He shared an internal medicine practice in Northeast Philadelphia for more than 20 years and later had an office in Wynnefield Heights. In 1980, he became the first medical director at Martin's Run, a retirement community in Media. He retired as medical director of the life-care facility at Logan Square. A former president of the board of the Jewish Employment and Vocational Service, he had also been chairman of the Hassel Foundation, which provides support for medical and educational purposes.

Donald M. Thomas, M.D. '55, Louisville, Ky., who developed one of the first departments of emergency medicine in the nation at the University of Louisville; March 26, 2008. Known as "The Chief," Thomas served nearly 30 years as a fire surgeon for the old Louisville Division of Fire. As assistant professor of anesthesiology during his first decade at the University of Louisville, he became an expert in resuscitation. He was an advocate for the use of CPR, which had not been practiced in Louisville in the 1960s. In 1970, he was named medical director of emergency services for the old General Hospital.

Frederick Cohn, M.D. '57, Albuquerque, N.M., a former obstetrician-gynecologist; November 28, 2007. He delivered more than 5,000 babies in Albuquerque during his 30 years of practice. He specialized in microscopic tubal surgery for fertility problems. A life member of the American Medical Society of Vienna, he lectured extensively throughout the world, served as an assistant professor at the University of New Mexico, and was invited to teach at Oxford University.

Miriam Molitch Kaye, M.D. '57, Austin, Texas, a former psychiatrist; April 25, 2008. After earning her medical degree, she opened a private practice in her home in South Orange, N.J., while commuting to Manhattan four nights a week to attend the New York Psychoanalytic Institute. She was board-certified in both psychiatry and neurology. After seven years at the New York Institute, she left South Orange for Austin, where she became the first woman solo psychiatric practitioner in 1975.

Bruce R. Cowen, M.D. '61, Edison, N.J., a retired physician; December 8, 2007. After interning at Womack Army Hospital at Fort Bragg, N.C., he spent two years in the Army, stationed at the United States Army Environmental Health Agency in Edgewood Arsenal, Md. In 1964, he settled in Edison and opened a medical office in general practice. Eventually board certified by the American Board of Family Practice, he practiced solo in Edison for 36 years, retiring in June 2000. He was a staff member of Perth Amboy General Hospital 1964-1967 and a staff member at John F. Kennedy Medical Center in Edison from 1967 until his retirement. He served as the school physician for Metuchen Public Schools. In addition, he was the "well baby" clinic physician for the Edison Township Division of Health from 1964 to 1995 and the college physician at Middlesex County College from 1969 to 1983. Cowen was a charter fellow of the American Academy of Family Physicians.

Warren W. Nichols, Ph.D., G.M. '61, Green Lane, Pa., a former professor of human genetics and pediatrics at Penn; November 19, 2007. He retired in 1999 as director of genetic and cellular toxicology at Merck & Co after 16 years with the pharmaceutical firm. For more than 30 years, he was associated with what is now the Coriell Institute for Medical Research in Camden, which investigates human genetic diseases. He was a professor in Penn's School of Medicine in the 1970s and also at the University of Medicine and Dentistry of New Jersey.

B. John Ashley Jr., M.D., G.M.E. '62, Topeka, Kans., a former ophthalmologist; January 17, 2008. He earned both his undergraduate and medical degrees at the University of Kansas. He spent two years as a flight surgeon in the U.S. Air Force before completing his residency in ophthalmology at HUP. He then returned to Topeka to join his father in private practice. In 1988, one of his sons joined the practice.

John J. Caesar, M.D., G.M.E. '65, British Columbia, Canada, a retired anesthesiologist; April 3, 2008.

Jerome H. Grossman, M.D. '65, Boston, April 1, 2008. He moved to Boston in 1966 to work at Massachusetts General Hospital and rose to be its director of ambulatory care. He then served as chairman and CEO of the New England Medical Center, now called Tufts Medical Center, for 16 years. During his tenure, the center added 100,000 square feet of research area, constructed an ambulatory-care building, added a maternity service, and opened a new emergency room and inpatient buildings. Widely recognized as an expert on outcomes and health-services research, he founded the Health Institute of New England Medical Center in 1988. He served as chairman of the Council of Teaching Hospitals and of the Academic Medical Center Consortium. He chaired committees for the Institute of Medicine of the National Academy of Sciences and led the academy's President's Circle for two years. He also was on the board

of the Mayo Clinic and spent seven years on the board of the Federal Reserve Bank of Boston, three as chairman. Recently, he served as a trustee of PENN Medicine. For the past decade, he was at Harvard University's Kennedy School as a senior fellow and director of its Health-Care Delivery Policy Program. In 1997, he received the School of Medicine's highest honor, the Distinguished Graduate Award.

Marvin A. Norcross, Ph.D. '66, V.M.D. '59, Germantown, Md.; September 11, 2007.

James A. Thomas, M.D., G.M.E. '69, Longwood, Fla., a former anesthesiologist; April 15, 2007.

Thomas Moshang Jr., M.D., G.M.E. '70, Blue Bell, Pa., emeritus professor of pediatrics and senior physician in the division of endocrinology at the Children's Hospital of Philadelphia; February 24, 2008. After serving on the staff of Hahnemann Medical College, he was appointed adjunct associate professor of pathology and laboratory medicine in Penn's School of Medicine. In 1983 he became the founding director of the Diagnostic and Research Growth Center at Children's Hospital and served as chief of its endocrinology division from 1995 to 2000. His world-renowned research focused on the endocrine function of children who survive cancer, with a special interest in disordered growth and sexual development related to pediatric cancer and/or the therapies for treating cancer. During the 1980s he was involved in research trials of human growth hormones. Widely published, he was editor of the textbook *Pediatric Endocrinology: The Requisites in Pediatrics*. Moshang was to begin a term as president of the Lawson Wilkins Pediatric Endocrine Society this spring. In recognition of his work, Children's Hospital endowed a chair of pediatric endocrinology in his name in February. Moshang had also been named one of *The Best Doctors in America*.

Larry S. Eisner, M.D. '74, Boca Raton, Fla.; March 4, 2008. He specialized in treatment of neurological disease in South Florida for more than two decades and



was a founding director of the Baumel-Eisner Neuromedical Institute.

John William Boor, M.D., G.M.E. '77, West Chester, Pa.; November 26, 2007. He practiced neurology in Delaware County for 29 years and was the chief of neurology at Riddle Memorial Hospital in Media.

Patricia Kordek Maud, M.D. '78, a former family practitioner, Villanova, Pa.; May 5, 2008. She completed an internship and residency in family medicine at Washington Hospital in Washington, Pa. She was then a clinician and medical director at Calhoun County Hospital in Arkansas and taught at the University of Arkansas College of Medicine. She practiced in Trappe, Medford, and Arlington, Mass., before moving to Villanova in 1987 and joining the staff of the St. Davids Health Center in 1987. She later was a physician at the Urgent Care Center in Havertown. She was with the Goshen Family Practice in West Chester from 1993 until 1996, when she interrupted her career to raise her family.

Joel D. Portnoy, M.D. '03, G.M.E. '04, M.B.A. '07, Wynne-wood, Pa., March 3, 2008. A pediatrician, he practiced in the Pediatric Intensive Care Unit of the Hospital of the University of Pennsylvania for eight years. He had received an Independent Scientist (K) Award from the Agency for Healthcare Research and Quality. More recently, he was a consultant for McKinsey & Company, where he specialized in business related to health care.

FACULTY DEATHS

Belmont G. Farley, Ph.D., Bala Cynwyd, Pa., a former faculty member in the Department of Biochemistry and Biophysics; February 28, 2008. He joined the School of Medicine in 1964 as a teacher and researcher on the electrophysiology of seizures and neural networks. He was a pioneer researcher who helped build computers to study how the brain works and was a co-developer of the first transistorized computer.

John R. Hoyer, M.D., Wynne-wood, Pa.; December 30, 2007. An emeritus professor, he was a professor of pediatrics and of medicine from 1983 to 2006. He continued his research in biomineralization at the University of Delaware in the Department of Biological Sciences.

John Keyser Knorr III, M.D. See Class of 1943.

John S. "Jack" Leigh Jr., Ph.D., Philadelphia, the Britton Chance Professor of Radiology; March 10, 2008. Leigh earned his B.Sc. degree in electrical engineering in 1961 from Penn and was a defensive lineman on its football team. He earned his Ph.D. degree in biophysics at Penn and went on to become a pioneer as a researcher and educator at the University. He was appointed to the radiology faculty in 1971. He also held a secondary appointment in the Department of Biochemistry and Biophysics. Leigh was instrumental in the founding of Penn's Metabolic Magnetic Resonance Research and Computing Center in 1984 and served as its director for almost 25 years. The center has made significant contributions to technological advancements and biomedical applications of magnetic resonance. In addition to receiving several N.I.H. fellowships, Leigh was a Guggenheim Fellow at Cambridge University (1974-1975) and in 1999 he was inducted as a fellow into the International Society of Magnetic Resonance in Medicine.

Thomas Moshang Jr., M.D. See Class of 1970.

Warren W. Nichols, Ph.D. See Class of 1961.

Henry A. Shenkin, M.D. See Class of 1942.

George W. Taggart, M.D. See Class of 1952.

Joseph Wallace, Jr., M.D. See Class of 1945.

LEGACY GIVING

Common Values, Uncommon Lives



From Arizona to Africa, during their 53 years of marriage, Avery Harrington, M.D. '56, and Carolyn Beckenbaugh Harrington, C.W. '52, have given generously of their time and resources. Many of their ideas and shared values – including a commitment to hard work, volunteerism, and philanthropy – were instilled in them by the University of Pennsylvania. Inspired by their appreciation of how Penn shaped their view of the world as well as their role in it, they decided to name the School of Medicine and the College of Arts and Sciences beneficiaries of their IRA.

"There are various convoluted ways to deal with an IRA in one's estate plans, but dividing it among our favorite causes was simple and tax-efficient," says Avery.

"We feel a great satisfaction in allocating some of our resources while we are still alive," says Carolyn.

Over the past five decades the couple has led a rich and interesting life, and they credit Penn with giving them a solid foundation for their careers and volunteer opportunities. Carolyn feels she widened her horizons as a journalism major and staff member of the University settlement house camp. For Avery, the School of Medicine opened doors to a variety of challenging opportunities for useful work.

Their devotion to social issues led them to Arizona, where they worked for three and a half years on the Mojave and Navajo Indian reservations. Eventually Avery became a nephrologist and taught at the University of Wisconsin Medical School, while Carolyn wrote for various non-profit organizations. They also volunteered for a year at several rural hospitals in Zimbabwe, later returning three times for different assignments.

"Our Penn education has served us well, and not just academically," says Avery. "The common values we learned have made us the people we are and gave us the rich experience that is our lives."

"This is our way of saying thanks," says Carolyn.

The Harringtons have chosen one of a multitude of creative gift opportunities that benefit both the School of Medicine and its donors. As you plan your financial future, 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., Director of Planned Giving, at 215-898-9486 or at PENN Medicine, 3535 Market Street, Suite 750, Philadelphia, PA 19104-3309. You can e-mail Christine at cewan@upenn.edu. Also, you can visit the Office of Planned Giving's web site at www.med.upenn.planyourlegacy.org.

A Roadmap for Turbulent Times

I suspect that it came as no surprise to anyone when, in December, economists officially declared the US economy in a recession. For several months prior, experts in the media had reformulated the question from whether we were in a recession to how deep and how long. That question is still with us today. And like all sectors in the economy, health care faces its future with enormous uncertainty.

In terms of what the economic downturn means for Penn Medicine, we are expecting deep cuts from the Commonwealth of Pennsylvania in the Medicaid program and reductions in state research and education funds. We can also expect more uninsured patients as the numbers of unemployed rise. And there is the possibility of decreased payments from private insurers and grant funders as well.

Yet despite these pressures, we remain totally committed to our mission of providing the finest care to our patients, conducting leading-edge research, and preparing the next generation of leaders. Furthermore, I remain optimistic about our future in fulfilling these vital tasks, although I am also realistic about what it will demand of everyone who is part of this great institution.

Today, we are seeing the advantages of some careful planning. Years before the current downturn, we had done what many financial consultants are now advising. We reduced our debt, formulated and followed a strategic plan that focuses on our strengths, grew our revenue, maintained a strong cash reserve, and improved our quality in each of our missions. In effect, we have followed the directive of Penn's president, Amy Gutmann, Ph.D., in her recent report to the University Trustees: followed prudent management with a keen focus on priorities. As a result, although significant challenges face us, we are



fortunate to find ourselves in a much stronger position to weather the current financial storm than many others.

In addition, as many of our sister academic medical centers have done, we have made a concerted effort to contain all nonessential expenses. Our effort includes slowing our spending on some capital projects and not filling open positions whenever possible. We are also working hard to increase our revenues through additional patient-care activities, new grant applications, and expansion of our educational programs. My optimism is also based on our superb clinical and research faculty that make Penn Medicine among the most respected institutions in the world. Our clinical programs are exceptionally strong, attracting patients from around the state, the nation, and the world. Our success as a leader in biomedical research, despite reduced federal funding, continues to produce exciting discoveries and attract the best and brightest who wish to come here to study, train, and work. Finally, we continue to be very attractive to M.D., Ph.D., and master's degree students.

Among the many external validations of our institutional strength is our showing in the annual *U.S. News &*

World Report surveys of medical schools and hospitals. Our school ranked among the top five research-oriented medical schools for the 11th consecutive year, and the Hospital of the University of Pennsylvania (HUP) placed in the top 10 in the nation on the magazine's exclusive "Honor Roll." Earlier this year, external reviewers from the Liaison Committee on Medical Education gave exceptionally high marks to our School. And as you can see in this issue's "Vital Signs," our faculty members continue to receive prestigious honors, such as election to the Institute of Medicine.

Part of Penn's tradition of excellence has been made possible by the ability of its faculty and staff to rise to meet the many difficult challenges that have faced us so often in our history. This occasion will be no different, and we will all be asked to "do more with less" while remaining true to our institutional values.

One thing is certain in these uncertain times, and that is the current downturn in the economy is not permanent. We, like the rest of the nation, have high hopes for positive change coming from the new administration in Washington. The prudent steps and forward-thinking actions we take today will enable Penn Medicine to emerge from this current cycle in an even better position to serve our patients, lead the way to new discoveries, and train the next generation of physicians and scientists.

The road ahead may not be easy, but with your help, we will remain focused on our mission. We will proceed with careful confidence, ready to turn challenges into opportunities and take the necessary measures to ensure that our organization emerges from these turbulent times stronger than ever. ♥

Arthur H. Rubenstein, M.B., B.Ch.
Executive Vice President of the University of Pennsylvania for the Health System
Dean, School of Medicine

UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM

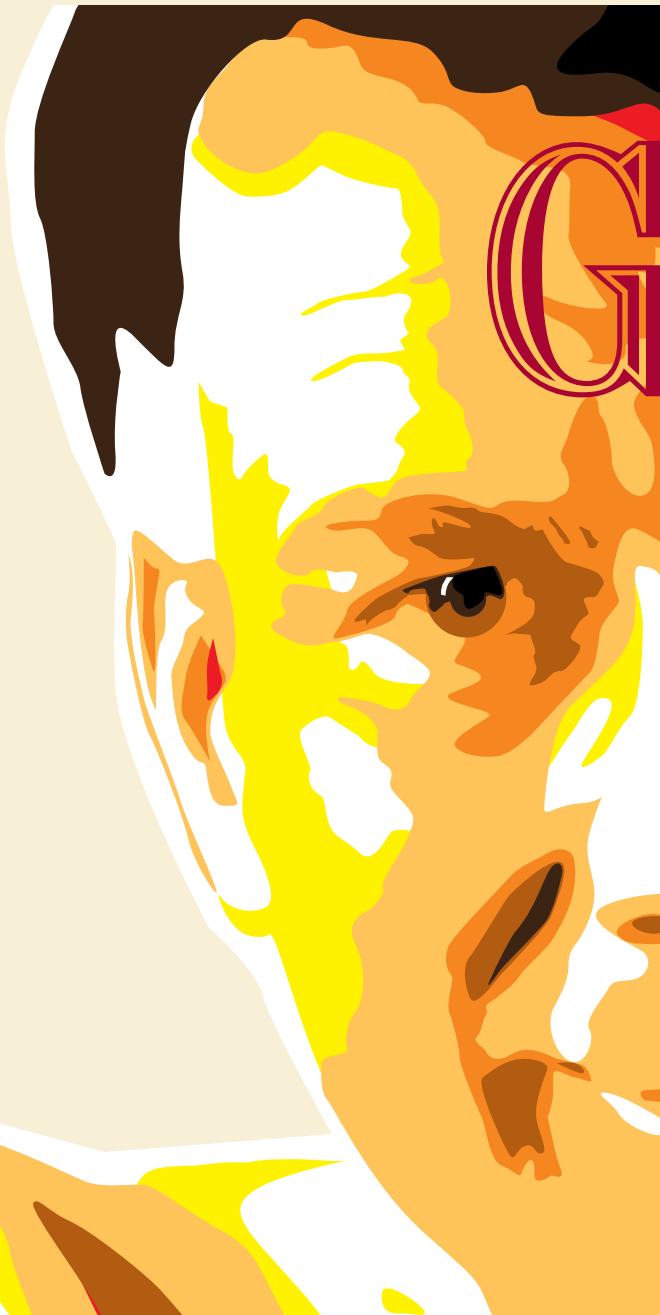
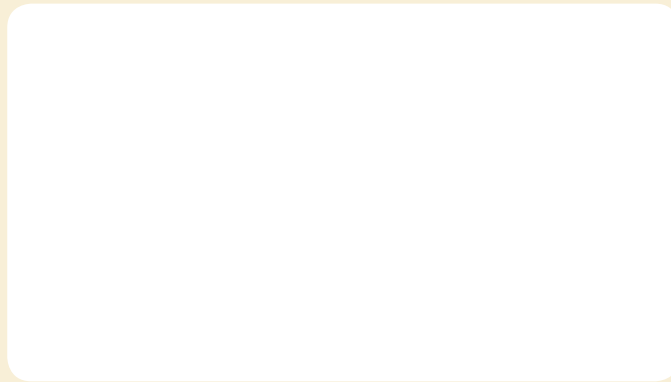
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George Cotsarelis, M.D. '87, has drawn wide – and sometimes fervent – interest for his research on hair loss. So far, his team has succeeded in generating new hair in mice. But the interim step may prove more significant: By generating hair follicles that produce the hair, the researchers accomplished the first successful regeneration of a mammalian organ.