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Yale Medicine



A new vision for
Route 34

4

The origin of
species

10

Physician Associate
Program at 40

18

autumn 2009

High-speed science

Tens of thousands of simultaneous experiments on gene function? It's all in a day's work at the Center for High Throughput Cell Biology, one of the first groups to move into Yale's West Campus.

12



ON THE COVER The Center for High Throughput Cell Biology relies on complex robots, laser microscopes, and vast computing power to determine the functions of genes. Automated plate handlers in the high throughput cell biology core can batch-process tens of thousands of cell-based assays simultaneously, using small interfering RNAs to silence individual genes.

THIS PAGE Vapor from a liquid nitrogen freezer hugs the floor in the center's laboratory space on Yale's 136-acre West Campus. The former Bayer Healthcare facility was purchased by the university in 2007; construction of the high throughput facility in a portion of the space began in July 2008.

ON THE BACK COVER Jason Ignatius is one of 16 people working in the new center at West Campus.

Photographs by Robert Lisak

AUTUMN 2009

CONTENTS

- 2 Letters
- 4 Chronicle
- 6 Rounds/Findings
- 8 Books & Ideas
- 10 Capsule

12 **Pioneering the West Campus**

The Center for High Throughput Cell Biology becomes the first scientific team at West Campus.

By Jenny Blair

18 **Yale's Physician Associate Program nears 40**

As it approaches its 40th year, the PA Program fills a niche in American medicine.

By Jennifer Kaylin

- 24 Faculty
- 26 Students
- 28 Alumni
- 32 In Memoriam
- 33 End Note

On the Web
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On our website, readers can submit class notes or a change of address, check the alumni events calendar, arrange for a lifelong Yale e-mail alias through the virtual Yale Station, and search our electronic archive.



HOW TO REACH US

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More premed courses should be required

I applaud and agree with the concepts expressed in "Reform of Premed Education Under Way" [*Yale Medicine*, Winter 2009].

My own case in point: I went to Stanford as an undergraduate, majoring in biology and chemistry. I took organic chemistry as a freshman, and took two statistics courses and a general psychology course, all of which should be required. I wanted to take biochemistry, but was not allowed to, since I was a premedical student and would have the same course in medical school. I took virtually every other chemistry course offered, including the second-year/graduate biochemistry courses—17 chemistry courses in all.

I would wish to require the following courses or the equivalent knowledge for premedical students, in addition to the liberal arts components: general statistics, biochemistry, and psychology. My own experience of 40 years in practice has made me aware of the need to understand business principles and such diverse topics as cultural and religious viewpoints toward health. I presume that computer literacy is a given (I typed my M.D. thesis in 1960 on a portable typewriter over and over until I got it right).

As the article by Jennifer Kaylin suggests, it would be wonderful if there were some preparatory coursework for beginning medical students covering the wide scope of world-views and personal interactions needed by caring and capable physicians. As an oncologist, I have developed productive and useful ways of dealing with terminal illness that are seldom shared with health care professionals. As Averill Liebow, M.D., told us in 1958, "You are students of medicine, not schoolboys." *Malin Dollinger, M.D. '60 Palos Verdes, Calif.*

Propaganda and the law of unintended consequences

I am sorry I cannot be in New Haven to see the exhibit of anti-VD posters used by the armed forces in World War II. It brings back some poignant memories ["Cautionary Tales for WWII GIs," *Yale Medicine*, Spring 2009].

I served in 1946 as radiologist to the 155th Station Hospital in Yokohama, Japan, also serving as pharmacy officer along with responsibility for two VD wards and VD education for our own hospital detachment. In the latter capacity I was required to give a series of lectures and to use posters, and more importantly, a series of excellent movies with story lines regarding the dangers of unsafe sex.

The Army was segregated in those days, and we had different movies for white and black soldiers. The femme fatale in the black movie was one of the most beautiful and provocative females I had ever seen. I was surprised when I received requests from our white GIs to show the black movie rather than the other. During this period I was

informed by 8th Army HQ that the VD rate in the hospital was starting to rise.

It was suggested by an old sergeant that I try showing the movies at the beginning of the day rather than just before the end. I was too inexperienced to realize that when the boys watched the temptress at work their hormone titers rose to astronomical heights and they immediately sought out the nearest brothel. When the film was shown early, its effects had a whole day to wear off. Although the new timing was not a popular move, the VD rate did drop to more manageable levels.

So while the propaganda might have had some positive results, it fell victim to the Law of Unintended Consequences. This was one of the best lessons I took home from my military career. *Raymond A. Gagliardi, M.D. '45 Boca Raton, Fla.*

CORRECTION

A photograph that appeared in "200 Years of Medicine at Yale," [*Yale Medicine*, Spring 2009, page 20] was incorrectly credited. The photograph is part of the A.C. Gilbert Papers, Manuscripts and Archives, Sterling Memorial Library.

A survey, a redesign, and a more frugal approach

Our thanks go to all of you who participated in our readership survey, not only for taking the time to reply, but also for the enthusiastic support you have shown for *Yale Medicine*. Most of you like what we're doing, but you also gave us ideas about how to do better. More than two-thirds of you ranked *Yale Medicine* "above average" or "among the best" alumni magazines you read, and almost 60 percent of you feel more engaged with the School of Medicine after reading *Yale Medicine*. You liked our mix of articles, but about half of you asked for more in-depth articles about medicine and science, and many of you asked for more news of alumni and faculty.

We will be thinking about your ideas, suggestions, and responses as we begin our redesign of *Yale Medicine*. The survey was the necessary first step prior to redesigning—we wanted to know what you, our readers, think about the magazine. For more on the survey, visit yalemedicine.yale.edu/readersurvey.

You will have noticed by now that the issue you hold in your hands is thinner than usual. The current economy has forced us to cut back, so this issue has just 32 pages, not the usual 48. To continue providing you with news of the School of Medicine, we've moved some of our content to the Web. Throughout the magazine you'll see references and links to online-only content.

We hope that you continue to enjoy *Yale Medicine* and that it continues to keep you in touch with friends, classmates, teachers, mentors, and others who made your time at the school so meaningful.

John Curtis
Managing Editor



Online Extra

This new icon will alert you to online-only content that can be found at yalemedicine.yale.edu.

yale medicine

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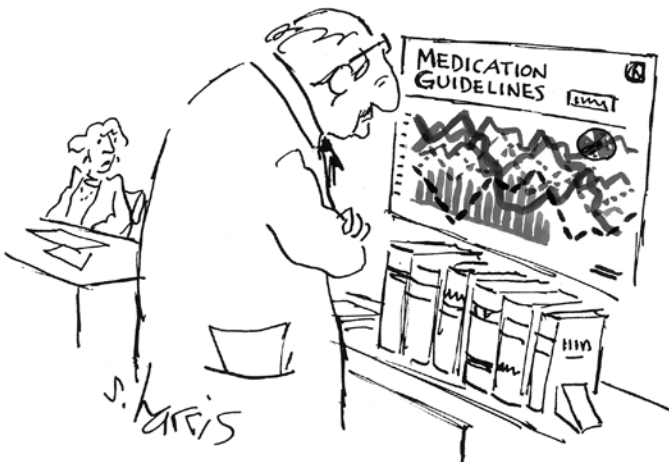
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SECOND OPINION BY SIDNEY HARRIS



Officials outline plans to reconfigure Route 34

Over the next decade the “highway to nowhere” will vanish and be replaced by new stores, offices, and homes.

In the 1950s city officials believed that New Haven needed a highway link to the towns of the Lower Naugatuck Valley. The Oak Street Connector, a free-way extending from I-95 northwest, and also known as Route 34, was thought to be the answer—but the project was an undisputed failure. To clear the way for a never-completed segment of highway that severed Yale’s medical campus and the nearby Hill neighborhood from the downtown, 881 families were displaced and 350 buildings razed.

Now, more than 50 years after it was built, New Haven Mayor John DeStefano Jr. has proposed a plan to remove the connector, restore the street grid, and reknit the city’s fabric.

The plan, which DeStefano announced at an April 20 press conference,

would nearly double the size of the city’s central business district; create 4.5 million square feet of new commercial, institutional, retail, and residential space; produce 12,000 permanent jobs; and generate more than \$100 million annually in tax revenue.

A joint effort of the city, Yale-New Haven Hospital, the School of Medicine, and the Economic Development Corporation of New Haven, the plan is by all measures ambitious. A \$5 million federal grant secured by U.S. Representative Rosa DeLauro has funded the project so far. The cost of the plan’s infrastructure, estimated at \$45 million, will be financed through federal, state, and private funding. Engineering work for this phase of the project has already begun, but it is expected to take years to complete.

A private-sector project will jump-start the initiative. Winstanley Enterprises, a property development firm based in Concord, Mass., is ready to break ground on a 300,000-square-foot office and laboratory “sister building”

to 300 George Street between the Air Rights Garage and College Street in the Route 34 right-of-way as soon as the state land and air rights are transferred. Developer Carter Winstanley, owner of 300 George, envisions closing Route 34’s Exit 3, with several lanes of traffic rerouted. An existing entrance to the Air Rights Garage would remain.

“We are just ecstatic with the vision that the downtown will extend to the medical center and that we will be a part of it,” said Dean Robert J. Alpern, M.D., Ensign Professor of Medicine. Alpern said the plan addresses two important issues: the medical school’s disconnection from “such a vibrant downtown” and its ability to grow. The only limitation on growth in research and clinical care is space, he said.

“We’ve been somewhat landlocked. But now, with plans for the conversion of the downtown, this will create opportunities for a lot of new research buildings,” Alpern said.

The plan is “going to be a positive circumstance for the university,” said Bruce D. Alexander, J.D., Yale’s vice president for New Haven and state affairs and campus development. “We’ve been working hard whenever we had the opportunity to reconnect the central campus and the medical campus. This will be a very significant step forward.”

DeStefano said the plan is meant to “create a footprint for what happens to New Haven over the next 15 years.”

—Charles Gershman



U.S. Rep. Rosa DeLauro and Dean Robert Alpern shared a laugh at a press conference on April 20 to announce the city’s plans to remake the Route 34 corridor that separates the medical campus from downtown New Haven.

et cetera . . .

A new ARRA for science as stimulus package boosts NIH grants around the country

In his inaugural address in January, President Barack Obama pledged to “restore science to its rightful place” and “not only to create jobs, but to lay a new foundation for growth.” These goals are intertwined in a \$10 billion allocation to the National Institutes of Health (NIH) in the economic stimulus package approved by Congress, officially known as the American Recovery and Reinvestment Act of 2009 (ARRA). The package comes as welcome relief to biomedical scientists at the School of Medicine and elsewhere who have endured years of flat NIH budgets that result in de facto cuts after adjusting for inflation.

The ARRA moneys provided to NIH for “extramural” distribution include \$8.2 billion for research grants, \$1 billion to support construction and renovation at NIH-funded research institutions, and \$300 million for the purchase of scientific equipment. An additional \$500 million will support improvements and construction at NIH’s own research facilities.

According to Carolyn W. Slayman, PH.D., deputy dean for academic and scientific affairs, as of June 1 Yale scientists had completed more than 650 ARRA grant applications requesting nearly \$387 million in support. Those grants are in addition to typical NIH awards, which last fiscal year totaled \$350 million.

More than 250 of the ARRA applications, totaling almost a quarter billion dollars, were made under two new NIH grant initiatives. Challenge Grants, which

will account for at least \$200 million of the stimulus funding, will provide up to \$500,000 per year for two years, and are aimed at what NIH terms “priority areas of research,” such as HIV therapy, pain management, and health disparities. Another \$200 million has been assigned to Grand Opportunities, or “GO,” grants, which are targeted at “high-impact, well-defined, large-scale” research projects in such areas as nanotechnology, genomics, and Alzheimer disease.

In addition to providing jobs for postdocs, lab techs, administrators, and other Yale staff members, Slayman says, the ARRA grants will also indirectly, but significantly, stimulate the economy by providing revenue and jobs to equipment vendors and manufacturers, and to construction firms. Given the high historical percentage of Yale grant applications funded by the NIH, Slayman hopes that a “tsunami” of ARRA funds will begin arriving on campus this fall.

—Peter Farley

YALE, CITY ADDRESS CHRONIC DISEASE

New Haven is the first U.S. city to participate in Community Interventions for Health (CIH), an international project to address chronic disease.

Working with Yale’s Community Alliance for Research and Engagement (CARE), CIH will study the effectiveness of community interventions in reducing the prevalence of chronic diseases. In New Haven, high rates of obesity put children and minority groups at elevated risk for heart disease, type 2 diabetes, and cancer.

CIH, which works with communities to improve health, is spearheaded globally by the nonprofit Oxford Health Alliance and locally by CARE, which is part of the Yale Center for Clinical Investigation.

“We hope that innovative research conducted at Yale can be translated into vital policies and programs to prevent disease and promote the health of our citizens right here in New Haven,” said Jeannette R. Ickovics, PH.D., professor of epidemiology and public health, professor of psychology, and director of CARE.

—John Curtis

EMERGENCY MEDICINE A DEPARTMENT

The Yale Corporation granted departmental status in June to the Section of Emergency Medicine, which had been part of the Department of Surgery since 1991. Gail D’Onofrio, M.D., the current section chief, was named chair of the new department.

A faculty committee recommended unanimously last fall that the section, which met standards for academic and programmatic importance, was ready to be elevated to departmental status. Emergency medicine has emerged as a distinct discipline during the past two decades, and 83 percent of all emergency medicine programs nationally are located within independent departments.

Emergency medicine is now the 28th academic department at the school. Since its creation as a section, it has grown from five to 33 faculty members, who have responsibility for 72,500 patient visits per year at Yale-New Haven Hospital and 21,600 visits annually at the Yale-New Haven Shoreline Medical Center in Guilford.

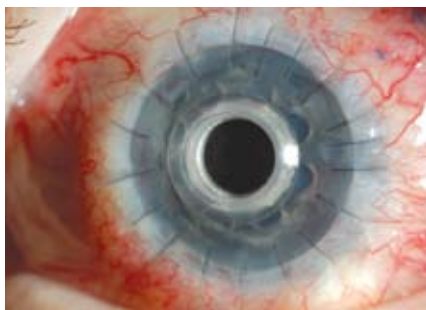
—J.C.

Sight restored with artificial cornea

When natural transplants fail, ophthalmologists turn to corneas made from polymers.

Sixteen years ago, when Awilda Irizarry was 33, glaucoma was diagnosed in her right eye. Over the years, her vision grew increasingly blurry and the pain became agonizing. Her doctor prescribed eyedrops to reduce pressure on her optic nerve; finally, however, the pain was so unbearable that Irizarry had her eye removed.

The pain on the right side was relieved, but Irizarry began to feel pain and lose peripheral vision in her left eye. She had four surgeries, including two



JIMMY K. LEE (2)

Ophthalmologist Jimmy Lee is one of a handful of surgeons in the country who perform artificial cornea transplants. These images show a patient's cornea before (top) and after the surgery.

donor cornea transplants, but still her vision dimmed and the pain worsened.

"She doesn't like people to help her much," said Irizarry's daughter, Maggie Morales. "She loves being independent, but she was frustrated losing her vision little by little. It got to the point where she was basically blind."

Last August, just as Irizarry's doctors were running out of options, Jimmy K. Lee, M.D., joined Yale as the new director of the cornea and refractive surgery sections at the Yale Eye Center. Lee, who had just completed a fellowship at the Wilmer Eye Institute at Johns Hopkins Hospital in Baltimore, came with a clinical interest in corneal transplantation, including artificial corneas. After hearing Irizarry's case history, Lee thought Irizarry would be an ideal candidate for an artificial cornea transplant. "The main indication for an artificial cornea is when patients have had multiple failed natural cornea transplants," Lee said. "The immune rejection rate is much lower because the center is an artificial implant."

The first artificial cornea implant was performed less than 20 years ago, after the device was approved for use in the United States in 1992. "It was uncomfortable for the patient, and there were complications," said Lee, one of a handful of surgeons in the country who perform artificial cornea transplants. The model Lee uses is the Boston K-Pro (also known as the Dohlman-Doane) developed at Harvard and Massachusetts Eye and Ear Infirmary in the 1960s by Claes H. Dohlman, M.D., PH.D., considered the founder of modern corneal science. The K-Pro is made of a transparent polymer that offers a visual field almost as wide as that of a normal

cornea—the transparent part of the eye that covers the iris, pupil, and anterior chamber and contributes to the eye's focusing power. A donor cornea is used as a "peripheral skirt" to provide tissue into which the prosthetic implant can incorporate itself.

The surgery takes about two hours, and the bandages are removed the next day. Patients are treated with steroids and antibiotics and usually recover fully in about a year. Glasses or contact lenses are typically prescribed to enhance sight restoration.

It's always an emotional moment when the bandages come off and a patient can see again, said Lee, who performs about two artificial cornea transplants per month. "These are patients who at best could only see light. After the surgery they can dress themselves, cook and watch TV again. There aren't many scenarios in medicine where there's such a dramatic change."

Morales said when Lee removed the bandage from her mother's eye, "she was laughing and crying at the same time" because she could see her children and grandchildren. "It's better in every way," Morales said. "Now she can see us."

—Jennifer Kaylin

et cetera ...

Nanoparticles loaded with siRNAs are new vehicle for silencing genes in pathogens

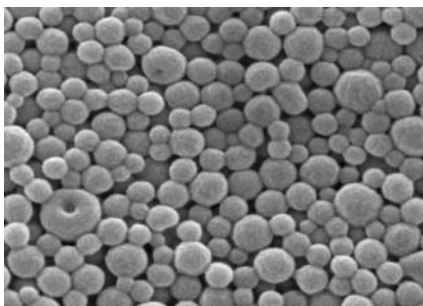
During the past 10 years researchers have puzzled over how best to deliver small interfering RNA (siRNA) molecules, whose therapeutic value lies in their ability to shut down genes in higher organisms and in pathogens that may cause sexually transmitted infections (STIs).

Lipid-based formulations, the most widely used siRNA delivery vehicles, suffer from certain limitations. In particular, they are unable to provide sustained release of siRNAs that may be required for many applications, and they may be toxic to target tissues.

Now, as reported in *Nature Materials* in May, Yale scientists have found a safe and effective way of administering siRNA molecules. “We wanted to develop a new strategy of delivering siRNAs with an FDA-approved material,” said lead author Kim Woodrow, PH.D., a postdoctoral fellow working with W. Mark Saltzman, PH.D., the Goizueta Foundation Professor of Biomedical Engineering and Chemical Engineering.

For this proof-of-principle work, the researchers designed siRNAs to target a gene expressed widely in the lining of the female mouse reproductive tract. Saltzman and Woodrow used densely loaded nanoparticles made of PLGA, an FDA-approved biodegradable polymer, to create a stable time-release vehicle for delivering siRNAs to mucosal tissue.

To convert an FDA-approved material into an siRNA delivery system, the particles needed to be small enough to penetrate tissue barriers and be taken up by cells. These nano sized particles also required stable incorporation of



To deliver small interfering RNAs that can silence genes, researchers turned to nanoparticles made of a biodegradable polymer. The nanoparticles were distributed throughout female reproductive tissue in mice and resulted in gene silencing for up to 14 days.

large quantities of siRNA. Saltzman and Woodrow demonstrated that their siRNA nanoparticles were distributed and retained throughout the female reproductive tissue. They also showed that delivery of siRNA by PLGA nanoparticles resulted in sustained gene silencing in the tissue for up to 14 days.

“Before human clinical testing can begin, our next step in research will be to test this approach directly in disease models—for example in the HIV-model mice that have an immune system genetically identical to that of humans,” said senior author Saltzman.

This approach may lead to antimicrobial treatments that patients can apply themselves. “It is safe and effective, and much easier than getting an injection of vaccine,” Woodrow said.

—Janet Emanuel

\$4 MILLION FOR STEM CELL RESEARCH

The state of Connecticut in April awarded close to \$4 million to Yale scientists to study ways in which human embryonic stem cells can be used to treat such ailments as spinal cord injuries, cancer, and mental retardation. The grants were made by the Connecticut Stem Cell Research Advisory Committee, formed in 2005 when the state allocated \$100 million over 10 years to promote such research. Connecticut was the third state to pass legislation allocating funds for the study of embryonic stem cells.

Five Yale researchers received grants worth a total of \$2.5 million, and seven others received seed grants worth a total of \$1.4 million. This latest round of funding will support such research projects as remyelination of nonhuman-primate spinal cords and the use of transposons—sequences of DNA that can change position within the genome of a single cell—for genetic manipulation of human embryonic stem cells.

—John Curtis

MARKERS FOR PROSTATE CANCER

Scientists at Yale and the VA Connecticut Healthcare System in West Haven have reported a link between molecular markers and higher death rates from prostate cancer. The paper appears in the May 5 issue of the *Annals of Internal Medicine*.

Amidst an ongoing debate in the medical community over whether screening and early diagnosis of prostate cancer save lives, or whether the aggressiveness of the tumor is more relevant in determining survival, the scientists studied tissue from biopsies of more than 1,000 veterans diagnosed with prostate cancer between 1991 and 1995. They found that abnormal expression of the *Bcl-2* gene or of the *p53* tumor suppressor gene increased the likelihood of patients' death from prostate cancer.

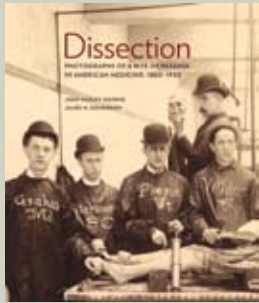
“Our results expand the current ability of clinicians to evaluate the aggressiveness of prostate cancer,” said lead author John Concato, M.D., M.P.H., professor of medicine. “Future research can help to define specific biologic mechanisms and develop new therapies.”

—J.C.

A questionable tradition

The dissection photo, now taboo, and its societal implications are explored in a history of the genre.

During the five decades from the Gilded Age to the Great Depression, American medical students created a distinctive genre of photograph: the group portrait with cadaver. First popularized in the 1880s, these tableaux commemorate the experience of dissection—what co-author John Harley Warner calls “a harrowing ritual of initiation.” His new book contains roughly 200 such photographs.



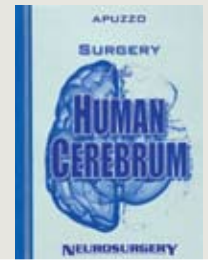
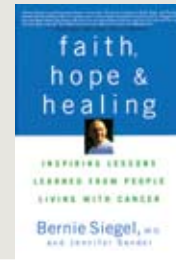
Dissection: Photographs of a Rite of Passage in American Medicine 1880–1930

by John Harley Warner, Ph.D., Avalon Professor of the History of Medicine; and James M. Edmonson (Blast Books)

Warner, chair of the Section of the History of Medicine at the School of Medicine, describes dissection as central to early medical education, and yet “transgressive, practiced on the social, legal, and moral margins.” He analyzes the photographs to explore societal ambivalence about dissection, gender roles, race, class, and the iconography of the white coat. Warner collaborated with the chief curator at the Dittrick Medical History Center at Case Western Reserve University to collect the portraits. These photographs proliferated during an era when dissection was performed on paupers, executed criminals, and corpses “resurrected” from graveyards—bodies that were disproportionately black. Some photos convey morbid humor, including pipe-smoking skeletons and propped-up cadavers seemingly dissecting a medical student.

Warner argues that the photographs express a violent impulse in early 20th-century society, with such captions as, “He lived for others. He was killed for US.” By the mid-20th century, bodies used for dissection were increasingly donated to medical schools rather than stolen, and the dissection photograph became taboo. Today, as Warner notes, even the act of dissection is in question: computer simulations may render the gross anatomy lab obsolete.

—Cathy Shufro



Genetic Diseases of the Kidney

edited by Richard P. Lifton, M.D., Ph.D., Chair and Sterling Professor of Genetics and professor of medicine, Stefan Somlo, M.D.; the C.N.H. Long Professor of Medicine and professor of genetics; Gerhard Giebisch, M.D., Sterling Professor Emeritus of Physiology; and Donald Seldin, M.D. '43, HS '46 (Academic Press) This book identifies and analyzes genetic abnormalities causing renal disease in humans.

Principles of Addiction Medicine, 4th ed.

by Richard K. Ries, M.D.; Shannon C. Miller, M.D.; David A. Fiellin, M.D., HS '95, associate professor of medicine; and Richard Saitz, M.D., M.P.H. (Lippincott Williams & Wilkins) This book blends scientific principles underlying addiction with practical essentials of clinical addiction medicine to help professionals who specialize in addiction medicine and who treat patients with addiction disorders.

The Soul of Medicine: Tales From the Bedside

by Sherwin Nuland, M.D. '55, HS '61 (Kaplan Publishing) This book is a compilation of stories in which more than a dozen specialists describe their most memorable patients. The contributors also recount instances of fallibility and vulnerability that prove that doctors are human and caring.

Faith, Hope & Healing: Inspiring Lessons Learned From People Living With Cancer

by Bernie Siegel, M.D., HS '61, and Jennifer Sander (Wiley) In this collection of first-person accounts, Siegel brings together almost three dozen cancer patients to share their stories and the lessons they have learned while living with cancer.

Surgery of the Human Cerebrum

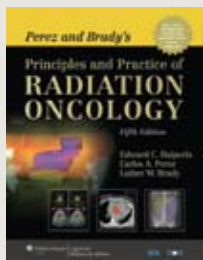
edited by Michael L.J. Apuzzo, M.D., HS '67 (Lippincott Williams & Wilkins) This book documents advances in surgery on the human cerebrum during the past 30 years, bringing together new and archival articles to provide sources of information on contemporary cerebral surgery.

Handbook of Radiation Oncology: Basic Principles and Clinical Protocols

by Bruce G. Haffty, M.D. '84, professor (adjunct) of therapeutic radiology; and Lynn D. Wilson, M.D., M.P.H. '86, professor of therapeutic radiology and dermatology (Jones and Bartlett Publishers) This handbook covers the issues most pertinent to patients undergoing radiation therapy, including general oncologic principles; workup, staging, and multidisciplinary aspects of treatment; basic principles of physics and radiobiology; and such specific technologies as brachytherapy and radiosurgery.

Otolaryngology: A Surgical Notebook

edited by K.J. Lee, M.D., associate clinical professor of surgery (otolaryngology); and Elizabeth H. Toh, M.D. (Thieme New York) This handbook uses a bullet-point format to present an overview of the fundamental concepts and core techniques for basic and advanced otolaryngologic procedures.



Perez and Brady's Principles and Practice of Radiation Oncology, 5th ed.

by Edward C. Halperin, M.D. '79; Carlos A. Perez, M.D.; Luther W. Brady, M.D.; et al. (Wolters Kluwer/Lippincott Williams & Wilkins) This book provides an understanding of radiation oncology; the physical methods of radiation application; the effects of irradiation on normal tissues; and site-specific applications of radiation therapy, either as a single modality or as part of a multi-modality treatment program.

ADHD Comorbidities: Handbook for ADHD Complications in Children and Adults

edited by Thomas E. Brown, M.D., assistant clinical professor of psychiatry (American Psychiatric Publishing) This book covers the multiple ways in which ADHD is complicated by other psychiatric and learning disorders in both children and adults. Clinicians will find help for patients whose ADHD appears in conjunction with 11 other syndromes ranging from mood disorders to developmental coordination disorder.

Laryngeal Physiology for the Surgeon

by Clarence T. Sasaki, M.D. '66, HS '73, the Charles W. Ohse Professor of Surgery (Plural Publishing) This book provides an understanding of the three principal functional priorities of larynx protection, respiration, and phonation and features numerous illustrations and tables. Most chapters are preceded by focused case presentations introducing relevant clinical descriptions.

Royal Maladies: Inherited Diseases in the Royal Houses of Europe

by Alan R. Rushton, PH.D., M.D., HS '80 (Trafford Publishing) The author provides an historical study of the effects of two hereditary diseases, hemophilia and porphyria, on the personal and political lives of European royal families.

Comprehensive Review of Psychiatry

edited by Rajesh R. Tampi, M.D., associate clinical professor in the Child Study Center; Sunanda Muralee, M.D., clinical fellow in the Child Study Center; Natalie D. Weder; and Heath Penland (Lippincott Williams & Wilkins) This text will prepare resident and practicing psychiatrists for all types of standardized examinations, including the Psychiatry Resident-In-Training Examination, the American Board of Psychiatry and Neurology (ABPN) written exam, and recertification exams. The book contains 2,000 multiple-choice questions divided into 10 200-question tests, each test covering all psychiatry and neurology topics in the ABPN curriculum.

The descriptions above are based on information from the publishers.

SEND NOTICES OF NEW BOOKS TO Cheryl Violante, *Yale Medicine*, 300 George Street, Suite 773, New Haven, CT 06511, or via e-mail to cheryl.violante@yale.edu



ROGER GLASS

A new vanguard to address global health

The fight against disease in the developing world has often been waged not by public health professionals, but by economists, politicians, and even military personnel, said Roger I. Glass, M.P.H., M.D., PH.D., director of the Fogarty International Center at the National Institutes of Health, during a talk at the medical school in April. Glass spoke at the spring symposium of the Wilbur Downs International Health Travel Fellowship Program.

"It was Colin Powell and Madeleine Albright saying the health of Africa was a security issue," Glass said, that launched the President's Emergency Plan for AIDS Relief (PEPFAR). "Global health has changed in the last 10 years," he said, noting the emergence, in addition to PEPFAR, of the Bill and Melinda Gates Foundation and the Global Alliance for Vaccines and Immunization, organizations that also address health issues in the developing world. "Global health in the 20th century was schools of public health and departments of international health at medical schools. In the 21st century global health is more than that. It is engineering. It's business and organization of delivery of care. It has to do with international ethics and law. It has to do with economics."

—John Curtis



ERIC CAMPBELL

Ubiquitous industry ties have risks and benefits

By the time they've reached their third year of medical school, said Eric G. Campbell, PH.D., virtually all medical students have accepted a free meal from drug companies. While this treat may appear to be a small gift, it could also be the first of many that lead young doctors and scientists into conflicts of interest and the erosion of trust between physicians and the public.

"There's a lot of eating going on in academic medicine," joked Campbell, an associate professor of medicine (health policy) at Massachusetts General Hospital and Harvard Medical School, who spoke at the *Perspectives on Medicine* series in March.

Relationships between industry and academia are not necessarily bad, Campbell said, noting that the pharmaceutical industry underwrites \$1.5 billion in research each year. "They have benefits that are very important," he said. But industry-sponsored junkets, along with ghostwriting, speaking, consulting, and advisory fees can create the impression that medical findings are "bought and paid for," he added.

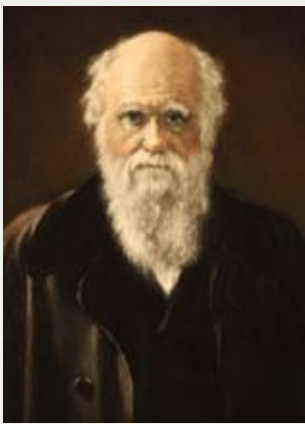
"Managing conflicts of interest is a fundamental part of medical professionalism today," Campbell said. "We need to disclose these things and we need to manage them."

—J.C.

The origins of Darwin's *The Origin of Species*

An exhibit at the Cushing/Whitney Medical Library traces the evolution of Charles Darwin's theory.

By Colleen Shaddox



MEDICAL HISTORICAL LIBRARY



JOHN CURTIS

A medical student, appalled at what he was witnessing, ran from the operating room. He was little more than a boy, having enrolled at the University of Edinburgh at 16, but his revulsion at the sight of human blood would stay with him throughout his life. That distaste was compounded by the horror of surgery before the advent of anesthesia. He had to admit to his family that he could not follow in his father's and grandfather's footsteps to become a physician. But Charles Darwin made a name for himself nevertheless.

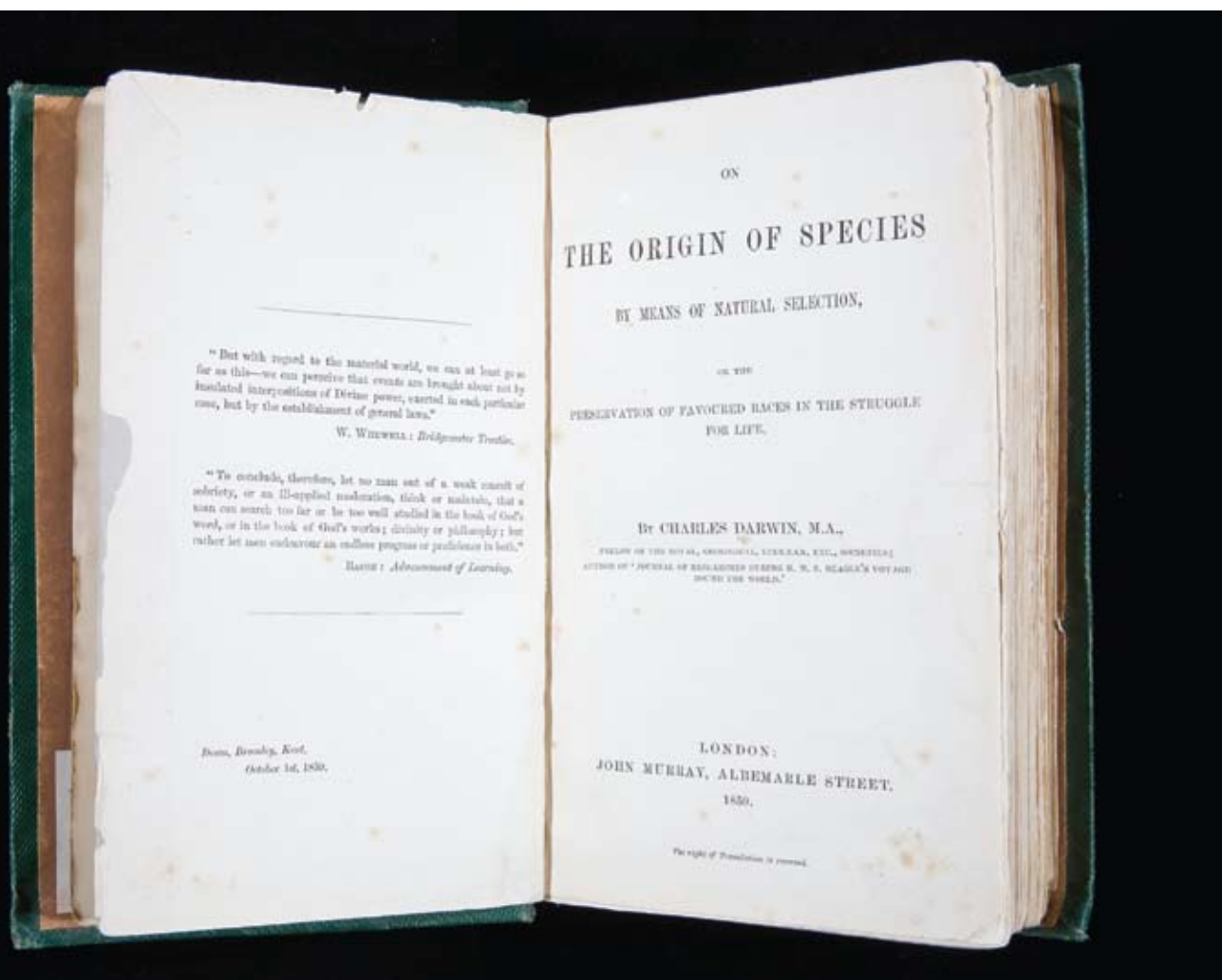
Marking the 150th anniversary of *The Origin of Species* and the 200th anniversary of its author's birth, an exhibit in the Cushing/Whitney Medical Library rotunda from February to April explored Darwin's groundbreaking theory in the context of the scientific and theological beliefs of his contemporaries. *From*

Natural Theology to Natural Selection: Celebrating the Darwin Bicentenary made use of the Historical Library's own assets, including a first printing of the first edition of *The Origin of Species* from Harvey Cushing's collection. Toby Appel, PH.D., the John R. Bumstead Librarian for Medical History, curated the exhibit.

The exhibition opened with 17th-century texts that sought to reconcile scientific discoveries with Christian beliefs. John Ray's *Wisdom of God Manifested in the Works of Creation* is an early example of "natural theology," a blending of religion and science that still had adherents when Darwin set sail for South America in 1831. Also in the exhibit is *Zoonomia*, a medical textbook by Erasmus Darwin, grandfather to the naturalist. Erasmus Darwin argued that organisms inherited useful characteristics, leading to the development

of higher animals. Though muddled with notions about spontaneous generation and not nearly as well supported as Charles Darwin's arguments, the book is a precursor to evolutionary theory.

While Darwin never acquired the family passion for medicine, he did inherit his grandfather's curiosity about the natural world. During the years he studied at Cambridge to become a clergyman, Charles Darwin's true enthusiasms were collecting insects and attending geology lectures. Not surprisingly, a professor recommended him for the post of naturalist aboard the HMS Beagle. The post was unpaid and designed not so much to serve science as to provide the captain with the company of a fellow gentleman on the long voyage. Journals and plates from the voyage were included in the exhibit. The plates—which contained



MEDICAL HISTORICAL LIBRARY/TERRY DAGRADI

new knowledge about plants, animals, native peoples, and geology—cemented Darwin's scientific reputation.

Darwin would wait more than 20 years to publish *The Origin of Species*. He wanted first to increase his own knowledge and come up with a coherent theory. He may also have been reluctant—he knew his findings would put him at odds with both the religious and scientific establishments. Stress over his concerns, some biographers speculate, may have caused Darwin's chronic headaches and cramps. He found relief in the “water cure” many Victorians took for all manner of complaints. A text on the cure was among the items on display.

Darwin was finally pushed toward publication when he learned that the naturalist and explorer Alfred Russell Wallace had developed a strikingly similar thesis. Friends of Darwin arranged

for the joint publication of the Wallace and Darwin papers, and *Origin* followed. Within two decades, most of the scientific community accepted Darwin's theory of evolution, though debate about natural selection stretched on for decades.

Darwin's landmark contribution to science—and the ongoing controversy it stirs in some circles—made the anniversary year a major public event. At Yale, it was observed throughout the campus. This spring and summer, the Peabody Museum took passengers aboard a wooden schooner to simulate the conditions on the HMS Beagle.

Colleen Shaddox is a freelance writer in Hamden, Conn.

OPPOSITE, LEFT Charles Darwin in a portrait by John Collier from 1881. The year 2009 marked the 200th anniversary of his birth and the 150th anniversary of the publication of his landmark *The Origin of Species*.

OPPOSITE, RIGHT On Santa Cruz in the Galapagos Islands, a crab climbs over volcanic rock to escape the pounding waves. Darwin's observations of the differences in flora and fauna in the islands of the Galapagos archipelago led him think about how life evolved.

ABOVE Among the Medical Historical Library collection is a first printing of the first edition of *The Origin of Species*, published in 1859. Darwin's ideas have held up and provide a unifying theory of evolution.



Center Director Lars Brandén became hooked on gene therapy after reading a science magazine in his native Sweden. He has done research at that country's Karolinska Institute and at Columbia University.

Pioneering the West Campus

Lars Brandén and his colleagues at the Center for High Throughput Cell Biology are the first scientific team to occupy space at West Campus. Others will follow in the coming years.

By Jenny Blair

Photographs by Robert Lisak

As an 11-year-old in Sweden in 1979, Lars Brandén read about retroviruses in a popular science magazine, and it occurred to him that they could introduce healthy genes into cells. “I told my father I would do gene therapy when I grew up,” he said, laughing. “When you’re 11 years old, you don’t know. But I did.”

Now director of the Yale Center for High Throughput Cell Biology, Brandén, 41, has kept that promise, and moved on to another frontier of genetic research, in keeping with his propensity for exploration and individualism. He wears his hair long and has been known to sport a handlebar mustache. The Thor’s Hammer around his neck is a replica from the era of an ancestor who was a henchman of a 12th-century Norse king. He smokes cigars and feeds the piranhas in the tank in his office with meat on a string.

That office is on the West Campus, where Brandén and his colleague James E. Rothman, PH.D., professor and chair of cell biology, Wallace Professor of Biomedical Sciences, and executive director of the center, run the first laboratory to move into the 1.6-million-square-foot former Bayer facility, which Yale purchased in 2007. The center is housed in a building just inside the West Haven town line, a few hundred feet from the tiny Oyster River. In the lobby is an old-fashioned popcorn wagon, a coffee table that used to be a packing crate for lab instruments, and a large photograph of 16 smiling scientists. Apart from several staff members from the Peabody Museum, these 16 people are the first Yale researchers to colonize the West Campus. There, in the first of three core science facilities planned for the West Campus, they are quietly performing genetic research on a scale that beggars the imagination.

Starting from scratch

When Brandén and the team arrived at Building B-31 on the West Campus in July 2008, they started from scratch. “Not even the toilets were working. ... We had to buy pens, even. We had no phones—nothing,” he says. The rooms were then gutted and painted, data jacks were installed, and the researchers began placing orders for the most state-of-the-art equipment available: automated liquid and plate handling platforms, an Opera confocal imaging system, a 24-CPU Linux computer cluster, and many other items, some of them custom-built.

But Brandén is used to being the first man in a new environment. The Center for High Throughput Cell Biology is the third such infant facility he has joined. In 1995, he was one of the first scientists to work at the new southern campus of the Karolinska Institute, just outside Stockholm. There he kept his childhood vow by studying gene therapy while earning his doctorate in cell and molecular biology. Several years later he helped design and set up Columbia University’s Genome Center and its high-throughput chemical compound screening facility, at which he served as associate director until last summer’s move to Yale with Rothman and several other colleagues.

Brandén’s experience in New York made the setup process faster. Whereas the Columbia institute took some 18 months to get up and running, Yale’s was ready in 13, even though it is a more complex operation.

Perhaps unsurprisingly for a man who takes pride in his Viking ancestry and sometimes hunts his own food with bow and arrow, Brandén relishes the role of pioneer.

At a new campus, he said, one has “freedom to explore novel approaches for doing science without having a preconceived idea as to how it should be done. [It gives] you more freedom to define what direction you want to go in yourself instead of having to battle old fiefdoms.”

First teams to use the core

Daniel DiMaio, M.D., PH.D., vice chair and Waldemar Von Zedtwitz Professor of Genetics, and his team are among the first Yale scientists to make use of the center’s services. Brandén’s group helps researchers learn how cellular processes unfold by examining the function of every gene in the human genome more or less at once. In each of thousands of tiny adjacent wells, a different gene is deactivated to determine how cells react. Laser microscopes scan the wells and send data to computers with between 10 and 80 terabytes of disc space. The final result is an inventory of genes that may be important to the cellular process being studied as well as information about the pathways those genes may affect, loaded on a jump drive that fits on a researcher’s key ring.

DiMaio and graduate student Alex Lipovsky study the human papilloma virus (HPV), 13 of whose 130 types can cause genital warts and cervical cancer. The researchers are interested in the crucial first steps of infection: how the virus enters human cells and expresses its genes. All HPV types consist of a protein shell around a length of DNA that encodes between six and eight genes. Human cells and the virus’ protein coat interact in such a way that the cells allow the virus to enter. The center is working with DiMaio’s team to design an assay to pinpoint the cellular genes involved in this event. Lipovsky began by creating a pseudovirus whose protein coat is identical to HPV’s but whose innards contain only a gene encoding a green fluorescent protein. This stand-in for the real virus is later mixed with cells in which one gene has been selectively deactivated.

The experiment takes place in tiny volumes and huge numbers. Within the center’s labs are machines that hold 70 plates, each plate containing 384 wells a few millimeters in diameter and holding 50 microliters each. Robots inject 1,000 human cells into each well. Then “bullets” that knock out specific genes are introduced: small interfering ribonucleic acids, or siRNAs. These short lengths of RNA, discovered 10 years ago in plants, are now available in synthetic form, several for each gene in the human genome. The siRNAs effectively disable the gene in question—a different gene in each well—and are available to

researchers in vast libraries. The siRNAs are mixed with the cancer cells for 48 hours; then the pseudovirus is introduced.

Cells that take up the pseudovirus glow green. Some cells take it up less effectively than others, and some never take it up at all. A cell that doesn’t glow either did not take up the virus, prevented viral transit to the nucleus, or failed to express the green fluorescent protein or express the virus—and that is important, since it may mean the specific gene silenced in that well by that siRNA is critical to virus uptake or gene expression. Those variations in the brightness of the green glow—the range of fluorescence—are examined, quantified, and sorted out by the automated microscope and software, leading to hits that may be crucial genes in the process of HPV infection. DiMaio’s group of researchers will then go on to study the candidate genes in their own lab.

Though suppressing genes to see how that alters cell behavior sounds straightforward, Lipovsky said that “the devil is always in the details.” There are countless technical steps that must be refined to perfection before the assay can be run, and it takes months of planning to hash them out. How long and at what temperature should the cells be incubated? How should the growth medium’s greater viscosity at the edges of the plates be accounted for? Many commercially available siRNAs have never been tested—will they do their job and knock out the genes? The center takes pride in its ability to guide researchers through these complex questions of experimental design. For several months Lipovsky spent several days a week driving to West Campus and meeting with assay-development specialist Michael Wyler, M.A., also formerly of Columbia, to discuss these details.

This kind of collaboration with clients, Brandén says, sets the Yale center—which charges both Yale investigators and outside parties a fee for service to cover some of its costs—apart from many of its competitors. At another university that offers high-throughput siRNA screening, he said, “referring investigators have to come and do the screens themselves. So you have access to instrumentations, and access to the facilities, but basically, you’re also inviting everyone to do the same mistake over and over again. ... We have a different approach, we’re taking the investigator here, we work with him to help him develop their assay, then we run it for him.” Wyler added that the approach at Yale is both fun and science-oriented. “We actually interact with the PIs, sit down, have science conversations, plan out the assays correctly, and work with them from the beginning to the end.”

In his lab at West Campus, Lars Brandén (right) looked over results with Leena Kuruvilla, Susanne Hasse, and Michael Wyler.

“You can definitely feel the enthusiasm. With this screen, we’re getting an integrated picture of how [HPV] infects the cell,” said Lipovsky. “And this has never been done before.”

A revolution in high-throughput screening

High-throughput screening (HTS) technology, which can also employ chemical compounds rather than siRNAs to knock out genes, was developed in the late 1980s and has since been a mainstay of drug discovery within the pharmaceutical industry. Only in the last 10 years has the technique moved to academia on an industrial scale. Yale is joining the wave of academic institutions to institute HTS capacity; other pioneering groups include the Broad Institute of the Massachusetts Institute of Technology and Harvard, and Stanford’s High-Throughput Bioscience Center.

Relying as it does on complex and costly robots, laser microscopes, and vast computing power, HTS might be thought of as research on a scale appropriate to the spectacularly complicated workings of the cell. A cell’s machinery comprises a series of chemical signals that, like a microscopic Rube Goldberg contraption, each set off a different process that cascades toward an end result. Unlike a Rube Goldberg gadget, though, these signals proceed across intricate networks rather than linearly.

Teasing out how each gene product interacts with the next one has historically taken years; to date researchers have pieced together only small parts of human cell networks. Most previous methods relied on chemical compounds alone to knock out one part of a cellular process. But the chemicals can deactivate more than just the process in question, complicating the analysis. “All drugs like that are dirty ... which made it very cumbersome to delineate,” said Brandén. The tidy specificity of siRNAs—their ability to deactivate a single gene—is part of what has allowed the HTS revolution to take place. Also, advances in automation and computing now allow thousands of experiments to occur within a day. The rich lodes of data from an HTS assay can be examined by advanced software for hits, or promising results. Many of the hits lead nowhere, but a few will point the way to genes or other compounds that are important to the process being studied. Gradually, a network of intracellular interactions becomes clear and can be mapped out graphically on powerful computing platforms. And once those networks are understood, scientists can begin to design drugs for tweaking them.



The frontiers so far seem limitless. Once one cell type’s networks are understood, the researchers can explore those of related cell types to pinpoint important differences. Genetic variations will lend yet another dimension to the hunt. “If you understand the differences,” said Brandén, “then you can also understand the side effects of drugs, how diseases are progressing in different tissues, and why they behave as they do.”

With dozens of CPUs crunching the data—and the center is able to tap up to 1,000 more at Yale’s High Performance Computing cluster in downtown New Haven—the sheer scale of the work is breathtaking. But the size of the human genome makes it necessary. After a half-century of research, only about one-tenth of the human genome’s function is understood. Some 20,000 to 25,000 genes are thought to exist, but how they and their protein products interact is still largely a mystery. High-throughput screening speeds up discovery by orders of magnitude. Currently, the center has the instruments to run experiments on 200,000 wells per day, but that level of production would need a team many times the size of the present.

As part of the center’s long-term plans, Brandén expects to design several hundred such cell-based assays that will allow an exploration of the entire human proteome. “If you cover the whole proteome, you can then get supremely detailed information about any unknown gene. You can profile drugs to understand what they would do on a global level.” This approach would vastly reduce the number of animal subjects needed in trials, he said. “You can actually understand what’s

The scientists and staff of the Yale Center for High Throughput Cell Biology come from a variety of backgrounds. Center director Lars Brandén is from Sweden and his team includes a former firefighter from Arkansas, a computer scientist from the Ivory Coast, and an informatics director who raises carnivorous plants.

Back row, from left: Steve Berman, Phil Williams, Marie-Aude Guié, Laurie Tomei, Lori Ortoleva-Donnelly, Lars Brandén. Front row, seated; Leena Kuruvilla, Yan Song, Adrian Poffenberger, and Susanne Hasse. Seated on ground: Michael Wyler and Jason Ignatius. Not pictured: James Rothman, Deborah Smith, Trisha D'Errico, and Michael Richo.



happening before you go there. You can direct the efforts of medicinal chemistry.”

The center will try to break even and it is run as a business. A small, early investment allowed Brandén to hire a marketing company and contact cell biology investigators in academic and industry centers around the world, thus creating a targeted database of potential customers.

The Center for High Throughput Cell Biology is a model for two other core research facilities planned for West Campus. A second facility will provide gene-sequencing services, and will be led by Richard Lifton, M.D., PH.D., chair and Sterling Professor of Genetics. The third group, which will perform high-throughput screens of drug-candidate chemical compounds, will be organized and overseen by Craig Crews, PH.D., professor of molecular, cellular, and developmental biology. Thanks to the campus’ vast size and resources, the three cores, expected to be up and running by December, will boast an information-gathering capacity rare in academia.

And the cores in turn will support departments and programs across the university, including five new interdisciplinary research institutes: the Institute of Cell Biology, also led by Rothman; and institutes of chemical biology, cancer biology, microbial diversity, and systems biology. Like the Center for High Throughput Cell Biology, these institutes will comprise groups of researchers from across the sciences, including engineers, chemists, geologists, and forestry experts as well as biologists of every stripe. “The strong sense of the science community at Yale and elsewhere is that it is going to be important to mix up these disciplines a little bit. There will always continue to be really strong science coming out of the core disciplines, but the most exciting opportunities might lie at the intersections [of different disciplines],” said Michael J. Donoghue, PH.D., vice president for West Campus planning and program development. “One of the ways that the West Campus can be useful is to break down those barriers by actually co-locating people from those different disciplines. It provides an opportunity to do something you can’t really physically do on the central campus.”

The wild, wild West Campus

In keeping with that wild West Campus culture of diversity, the center’s team members have a broad spectrum of training, backgrounds, and interests. (They also hail from several different countries; their potlucks, featuring international cuisine, are reportedly superlative.) Bioinformatics investigator Phil H.

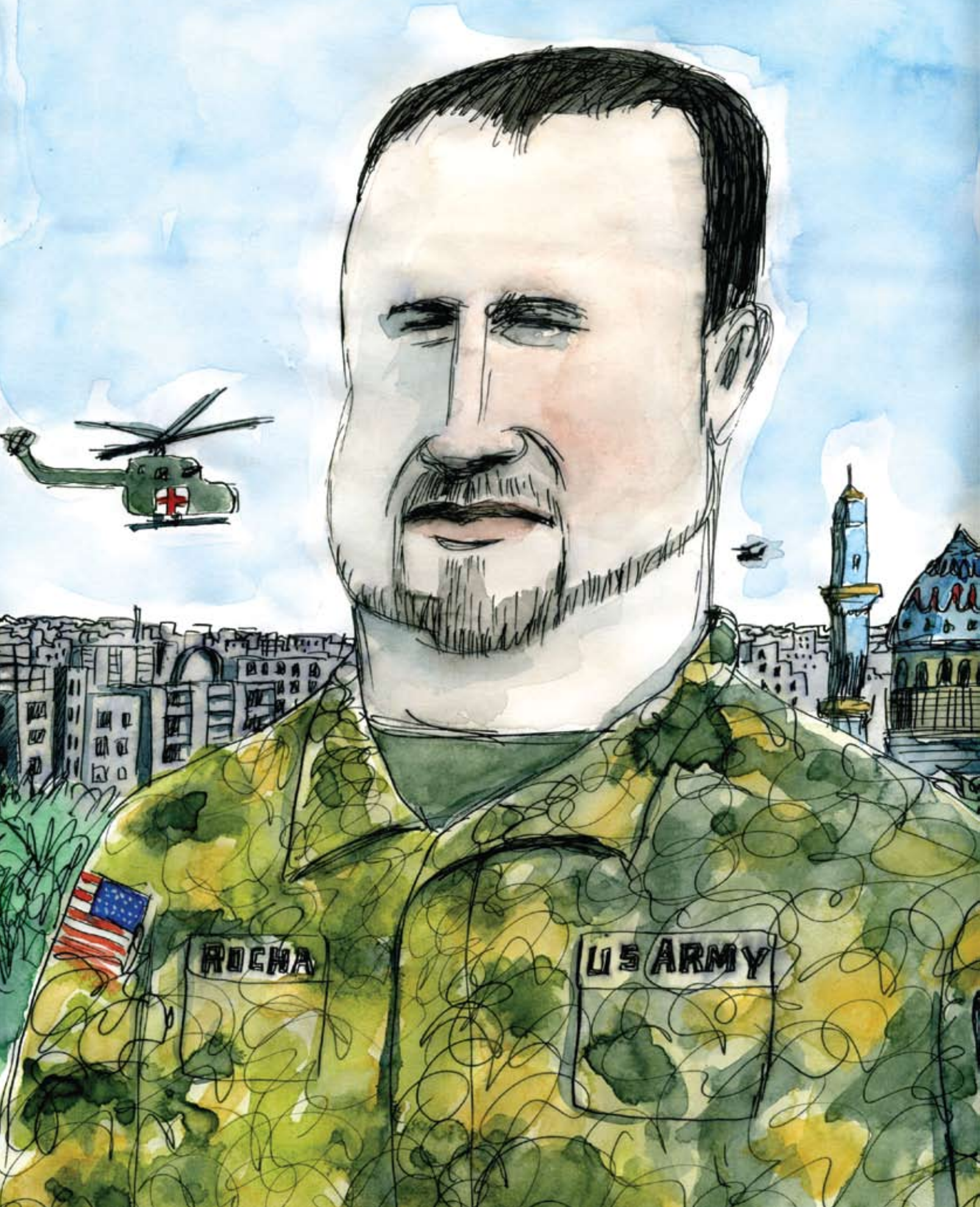
Williams, PH.D., grew up in Horseshoe Bend, Ark., where he worked as a volunteer firefighter and helped his father run a lawnmower-repair business. After his father bought an IBM 386 to keep track of inventory, Williams was hooked, developing a deep fascination with computers. He eventually left Horseshoe Bend and studied bioinformatics at the University of Arkansas. Research informatics scientist Marie-Aude Guié, M.S., is a computer scientist who hails originally from the Côte d’Ivoire. She puts up with good-natured teasing about being a princess, as her father is king of their ethnic group, the Baoulé, in her home country. Ashima Bhan, PH.D., is the team’s cell culture biologist and has a background in toxicology. Informatics director Adrian Poffenberger, M.S., who grows carnivorous plants in his office, has studied biology, mathematics, and cheminformatics, and has 14 years’ experience in drug discovery research.

With researchers of such disparate backgrounds bringing their ideas to the table, “intense brainstorming” are the norm, and Brandén says team meetings are a lot of fun. “We’ve had more positive science interactions in the last six months here than we had over four years at Columbia,” he said. (The transition from New York to suburbia also appears to have gone relatively smoothly. Brandén has a house in the Woodbridge countryside where he barbecues on his riverside deck, while Wyler, formerly a Brooklynite, says he likes being able to drive to work and park in front of the building.)

The center’s HTS assays hold the potential to reveal more information about cells and in greater detail than has ever been possible at Yale. HTS, said Lipovsky, is itself a marker of a shift toward greater complexity in science. “If we’re to make the next leaps in science, we need to understand not only how genes work by themselves, but also how they work together,” Lipovsky said. “We need to understand processes, not just genes.” He is excited not only for the HPV results that will come from his carefully designed assay, but also to be a part of the center’s maiden voyage. After all, he said, “the reason I’m in science is to pioneer things.”

For his part, Brandén says he is in the perfect job. “I’m dying to know things,” he said. “I’m a very curious kind of person.” With high-throughput screening, “you’re exposed to new science every single project that you run. And the allure of visualizing and understanding a complete transduction network—not only one pathway, but the global one—that is intense.”

Jenny Blair, M.D. ’04, is a writer and physician in New Haven.



Yale's Physician Associate Program nears 40

A medical profession that began in the 1960s has become an essential participant in health care.

By Jennifer Kaylin
Illustrations by Gary Clement

In 2002, a year after graduating from high school in Brigham City, Utah, Gabriel Rocha enlisted in the U.S. Army. He decided to become a medic, in large part because the position included airborne training and he thought the idea of jumping out of planes sounded adventurous and exciting. But it wasn't long before he got to see what a medic's job is really about. In 2003, the United Nations headquarters in Baghdad was bombed; many of the casualties were brought by helicopter to the aid station where Rocha was deployed.

"People had been dug out of the rubble," he recalled. "There were burns, shrapnel injuries, blunt force trauma, and head injuries." The number of wounded was so overwhelming that even the senior medics were treating patients independently, along with the doctors and physician assistants.

Rocha worked closely with the PAs—as physician assistants have been known since the mid-1960s, when their profession was born—as well as doctors. "Basically, you couldn't tell the difference between them, that's how knowledgeable and professional the physician assistants were," he said. That event, like so many others, combined with the daily occurrence of treating Iraqi civilians—including many children—who came

As did the first physician associates, Gabriel Rocha started his route to medicine in the military. As a U.S. Army medic based in Baghdad, Rocha treated many of those injured when the United Nations headquarters were bombed in 2003. After leaving the army, Rocha came to Yale for training as a physician associate. While at Yale, he was inducted into the U.S. Navy, where he will serve upon his graduation.



Alfred Sadler Jr., M.D.

Alfred Sadler Jr. and his twin brother, Blair, were co-founders of Yale's Physician Associate Program in 1971. The young program offered an opportunity for medical corpsmen returning from Vietnam to apply skills learned on the battlefield to a civilian setting.



Ann Bliss, R.N., M.S.W.

Nurse Ann Bliss helped launch Yale's Physician Associate program and also worked to set national standards for the profession. Yale's was one of the first programs to set a full-fledged curriculum so that students would leave, Bliss said, with "clinical skills and acumen."

to the aid station for care, convinced Rocha that he wanted to pursue a career as a PA.

"When I joined the military I wasn't thinking at all about the health care field, but then I saw how rewarding it was, taking care of patients and helping people," Rocha said. "Becoming a PA just seemed like the most direct and efficient way possible to get to do what I wanted to do, which was help others."

Rocha, who is in his second year of Yale's 28-month Physician Associate Program, is following a trail blazed almost 40 years ago by a previous generation of former military personnel who used medical experience acquired on the battlefield as a springboard to a civilian career in health care. (Although the preferred term is physician assistant, the Yale program uses the term physician associate.)

A new program fills a gap

The physician assistant profession began at Duke University in 1965; it was originally designed to train assistants who could relieve the burdens of overworked general practitioners. In the early 1960s, the Graduate Medical Education National Advisory Committee had issued a report that identified a shortage of primary care providers in rural and underserved areas. It was thought that physician assistants could help fill that gap.

At the same time, the nascent profession quickly provided an opportunity for medical corpsmen returning from Vietnam to find a civilian application for their battlefield experience. During the war, about 30,000 men with medical experience were being discharged each year; of those veterans, 6,000 had extensive medical training.

"These guys saved lives and made tremendous sacrifices," said Alfred Sadler Jr., M.D., who served with his twin brother, Blair, as founding co-director of Yale's PA program, which began in 1971. "It was a way to show our appreciation and to help them assimilate into civilian life."

Sadler said the birth of this new medical profession was also aided by a national mood of openness toward progressive solutions to social problems. "We encountered no real obstacles to what we'd set out to do," Sadler recalled. "The late '60s and early '70s was a time of great innovation in health care in the United States." Noting the creation of the National Health Service Corps in 1972 and President Lyndon Johnson's Great Society initiative, which had established Medicare and Medicaid in 1965 and 1966 respectively, Sadler said "there was a willingness to experiment with new health care models."

Yale's program got its start when Jack Cole, M.D., then the chair of surgery, received a trauma training grant from the Commonwealth Fund, a private foundation dedicated to improving the health care system. Sadler, who, along with his brother, a lawyer, had written the original 911 emergency dispatch legislation and created the region's emergency medical service infrastructure, thought PAs would be ideally suited to emergency medical care. (In 1968 the Sadler brothers also drafted and helped implement the Uniform Anatomical Gift Act, which governs organ donations in all 50 states.) As director of Yale's trauma program within the Department of Surgery, Sadler convinced Cole to use the grant money to create a PA program—or, as he put it, “the medical school's first experiment in non-physician education.”

Almost four decades later, Sadler calls the experiment “a tremendous success.” The numbers would seem to support the growing popularity and acceptance of PA programs globally, as well as at Yale. In 1973, Yale graduated five students who received a certificate in physician associate studies. Since then, Yale has graduated 895 physician assistants. Nationally, 77,000 PAs are practicing in virtually all medical specialties, including surgery. There are now 145 accredited PA programs in the United States, with a growing number in foreign countries, including the United Kingdom, Canada, Japan, and many African countries studying the American PA model with an eye toward implementing something similar.

Setting the standards

Ann Bliss, R.N., M.S.W., was part of the team that launched Yale's PA program and established national guidelines and standards. “When we got started,” she recalls, “not many leading medical schools had taken this up.”

She said the architects of Yale's PA program set two basic rules: “One was to take college graduates.” The second rule was that “It had to be equal. We didn't want anyone saying nursing is for girls; medicine is for boys.” They also set out to create a program that would produce leaders in the new profession, in keeping with Yale's mission as a university.

The founders were determined to create a challenging course of study with both didactic and clerkship components. “We were one of the first programs to launch a full-fledged curriculum,” Bliss said. “We didn't want our students to graduate without acquiring clinical skills and acumen.”

The other important ingredient for success, Bliss said, was accepting students who embraced the philosophy of the PA program. Bliss was responsible for evaluating each applicant's psychological readiness. In addition, “I watched their backstage behavior. For instance, were they rude to the secretaries?” she said. “We wanted people who would take a more humanist approach to patient care, who were team players,” and who would work well with the doctors.

The curriculum established by Bliss and the Sadler brothers—a nine-month didactic phase followed by 15 months

of clinical rotations resulting in a PA certificate—remained the same until the late 1990s. In 1995, students approached Lawrence S. Cohen, M.D., HS '65, then special advisor to the dean, requesting that Yale PA graduates receive a master's degree instead of a certificate. They argued that by offering a degree, Yale would be able to compete for the top students and that a Yale degree would in turn improve the graduates' job prospects.

Cohen raised the issue with David A. Kessler, M.D., J.D., when Kessler took over as medical school dean in 1997. The new dean appointed a committee led by Walter Kernan, M.D., professor of medicine, to review the program. “The PA program had been a bit under the radar at the institution for a number of years,” Kernan said. “It was doing a great job of training PAs, but its visibility in the larger academic community of the medical school wasn't high, because it had never been fully integrated into the training of medical students and residents.”

The committee found that Yale was in the minority in giving its PA graduates certificates rather than degrees. “But we decided we didn't simply want to grant a degree to get the best students,” Kernan said. “We wanted to grant a degree only if the curriculum warranted a graduate degree.”

After a thorough analysis of the curriculum, including comparing it to the curricula of the university's nursing, medical, and graduate schools, the committee determined that with certain changes, a Yale PA education would be worthy of a master's degree. Their main suggestion was that PA students should be required to write a thesis like their medical school counterparts. The program wasn't long enough for students to conduct independent research and analyze the results; however, they could produce a finished product comparable to a biomedical research grant application.

The other recommendation was that the medical school had to take more ownership of PA training. “At the time we met, it was common practice for the PA students to get their training away from campus and away from Yale-New Haven Hospital at other hospitals and community practices,” Kernan recalled. “We felt that the faculty of the medical school needed to be more engaged in the teaching of these students.”

After the committee's recommendations were implemented, the program grew in length to 25 months to give students time to write a thesis, and students began doing their clinical rotations alongside medical students at Yale-New Haven Hospital. In addition, it became a requirement that PA instructors have a strong affiliation with or a faculty

appointment in the medical school. Directed by Associate Dean Mary Warner, M.M.Sc., PA-C, the PA program is under the umbrella of the medical school, with academic oversight from the deputy dean of education and administrative oversight from the medical school dean. Starting in 1999, PA graduates began receiving a full master's degree.

Kernan says that the move from granting a certificate to conferring a degree was a necessary next step in the program's coming of age. "I heard from some PA students just recently," he said. "They said that if Yale were not granting degrees, they wouldn't have come here."

Another milestone for the PA program came in July 2003, when the national Resident Review Committee (RRC) mandated that resident physicians be held to an 80-hour work week. "We went into crisis mode," said Robert Udelsman, M.D., M.B.A., the William H. Carmalt Professor of Surgery and Oncology and chair of the Department of Surgery. "If residents were held to an 80-hour work week, there was no way we could comply with our then-workload, which has since tripled."

The solution? More PAs. There were two full-time PAs on surgical services before the RRC mandate; now there are 26. "It's been extraordinarily successful," Udelsman said. "It basically solved the crisis." Beyond that, Udelsman says the presence of PAs to help with floor management of patients has benefited the physicians as well as patients. "The PAs are here long term, whereas the residents cycle through," he said. "The PAs have played an incredibly important role in stabilizing services. They are fully integrated into our patient care model, and without them we could not function at the level that our patients and their families deserve."

The most recent change in the PA program, which went into effect a year ago, was to extend it from 25 to 28 months. The three extra months were added to the didactic phase to enable instructors to cover all the material that is now required. "We found it increasingly difficult to cover all the mandated topics," said PA Program Director Warner, "and we also wanted to reduce the stress on our students and give them enough time to participate in the Yale community."

Assistant v. associate

Yale may have joined the majority of PA programs a decade ago in offering a master's degree, but it has remained resolutely independent when it comes to the name of the Yale program—for reasons that run deeper than mere tradition. In the early

days, more than half the PA programs nationally were called physician *associate* programs, but as time went on, the preferred term became physician *assistant*, which is the term used by the American Medical Association (AMA).

"It comes up for debate within the profession every five years or so," said Warner, "But we feel that *assistant* sounds hierarchically lower and that *associate* is a more accurate reflection of the PA's role with respect to patients and physicians. Our program is called *physician associate*, because that's what it was called when it started, and I'm not changing the name; the alumni would revolt."

But this debate enters into a deep current that runs through the profession—one that seeks healthy relationships between men and women, care and cure, colleagues and subordinates.

From the outset, there were those who questioned the need for another allied health profession. After all, nurses, a known quantity to both physicians and patients, had successfully been carrying out many of the same functions for years. Indeed, as early as 1969, the AMA had held discussions with the American Nurses Association about the possibility of nurses becoming physician assistants. The women's liberation movement was starting to resonate with professional women, however, and the nurses emphatically rejected the proposal for fear that they would become handmaids of patronizing male physicians. That refusal to broaden the scope of their practice led directly to the creation of the new midlevel profession of physician assistant, which was largely male-dominated in its beginning.

The profession of nurse practitioner was established at around the same time as the PA program; however, the two programs have different curricular emphases, according to Warner. "We emphasize medical sciences in PA training, similar to the medical school model," she said, "whereas advanced practice nursing emphasizes integration of the physical and psychosocial assessment, health promotion, and disease management. Another difference in the two professions is that PAs work with physician supervision while nurse practitioners may opt for independent practice in many parts of the country."

When the PA program got started, the majority of students were military veterans, but as time has passed the profession has become feminized as women have turned to it as a way to strike a balance between a meaningful career in health care and family life.

Warner, who became a certified PA in 1992, is one such woman. She had planned to become a doctor since she was a child of 10. After college, she worked for two years in a health care environment to gain some experience and pay off student loans. It was then that she met her first PA and became intrigued. She began to weigh the years of medical training required to become a physician against her desire to raise children and decided that becoming a PA was the better route to take.

“I thought this would be a very efficient way to do a lot of what I love without having to turn off or postpone the rest of my life,” she said. Has it been a good decision? “Absolutely.” The added plus, which Warner didn’t foresee when she started out, is that unlike medical students, who must choose a specialty, PAs train in a generalist model. That means that they can move from one specialty to another with on-the-job training from a supervising physician.

After getting her PA degree from Emory University School of Medicine Physician Assistant Program, Warner worked in orthopaedic surgery for three years. Then she switched to cardiac surgery for five years before returning to orthopaedic surgery. When she came to Yale, she worked in emergency medicine.

Mathew Simmons, M.M.Sc., PA-C ’06, went so far as to apply to and get accepted by a medical school, Florida State University College of Medicine, before deciding to become a PA instead. “The summer before my senior year, I volunteered in an operating room at a local hospital,” Simmons recalled. “The whole time I didn’t feel great about medical school. Then I got engaged and realized I wanted to put my family and home life first. My stepdad is a doctor, so I know how much you have to sacrifice.”

Simmons, who works in a gastroenterology practice in Florida, has no regrets about not going to medical school. “I still have plenty of responsibility, and I take care of patients every day,” he said. “It’s very challenging and intellectually stimulating.” The only downside, Simmons said, is the frequently asked question, ‘Are you going to go on and become a doctor?’ “I have to tell them, no, that’s not how it works. It’s a little annoying, but you get used to it.”

According to Warner, about 92 percent of Yale’s PA students receive some form of financial aid, compared to 83 percent of medical students. “If you look at who we train, our students have smaller parental contributions with less money, so time and money are important factors.”

Warner said many people who apply to become PAs are looking for second careers. Thea Cogan-Drew, who enrolled in Yale’s program in 2007 and will graduate in December, worked as a photographer, graphic designer, and art director for several years before she “hit a plateau,” and began looking for a more satisfying career.

“I explored a lot of career options before coming to medicine,” she said. “Then, based on where I was in my life



Mary Warner, M.M.Sc.

During her tenure as director of the program, Mary Warner has overseen an expansion of the program from 25 to 28 months. The additional three months allow instructors to cover all the didactic material that is now required.

personally and professionally (she is the mother of a 4-year-old son and pregnant with her second child), I decided that the PA degree was the best route for me, as opposed to medical school.”

The National Commission on Certification of Physician Assistants estimates that PAs do 80 to 90 percent of what physicians do but bill at 15 percent less. As the nation grapples with ways to overhaul the health care system to make it more accessible and affordable, many people see an expanded role for physician assistants as a key part of the solution. “From the country’s point of view, it’s an incredibly important program,” said medical school Dean Robert J. Alpern, M.D., Ensign Professor of Medicine.

“Access to cost-effective care is who we are,” said John Bond, PA-C ’76, who has worked as a PA in Vermont since his graduation. “We’re talking about people who are interested in providing care to patients in underserved areas and training those people in less time and at a lower cost. What isn’t there to like about what PAs can do in this time of health care crisis?”

Jennifer Kaylin is the Web editor of the YSM Office of Institutional Planning and Communications.



David
Hafler

MS expert named to head neurology

DAVID A. HAFLE, M.D., a leader in multiple sclerosis (MS) research, was named chair of neurology at the School of Medicine and chief of neurology at Yale-New Haven Hospital, effective September 1.

An expert on the mechanisms of autoimmunity and inflammatory diseases of the central nervous system, Hafler was director of molecular immunology in the Department of Neurology at Harvard Medical School and an associate member of the Broad Institute of Harvard and MIT. He was the Jack, Sadie, and David Breakstone Professor of Neurology (Neuroscience) at Harvard Medical School, and a neurologist at Brigham and Women's Hospital.

Hafler's recruitment complements ongoing research at Yale in neurology, genetics, and translational immunology. Hafler will build upon existing neurology research in such areas as spinal cord injury and repair, epilepsy, and neurodegeneration, and he will expand research in MS and in other areas of neurology and the clinical neurosciences.

Hafler succeeds Stephen G. Waxman, M.D., PH.D., the Bridget Marie Flaherty Professor of Neurology, Neurobiology, and Pharmacology, who has led the department since 1986 and will remain on the faculty and continue as director of the Center for Neuroscience & Regeneration/Neurorehabilitation Research.



John
Krystal

Psychiatry professor named chair

JOHN H. KRYSAL, M.D. '84, was named chair of the Department of Psychiatry, effective July 1. Krystal, the Robert L. McNeil, Jr., Professor of Translational Research, will also serve as chief of psychiatry at Yale-New Haven Hospital. He is director of the Center for the Translational Neuroscience of Alcoholism, and he also heads the Clinical Neuroscience Division of the Veterans Affairs National Center for Post-Traumatic Stress Disorder and the Veterans Affairs Alcohol Research Center at Yale. Since 2000, he has served as the department's deputy chair for research.

Krystal is an internationally renowned expert on the neurobiology and treatment of schizophrenia, alcoholism, depression, and PTSD. His work is distinguished by its emphasis on translational neuroscience, the effort to combine emerging brain imaging and molecular genetic technologies with psychopharmacology to better understand alterations in brain function associated with psychiatric disorders. His research on the glutamate system in the brain has led to new experimental treatments for several psychiatric disorders.

Krystal succeeds William H. Sledge, M.D., who led the department as interim chair during the past year, and Benjamin S. Bunney, M.D., who served as chair for two decades until his retirement in 2008.



Stephen
Waxman



Peter
Salovey

Stephen G. Waxman, M.D., PH.D., the Bridget Flaherty Professor of Neurology, Neurobiology, and Pharmacology, received the William S. Middleton Award, the highest scientific honor bestowed by the Department of Veterans Affairs, at the U.S. Capitol in Washington in April. The award includes a cash prize of \$150,000 in research support.

Waxman was honored for his research on spinal cord injury, multiple sclerosis, and painful nerve injuries. His research was the first to show the changes in molecules within nerve cells that permit remissions—recovery of such lost functions as vision and motor control—in multiple sclerosis. He has also identified key molecules responsible for pain after nerve and spinal cord injury.

Waxman is the director of the Neuroscience and Regeneration Research Center, a collaborative enterprise of Yale University, the Department of Veterans Affairs, the Paralyzed Veterans of America, and the United Spinal Association. He is also co-director of the Yale-London Collaboration on Nervous System Injury at University College London. Having served as chair of neurology since 1986, Waxman is now making the transition to a full-time role as director of the research center at the VA Connecticut Healthcare System in West Haven.

Eleven Yale faculty members, including six from the School of Medicine, were elected to the Connecticut Academy of Science and Engineering in April in recognition of their contributions to the advancement of science. Scientists and engineers elected to the academy must achieve distinction through original



William
Sessa



Robert
Sherwin

contributions to theoretical or applied science or engineering.

The newly elected members, who were introduced at the academy's annual meeting at the New England Air Museum in May, are **Michael Donoghue**, PH.D., the G. Evelyn Hutchinson Professor of Ecology and Evolutionary Biology and vice president for West Campus Planning and Program Development; **Peter Jones**, PH.D., the James E. English Professor of Mathematics and Applied Mathematics; **John H. Krystal**, M.D. '84, the Robert L. McNeil Jr. Professor of Translational Research; **Lynne J. Regan**, PH.D., professor of molecular biophysics and biochemistry and of chemistry; **Peter Salovey**, PH.D., University Provost and the Chris Argyris Professor of Psychology; **William C. Sessa**, PH.D., professor of pharmacology; **Robert S. Sherwin**, M.D., the C.N.H. Long Professor of Medicine and director of the Diabetes Endocrinology Research Center; **Abraham Silberschatz**, PH.D., chair and Sidney J. Weinberg Professor of Computer Science; **Joann B. Sweasy**, PH.D., professor of therapeutic radiology and genetics; **William V. Tamborlane**, M.D., FW '77, professor and section chief of pediatric endocrinology; and **Kyle T. Vanderlick**, PH.D., dean of the Yale School of Engineering and Applied Science and professor of chemical engineering.

The Michael J. Fox Foundation awarded \$125,000 in April to Yale biomedical engineers **Mark Saltzman**, PH.D., chair and the Goizueta Foundation Professor of Biomedical Engineering in the School of Engineering and Applied Science, and **Michael Levene**, PH.D., assistant professor of biomedical engineering, for research on the obstacles to



**William
Tamborlane**



**Michael
Crair**



**Pietro
De Camilli**



**Thomas
Gill**



**Jeffrey
Gruen**



**Susan
Kaech**



**Shirleen
Roeder**



**Michael
Sernyak**

drug delivery in regions of the brain affected by Parkinson disease. Saltzman and Levene will develop new imaging techniques that observe the movement of molecules in the brains of living animals. These techniques will make it possible to track the way in which drugs important for the treatment of Parkinson disease move to their target areas under different conditions.

Levene is a pioneer of deep brain imaging using multiphoton microscopy in living animals. This study will expand the technology to include molecular tracking of drugs as they traverse the brain.

Saltzman has published widely on the development of efficient drug delivery technology, including the recent addition of water-soluble polymers to chemotherapeutic drugs to allow deeper and more stable delivery to various locations in the brain.

Michael C. Crair, PH.D., was named the inaugural William Ziegler III Associate Professor of Vision Research at the School of Medicine this spring. Crair studies the ways in which the eye gets wired to the brain during fetal development. He uses a broad range of experimental techniques, including *in vitro* and *in vivo* electrophysiology and optical imaging, to examine neural-circuit development and to investigate the cellular and molecular mechanisms for sensory map development. Research from his lab will help advance understanding of the ways in which a combination of genetic instruction and sensory experiences can lead to developmental disorders related to vision.

Pietro De Camilli, M.D., FW '79, the Eugene Higgins Professor

of Cell Biology, has received a \$100,000 Distinguished Investigator Award from NARSAD, the leading charity advancing treatment of mental health disorders. The one-year grant will help support his research into the role metabolism plays in the regulation of brain function and its impact on autism, bipolar disorders, and schizophrenia. De Camilli is one of 16 scientists honored by NARSAD this year.

Thomas M. Gill, M.D., FW '94, a leading authority on the epidemiology and prevention of disability among older persons, was named the Humana Foundation Professor of Geriatric Medicine this spring. Gill is co-director of the Yale Program on Aging and of the Claude D. Pepper Older Americans Independence Center. His research is focused on understanding the mechanisms underlying the development of functional decline and disability among community-living older persons and on developing preventive strategies to forestall the onset and progression of disability among frail at-risk elders. His other research interests include the epidemiology and prevention of bathing disability and the epidemiology of frailty among older adults.

Jeffrey R. Gruen, M.D., HS '83, associate professor of pediatrics and genetics, has received a \$5.2 million grant from the Manton Foundation in New York City to further his research on the genetics of dyslexia. Gruen's discovery of a gene involved in dyslexia was named one of the top 10 scientific breakthroughs of 2005 by the journal *Science*. Gruen will use the grant monies to launch a new study that will

compare the complete genomes of 1,000 dyslexic children with those of 1,000 fluent readers to obtain a fine-grained view of genes known to play a role in reading disabilities, and possibly to identify new genes that increase the risk of developing dyslexia.

Susan Kaech, PH.D., assistant professor of immunobiology, is one of 50 researchers named Early Career Scientists by the Howard Hughes Medical Institute (HHMI). This award was created by the HHMI to fuel the creative energy of young scientists strained by reductions in federal funding in scientific research and education. The award includes a research grant of \$1.5 million over six years to support Kaech's research. Kaech is an expert on protective T-cells generated by the immune system to combat infections. In particular, she is focusing on memory T-cells, which are long-lived cells that remember pathogens from prior infections and can provide long-term protection against reinfection. Kaech is working on ways to enhance responses to infection and to improve vaccines.

Shirleen Roeder, PH.D., professor of molecular, cellular, and developmental biology, the Eugene Higgins Professor of Genetics, and a Howard Hughes Medical Institute investigator, has been named to the National Academy of Sciences. Roeder is at the forefront of scientific research in molecular genetics; she was part of a Yale team that fully characterized the function of the yeast gene. Roeder specializes in meiotic chromosome behavior and cell cycle checkpoints. In the laboratory, she is studying a special type of cell division

called meiosis, which is necessary for sexual reproduction, by isolating and characterizing yeast mutants with defective meiotic processes. She has written nearly 100 scientific articles that have appeared in such journals as *Cell*, *Science*, *Genetics*, and *Molecular Cell Biology*.

Michael Sernyak, M.D., HS '87, professor of psychiatry, was appointed director of the Connecticut Mental Health Center (CMHC), effective July 1. Sernyak was nominated by Yale University and appointed by Thomas Kirk, PH.D., the commissioner of the Connecticut Department of Mental Health and Addiction Services. Sernyak, who replaces the retiring Selby Jacobs, M.D., served as unit chief of the Psychosis Studies Unit at CMHC for five years. In 1996 he joined the staff at the VA Connecticut Healthcare System in West Haven and in 2001 was appointed chief of the psychiatry service. Sernyak is a nationally recognized health services researcher who specializes in treatment issues of the severely mentally ill. His most recent areas of focus have been the development of such metabolic abnormalities as diabetes and the delivery of medical care in patients with schizophrenia.

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JOHN CURTIS (3)

A day to reflect on becoming a doctor

The Class of 2009 enters medicine at a time of change and an ongoing debate over health care.

For the 96 members of the Class of 2009, Commencement was a day of sunshine and serious reflection on the nature and responsibilities of being a doctor.

Commencement speaker David Blumenthal, M.D., national coordinator for health information technology at the U.S. Department of Health and Human Services, exhorted the

graduates to engage in the debate on health care reform. “We are witnessing a crisis in the system of care, upon which we all rely as patients and without which you, and all the classes that follow you, cannot effectively apply your art and skills,” Blumenthal said. He spoke of the rising cost of health care in the United States, and he framed the current economic and political climate as an ideal moment for change as more people lose employment-based health insurance. “Timing is everything, and we are now seeing a combination of circumstances that is rare in the history of our country and of health reform.”

Blumenthal drew parallels between the Obama administration and that of President Lyndon Johnson, which enacted Medicare and Medicaid. Then as now, he said, three forces converged—a crisis in health care, a bipartisan desire to effect change, and presidential leadership on the issue. No true health care reform can take place, Blumenthal said, without the support of the nation’s young physicians, and he encouraged the graduates to stay involved in reform efforts throughout their careers. “It can make you a better physician, and it can certainly make the lives of your patients better.”

In his invocation at the ceremony in Amistad Park, Jason Frangos, M.D. ’09, described the process of moving through medical studies into the heart of doctoring. “We may look back to when we first arrived, when we first received our portions of unrefined ore,” he said. “We smelted and forged and hammered into iron in the blast heat of hard work, studying and memorizing, dissecting and discovering, listening and loving. ... We hammered, tempered, and wrought into a



TOP Lawrence Cohen and bagpiper Glenn Pryor led the procession to Commencement ceremonies at Amistad Park.

ABOVE Fabienne Meier-Abt, Sarah Milgrom, Kathleen Samuels, Aviva Romm, and Titilope Oduyebo waited at Cross Campus for the procession to Old Campus for the university Commencement.

RIGHT Sheela Smith-Rohrberg Maru and Duncan Smith-Rohrberg Maru bottle-fed their infant sons as they waited to receive their diplomas.



tiny spinning needle ... a compass that is our heart.”

Commencement awards

This year's Bohmfalk Prizes for excellence in teaching went to Michael L. Schwartz, PH.D., associate professor of neurobiology, for basic science; and to Frederick D. Haeseler, M.D., associate clinical professor of internal medicine and director of primary care clerkships, for clinical science.

Grace Y. Jenq, M.D., assistant professor of medicine (geriatrics), received the Leonard Tow Humanism in Medicine Award. The Leah M. Lowenstein Award went to Laura R. Ment, M.D., associate dean for admissions and financial aid and professor of pediatrics and neurology.

The Alvan R. Feinstein Award went to Robert M. Rohrbaugh, M.D., associate professor of psychiatry. Karen J. Jubanyik, M.D., assistant professor of surgery (emergency medicine), received the Francis Gilman Blake Award. The Betsy Winters House Staff Award went to Joshua Silverstein, M.D.

The Class of 2009 donated its class gift to the Mila Rainof Memorial Fund, to help those “who choose the same path we have chosen,” according to the class presidents.

—Ayelet Amittay



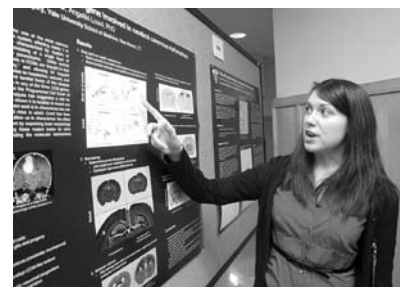
Online Extra

A complete Commencement photo gallery can be found at yalemedicine.yale.edu.



Online Extra

Visit the Online *Extra* section of *Yale Medicine's* website at yalemedicine.yale.edu to access more photographs and full coverage of student events, including Match Day and Student Research Day.



JOHN CURTIS (3)



TOP LEFT In March, Heather Wachtel celebrated her match to a general surgery residency at the Hospital of the University of Pennsylvania.

TOP RIGHT Medical student Aimee Two explained her neurobiology poster at Student Research Day in June. She was one of 70 students who presented posters on research in laboratory science, clinical findings, medical humanities, and international health.

ABOVE Ongoing renovations caused Student Research Day to move from its traditional home in the Jane Ellen Hope Building to The Anlyan Center this year.

A Navajo doctor tends to the spirit and body

Patricia Nez Henderson integrates a concept of balance and harmony into her thinking about medicine.

When **Patricia Nez Henderson**, M.P.H. '94, M.D. '00, was a child in rural Arizona, her grandfather would come to her house early in the morning and splash water on her and her siblings. "Get up! Get up! Go run and meet the rising sun," he told them in Navajo. "If you sleep too much, you're going to be left behind, and the morning gods are ready to bless you." The children would jump out of bed and run toward the glow in the east.

From growing up in a Navajo-speaking community without electricity or running water to completing medical school as Yale's first female American Indian graduate, Nez Henderson's was a remarkable journey. Her interest in medicine began early, influenced by her



Patricia Nez Henderson, the first female American Indian graduate of the Yale School of Medicine, combines science and the spiritual in her practice of medicine.

grandfather—a medicine man—and other traditional healers in her family. Most of her relatives worked as shepherds, and she recalls listening to lambs' hearts with a stethoscope her mother had bought her. "I'd come home smelling like manure," she said. "My mother says that's when she first realized I'd go into medicine."

Nez Henderson earned her M.P.H. at the School of Public Health in 1994 after earning a degree in biochemistry at the University of Arizona. Then it was on to medical school.

It was there that culture shock took hold. Having grown up among healers who took patients' spiritual as well as physical health into account, Nez Henderson felt miserable at an allopathic school. "My heart was dissected from my head," she said. "I felt it immediately upon getting into med school, and there were no other Native students there, so it was hard to explain to students or even my professors what I was going through." One day a faculty member made a thoughtless comment about her imperfect command of English. It devastated her. At that moment, she said, she understood why so many American Indian students leave school. "All I saw was a room full of men in white jackets, predominantly white, and I just began to cry, [thinking] 'I don't belong here.'"

Shortly afterward, Peterson Zah, a former president of the Navajo Nation, came to speak at Yale. Before his speech, Nez Henderson met with him privately and told him what had happened. Later, as he addressed the crowd, he turned directly to her and spoke words of encouragement in Navajo, whereupon she decided to stay at Yale.

After earning her M.D., along with an award in her name given to recognize a graduate committed to improving health among American Indians, Nez Henderson went to Colorado. Her sense that allopathic medicine is insufficient—as well as the frustration among physicians she had witnessed during clinical rotations at underfunded Indian Health Service sites—had

convinced her to pursue public health research. She joined the faculty of the University of Colorado Health Sciences Center's Native Elder Research Center for a two-year program that trains Native health professionals for research careers. Funded by grants from the National Institutes of Health, the Centers for Disease Control and Prevention, and the Robert Wood Johnson Foundation, she began to study tobacco control and prevention among American Indians, an interest that continues today.

Tobacco has long been sacred to Native communities, but its abuse leads to disproportionately severe health consequences for them. Nez Henderson studies American Indians' reactions to nicotine, which may have genetic underpinnings. She has also designed Web-based interventions and smoking cessation classes that incorporate tribal practices like prayers, visits to sweat lodges, and fasting, and that emphasize the sacredness of life. "Navajo tribes use a word, *hozho*, which means 'in balance' or 'it's beautiful.' There's that harmony," she said. "Anything that impacts *hozho* and makes it go out of balance, we know that's toxic, like cigarettes. ... It's a more holistic approach. Instead of just telling a person to do these things that are backed by evidence, you combine it with things that are spiritual."

Nez Henderson lives in South Dakota with her husband Jeffrey A. Henderson, M.P.H., M.D., an internist who is Lakota Sioux, and their daughter, Zahlianii, 7, and son, Mato, 5. They head the Black Hills Center for American Indian Health in Rapid City. In addition to her research, Nez Henderson works with tribal leaders to effect tobacco policy changes within the Indian nations. "With sovereignty comes responsibility," she said. "A lot of tribes are looking at ways to bring economic development into their communities, but if they put health first, all that they're looking for will come next.

"I work all the way from prevention to cessation to policy," she said. "I absolutely love what I do."

—Jenny Blair

At 86, head and neck surgeon still contributes to medicine and hospice cause he helped found

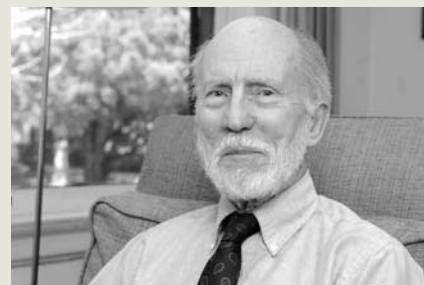
One medical school memory that **Donald P. Shedd**, M.D. '46, HS '53, holds dear is of the day he walked into the “croup room” at Grace-New Haven Community Hospital and peered through the mist that was then used to treat children with the characteristic barking cough. There he caught his first glimpse of his future wife, a Yale nursing student named Charlotte Newsom. “You can imagine how glamorous a woman looks in a steam room,” he said. She turned out to be lovely, a gifted pianist who played Chopin beautifully. They married and launched two brilliant careers.

Shedd, now 86, ended up joining the Yale faculty, later became chief of head and neck surgery at the Roswell Park Cancer Institute in Buffalo, New York,

and serving as national president of the Society of Head and Neck Surgeons, which became the American Head and Neck Society in 1998. Charlotte Newsom Shedd, M.N., R.N. '46, who passed away two years ago at the age of 84, co-founded Hospice Buffalo, often working from the dining room table while caring for her aging mother and the youngest of the four Shedd children. She traveled around the country as an early pioneer of the hospice movement at the national level.

Both Shedd's had high levels of energy. Now professor emeritus at SUNY Buffalo, Shedd still attends weekly tumor board meetings. He also maintains a database of head and neck operations at the cancer institute, where he was chief of head and neck surgery for 29 years. In 2007, the department published his fifth book, a history of head and neck surgery at Roswell. Shedd is also the author of *Historical Landmarks in Head and Neck Cancer Surgery* and *The Early History of Hospice Buffalo*.

“You become conscious of a decrease in energy in your mid-80s,” said the surgeon, who gave up windsurfing on Lake Erie around age 75. But he still plays tennis and maintains a regular exercise schedule. He has helped build



Donald Shedd, a head and neck surgeon in Buffalo, N.Y., was an early supporter of the hospice movement in this country, as was his wife, Charlotte.

houses for Habitat for Humanity and is an active member of the Unitarian Universalist Church of Buffalo, where he moderates a discussion group, serves on committees, and participates in a monthly book club.

Shedd earned his bachelor's degree at Yale and began his study of medicine in an accelerated program during



Online Extra

Visit the Online *Extra* section of *Yale Medicine's* website at yalemedicine.yale.edu to access more photographs and full coverage of this year's reunion events.

ALUMNI TOUR SMILOW CANCER HOSPITAL

During this year's reunion, about a dozen alumni toured Smilow Cancer Hospital, which is scheduled to open in October. From the ground floor, the group took elevators to the upper floors for views of still-unfinished offices and suites, with grand views of New Haven. The tour also took in new operating rooms—where all cancer surgery at Yale-New Haven Hospital will take place—and infusion suites. The 14-story facility will contain nearly 500,000 square feet and will include 112 inpatient beds, outpatient treatment rooms, expanded operating rooms, infusion suites, diagnostic imaging services, and floors for diagnostic and therapeutic radiology.



World War II, when faculty members were leaving to serve in the military and medical students were hired to deliver emergency anesthesia at night. During his 14 years on the Yale faculty, he became increasingly interested in the care of head and neck cancer patients. He moved to Roswell Park in 1967. “The job offer in Buffalo was an excellent one,” Shedd said. “It was one of the best positions in the field in the country.”

Shedd describes himself as “a modest contributor” to head and neck surgery during what he calls “a fascinating period” of advances in medicine. “I’d say there have been modest gains in head and neck cancer survival and major gains in quality of life, both cosmetically and functionally,” he said. “One of my contributions to care at Roswell Park was the incorporation of the use of the surgical microscope in endoscopic diagnosis. It made diagnosis more precise,” he said. As a faculty member at Yale, he conducted radiographic studies of swallowing in inpatients after head and neck surgery. “I did some work at Roswell in surgical approaches to speech rehabilitation after laryngectomy,” he said.

In addition to his clinical work and research, Shedd helped train fellows and residents who began their careers at Roswell Park. He was involved in medical service in Peru and Nicaragua, as well as short surveys of oral cancer research in India, Pakistan, and Ceylon (now called Sri Lanka). He also held a visiting professorship in South Africa.

While his own career was demanding enough, Shedd shared his wife’s passion for hospice care. The contemporary American hospice movement began in New Haven when the Shedd and others attended a talk at Yale by Dame Cicely

Saunders, the Englishwoman regarded as the founder of the modern hospice movement. “We kept talking about it after we came to Buffalo. We realized there was a need for such a facility here, so we formed a founding committee, then Charlotte took the initiative,” he said. The couple also collaborated on a survey of the final period of life in 60 head and neck cancer patients. Charlotte received a distinguished alumna award from the School of Nursing in 1992.

Shedd said the support he and his wife provided each other throughout their careers and retirement was crucial. He considers it a privilege to have been able to care for Charlotte at home during her encounter with Alzheimer disease. She spent her final day in the hospice inpatient unit she had helped to establish.

“Joseph Campbell said something about following your bliss,” Shedd said, referring to the scholar who wrote about the power of mythology to explain human experience. “I think I have been able to do that.”

—Kathy Katella

Familiar Faces

Do you have a colleague who is making a difference in medicine or has followed an unusual path since leaving Yale? We’d like to hear about alumni of the School of Medicine, Physician Associate Program, and the medical school’s doctoral, fellowship, and residency programs. Drop us a line at yymm@yale.edu or write to Faces, Yale Medicine, 300 George Street, Suite 773, New Haven, CT 06511.

2009-2010

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Aaron Beck



Richard Lamb



Anthony Proto

Eduardo
Alfonso

Jiyon Lee

Gualberto
Ruaño

1940s

Aaron T. Beck, M.D. '46, received the 2009 Award for Extraordinary Accomplishment in Medical Research from the Robert J. and Claire Pasarow Foundation in May. The \$50,000 award is one of three given each year for basic or clinical research in cancer, cardiovascular disease, and neuropsychiatry. Beck, the University Professor Emeritus of Psychiatry at the University of Pennsylvania School of Medicine, is a member of the Institute of Medicine and the National Academy of Sciences.

1950s

Richard Lamb, M.D. '54, received the 2009 Distinguished Service Award from the American Psychiatric Association. The award honors individuals and organizations that have contributed meritorious service to American psychiatry.

1970s

Katherine Benesch, M.D. '70, J.D., a partner in the health law practice group at the Princeton, N.J., office of Duane Morris LLP, was appointed to the American Arbitration Association (AAA) Health Care Advisory Council in March. The council is a national group appointed by the AAA to develop dispute resolution solutions for the health care industry.

Anthony V. Proto, M.D. '71, was awarded the 2008 Gold Medal of the Radiological Society of North America (RSNA) for his contributions to radiology. The Gold Medal requires the unanimous approval of the RSNA board of directors. Proto, who recently completed more than 10 years as editor of the journal *Radiology*,

is a professor of radiology at Virginia Commonwealth University Medical Center.

1980s

Eduardo C. Alfonso, M.D. '80, the Edward W.D. Norton Professor of Ophthalmology, was named chair of Bascom Palmer Eye Institute, the Department of Ophthalmology of the University of Miami Miller School of Medicine, in June. A 1984 graduate of the institute's residency program, Alfonso has been on the faculty since 1986. He is known for his clinical expertise in diseases and surgery of the cornea and in ocular microbiology and laser vision correction.

1990s

Matthew B. Klein, M.D. '97, has been named the David and Nancy Auth-Washington Research Foundation Endowed Chair for

Restorative Burn Surgery at the University of Washington. Klein is associate professor of plastic surgery, associate director of the University of Washington Burn Center, and director of the plastic surgery residency program.

Jiyon Lee, M.D. '96, assistant professor of radiology (breast imaging) at New York University (NYU) School of Medicine, was honored at the American Cancer Society's (ACS) Diamond Luncheon in May for her volunteer work with the ACS in Westchester County, N.Y. Lee has been serving as medical director and a member of the board of advisors for the past five years. She is a mammographer at the NYU Clinical Cancer Center and at Bellevue Hospital Center in New York City.

Gualberto Ruaño, Ph.D. '92, M.D. '97, was inducted into the American Institute for Medical

and Biological Engineering's College of Fellows in April at a ceremony in Washington, D.C., at the National Academy of Sciences. Recipients of this honor are chosen for exceptional leadership and achievements in medical and biological engineering. Ruaño is president and chief executive officer of Genomas Inc., a biomedical company based in Hartford, Conn.; director of genetics research at Hartford Hospital; and adjunct professor in the medical faculties of George Washington University and the University of Puerto Rico.

SEND ALUMNI NEWS TO Claire M. Bessinger, *Yale Medicine*, 300 George Street, Suite 773, New Haven, CT 06511, or via e-mail to claire.bessinger@yale.edu

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WANTED: IMAGES OF YESTERYEAR

In preparation for the School of Medicine's Bicentennial in 2010, *Yale Medicine* is seeking archival photographs, motion pictures, videos, and sound recordings depicting the history of the school and its students, faculty, and alumni.

Areas of interest include medical education, student life, medical practice, and scientific research. Please let us know if you have materials that could be borrowed or duplicated. All formats are acceptable, including photographic prints, slides, digital files, film and tape reels, and cassettes. Write to us at yymm@yale.edu [subject line: Bicentennial images] or via U.S. mail to Bicentennial Images, *Yale Medicine*, 300 George Street, Suite 773, New Haven, CT 06511. To join the Bicentennial news and events mailing list, visit medicine.yale.edu/alumni.



John R. Brobeck, PH.D., M.D. '43, died of pneumonia on March 6 at a retirement community in Media, Pa. He was 94. Brobeck served on the Yale faculty from 1942 until 1952. Brobeck then chaired the physiology department at the University of Pennsylvania School of Medicine from 1952 until 1973 and for 10 years served as assistant to the vice president for health affairs. He was elected to the National Academy of Sciences in 1975.

Seth D. Charney, M.D. '69, died at his home in San Francisco on March 8. He was 64. Charney served as a student editor of the *Journal of the History of Medicine* during his years at Yale. He practiced psychiatry in San Francisco, owned real estate throughout California, and was a lifetime champion of human rights causes.

Edwin L. Child, M.D. '56, died on February 14 of brain cancer at his home in Manchester, N.H. He was 78. Child was an obstetrician/gynecologist who delivered thousands of babies during his career and made medical mission trips to Liberia, Jamaica, and Kenya.

William F. Collins Jr., M.D. '47, the Harvey and Kate Cushing Professor Emeritus of Neurosurgery and former chair of surgery, died on June 17 in San Diego. He was 85. Collins accepted the position of professor and chief of neurosurgery at Yale in 1967. In 1970, he was appointed the Harvey and Kate Cushing Professor of Surgery. He remained chief of neurosurgery at the medical school and neurosurgeon in chief at Yale-New Haven Hospital until 1984, when he was appointed chair of the Department of Surgery. He retired as chair in July of 1993 and assumed emeritus status in the Department of Surgery on July 1, 1994.

Lycurgus M. (Bill) Davey, M.D. '43, died on June 15 in New Haven as a result of injuries from a fall. He was 91. Davey was a clinical professor of neurosurgery who devoted much of his career to

clinical teaching and the training of Yale neurosurgical residents. He served as president of the Association of Yale Alumni in Medicine from 1995 to 1997. He read five languages and drew on his classical education as he explored and wrote about the history of medicine, including an article about the Greek inscription above the entrance to Sterling Hall of Medicine. He was an active consultant and clinical professor in the Department of Neurosurgery at Yale from 1951 to the present. His recent awards include the Distinguished Alumni Service Award in 1997 and the Peter Parker Medal in 2003 for outstanding service to the School of Medicine.

William K. Frankenburg, M.D., M.S.P.H., FW '63, an internationally recognized pioneer in child development and pediatric preventive medicine, died on April 3 of acute myeloid leukemia at his home on Bainbridge Island, Wash. He was 78. In 1967, Frankenburg and his colleague at the University of Colorado, Josiah Dodds, PH.D., published the Denver Developmental Screening Test, known as the Denver II, which has been used to screen millions of children around the world for developmental delays.

Stuart L. Joslin, M.D. '43, died on January 25 after a short illness in North Adams, Mass. He was 93. Joslin was one of the founding directors of the Mid-Fairfield Child Guidance Center and chair of the Well Baby Clinic, both in Connecticut, where he practiced pediatrics until his retirement in 1991.

Alan D. Lieberman, J.D., M.D. '62, died at his home in Westport, Conn., on February 10. He was 71. Lieberman used his knowledge of law and medicine to tackle such medical questions as euthanasia, living wills, and health care rationalization. He was a partner at Internal Medicine of Westport for 15 years and served on the medical ethics committee of Norwalk Hospital.

Daniel L. Macken, MED '59, M.D., died on March 1 in New York City. He was 75. Macken served as a lieutenant colonel in the Army Medical Corps during the Vietnam War. He was honored by the United States and the Republic of South Vietnam for his wartime medical service. At Columbia University he founded the Medica Foundation to support medical research and activity.

Henry E. Markley, M.D. '43, died on February 26 in Greenwich, Conn. He was 90. Markley practiced medicine in Greenwich from 1950 until 1979, and in 1955 launched Greenwich Hospital's Home Care Program for the elderly, sick, people with disabilities, and children with special needs.

Robert W. Ollayos, M.D. '41, died on February 23 in a nursing facility near St. Louis of complications of Alzheimer disease. He was 92. Ollayos, a flight surgeon in the Army Air Corps during World War II, conducted research that contributed to the development of lifesaving equipment for babies born with Rh-blood type incompatibility.

Vincent Pepe, M.D. '46, HS '52, an obstetrician-gynecologist who delivered more than 10,000 babies during 60 years in private practice, died on June 20 of congestive heart failure in Meriden, Conn. He was 87.

Pepe, a native of New Haven, began his practice in the Meriden-Wallingford area in 1952. In the 1950s, he helped to forge the use of prenatal folic acid to prevent birth defects and later helped to pioneer work in urological gynecology. He also helped to advance surgical treatments for urinary incontinence for women as well as laparoscopic operative techniques and ultrasound procedures in community-based ob-gyn practice.

Richard C. Petersen, M.D. '48, died on February 1 at his home in Southbury, Conn. He was 85. In 1955 Petersen opened a pediatric practice in Stratford, Conn., and

became a leader in preventive pediatric care.

Samuel M. Rice, M.D. '49, died on March 3 in Cranberry, Pa. He was 86. After graduating from medical school, Rice returned to the Pittsburgh area and practiced medicine out of his house in Cranberry from 1953 until 2003, making house calls and seeing the same patients for decades.

Micky Ray Riggs, M.D. '92, died on December 26 in Seattle. He was 52. Riggs was remembered for his insights on topics ranging from global politics to serial killers to SpongeBob SquarePants.

Susan S. Spencer, M.D., professor of neurology and neurosurgery, died suddenly on May 21 in Salt Lake City. She was 60. Spencer was an internationally recognized expert in epilepsy, and particularly in epilepsy surgery. She was the co-director of the Yale Epilepsy Program with her husband, Dennis D. Spencer, M.D., HS '77, chair of neurosurgery. She came to Yale as a resident in neurology in 1975, following undergraduate and medical school education at the University of Rochester, and joined the faculty in 1980. She soon wrote major papers in epilepsy surgery and published more than 200 original manuscripts and chapters on the subject. Her contributions were recognized by the American Epilepsy Society Clinical Research Award in 2003.

SEND OBITUARY NOTICES TO
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 to claire.bessinger@yale.edu

A TOUCH OF GLASS

At this most modern of universities, with its particle accelerators, radiochemistry facility, and stem cell center, a lone craftsman in a small workshop helps unravel today’s scientific mysteries using techniques developed centuries ago.

Daryl Smith is Yale’s scientific glass blower. At the Yale Glass Shop in the Sterling Chemistry Laboratory, Smith helps scientists and researchers design the equipment they need for their experiments. “Anything they see in a catalog I can make and customize to fit their specific needs,” said Smith, who came to Yale in 2005 after working for private glass companies. He completed his undergraduate degree in aquaculture from Texas A&M University in College Station and studied scientific glass technology at Salem Community College in Carneys Point, N.J. “I like working with my hands,” he said, “but I like the science part of it, too.”

Smith also teaches a semesterlong course titled “Introduction to Scientific Glass Blowing,” which focuses on the dexterity needed to be a glass blower as well as the tools and materials. Last spring, his six students watched a brief demonstration by Smith before beginning their final project, a Hero’s engine—a device invented by Hero of Alexandria around A.D. 10 that propels itself by shooting steam from one or more orifices.

Many research universities outsource their glasswork to private companies, but Smith can meet face to face with researchers to develop customized products, and he can create or repair a device the same day if necessary. But perhaps most important, Smith’s loyalty is to Yale, so when he and a researcher develop a new design, he treats it as proprietary information; he won’t share it as an outside contractor might.

When Smith isn’t creating or repairing scientific equipment at Yale, he enjoys the artistic side of glass blowing, creating glass ornaments and gifts at his home studio. Not surprisingly, the Christmas season is his busiest time. “You’ll find me sitting in front of my bench torch,” he said, “instead of going to the mall.”

—Jennifer Kaylin



JOHN CURTIS

Glass blower Daryl Smith produces made-to-order glass implements and instruments for Yale scientists. “I like working with my hands, but I like the science part of it, too,” he said.



Online Extra

Video of Daryl Smith at work can be seen at yalemedicine.yale.edu/glassblower.

