# **Yale Medicine**

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## autumn 2008

A huge NIH grant boosts bench-to-bedside research, but many scientists still want to follow their noses



# AUTUMN 2008

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## We should expect our students to be literate

It was with some sadness that I read of the teaching of ethics by my colleague, Alan A. Stone, м.D. '55, to his students at Harvard Law School. ["A Passport to the Young," Yale Medicine, Spring 2008] Stone felt obliged to turn to the movies because "few students had read Sophocles or Dostoevsky, Austen or Flaubert." I was reminded of how startled I was some years ago to discover that one of my patients, a graduate student in literature at Yale and a magna cum laude graduate of Yale College, had never read a work by Shakespeare.

Should our top law and medical schools be admitting people who haven't even a rudimentary reading knowledge of the Western canon? Perhaps what is needed is not a "new passport to the young," but a reactivation of the old one. And perhaps we cannot absolve ourselves of some of the blame for the illiteracy of the young until we make it clear to them that we expect them to be literate.

Victor A. Altshul, м.D. '6o Associate Clinical Professor of Psychiatry

## Med school missing from cover

I find an interesting example of the complex relationship between the School of Medicine and the main campus represented by the absence of the topography of the medical campus on the cover of last spring's issue of Yale Medicine. Robert B. Duckrow, M.D. '75, HS '79 Associate Professor of Neurology and Neurosurgery

## vale medicine

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## starting Point

## Basic science vs. translational research, and medicine and rain forests

In the autumn of 2006, Yale became one of a handful of medical schools to receive a CTSA grant from the National Institutes of Health (NIH), a boon to translational research here and around the country. Once the program was up and running we asked writer Jill Max to take a look at the new Yale Center for Clinical Investigation, created and funded with the goal of supporting clinical research. This enhanced emphasis on translational research also prompted us to explore the tension between basic-science researchknowledge for knowledge's sake-and the bench-to-bedside goals of those who start out with a cure or treatment in mind. Boston-based science writer Pat McCaffrey talked to scientists at Yale and found that, largely due to a flat NIH budget, scientific research is going through hard times. But some scientists also worry that basic research is taking a back bench to translational research.

More than two years ago, in May 2006, we heard from Kinari Webb, M.D. '02, who asked if we'd be interested in an article about her work in Indonesia. Four years out of medical school, Webb had laid the groundwork to open a clinic in a remote area of Borneo. In addition to her desire to provide medical care to an underserved area, she and her husband, a Harvard ecologist, wanted to link that to preserving the region's rain forests. For more than a year Jill Max has been in contact with Webb, following the progress of the clinic, which opened in the summer of 2007. Her report begins on page 30.

> John Curtis Managing Editor

SECOND OPINION BY SIDNEY HARRIS



"LET'S SEE NOW ... "



The death of Mila Rainof, a month before her graduation, sent a shock throughout the medical school. Her classmates posted her photo and left flowers at the site of the accident.

## A student's warm heart and "amazing" smile

Mila Rainof's embrace of others has inspired an enduring memorial at the medical school.

As the 96 members of the Class of 2008 processed to Old Campus for Commencement on May 26, they paused at the corner of York Street and South Frontage Road. One by one, each graduate placed a carnation in memory of Mila Rainof, a classmate who was not with them in the procession.

On April 19 Rainof was struck by a car as she crossed the intersection. She died the next day of her injuries. At a medical school town meeting called by Dean Robert J. Alpern, M.D., on the Monday after Rainof died, Alpern said, "The medical school family has lost a member way too young in age."

In the wake of her death, Rainof's friends and classmates have found many ways to honor her. Her close friends stood by Rainof's parents and sister when they came to New Haven and organized a memorial service in the medical school's Rose Garden. Others began collecting photos and remembrances for a book to be given to her family. Students have organized efforts to improve safety at intersections near the medical school. (See sidebar.) A memorial scholarship and award fund is being established at the School of Medicine to honor and perpetuate Rainof's memory, in particular her compassionate spirit and humanistic approach to medicine. Students also planted a cherry tree in her honor on Harkness Lawn.

Rainof's parents have shared with Merle Waxman, director of the Office for Women in Medicine and a mentor to Rainof, that their daughter loved Yale and was happy here. Her phone calls, they told Waxman, were always filled with her enthusiasm for her classmates, teachers and patients.

What friends remember best about Rainof is her warm and welcoming smile. "Like everyone else," her boyfriend and classmate James Troy said at the Rose Garden memorial, "I was instantly won over by her amazing smile." A friend and classmate, Ellen House, recalled sharing clinical rotations with Rainof and all the patients asking for "the smiley one."

Margaret A. Drickamer, M.D., associate professor of medicine, recounted a trip to Seattle with Rainof to attend a conference. They walked all over the city, she said, talking and telling stories. "We laughed, we cried—and we did go to some poster sessions." Beyond Rainof's warm and friendly demeanor, Drickamer said, was a determination to help people. "Mila really cared about people, especially when she felt a responsibility for their welfare, and she steadfastly refused to let anything get in the way of that caring," Drickamer said.

Karen J. Jubanyik, M.D., assistant professor of surgery (emergency medicine), described a difficult shift at Yale-New Haven Hospital the day after Rainof died. "I just thought, 'What would Mila do?' " Jubanyik said. "She would contribute any way she could. She would go to the patient's side, hold their hand and genuinely listen to them." Friend and classmate Maggie Samuels-Kalow said, "Mila was the person that you wanted at your side when the patient was getting sicker and you didn't know what to do."

Kristina Zdanys, one of the class copresidents, said that the students in the Class of 2008 are a close-knit group and would have felt the loss of any of their members, but that Rainof was special.

## After a tragedy, the medical school community mobilizes around traffic safety

On the afternoon of May 22, about two dozen students, faculty and staff from the School of Medicine marched from Cedar Street to the corner of York Street and South Frontage Road, where Mila Rainof, a fourth-year medical student, died after being struck by a car a month earlier.

Pedestrians have long dreaded this and other intersections near the medical school. Drivers in a hurry to reach the Route 34 Connector feeding into Interstate 91 and Interstate 95 routinely run red lights and ignore pedestrian crossing signals.

Students have organized a Traffic Safety Group since Rainof's death their goal is to make the streets safer for pedestrians.

"It is important that we honor Mila and keep the traffic safety effort in the spirit of what she would have done," said Rachel Wattier, a fifth-year medical student who is leading the traffic group. "A lot of people have deep-seated concerns about traffic that they were never able to act on. People see an opportunity to have their concerns addressed." Plans are already under way to improve four intersections adjacent to the medical school area. They are part of a larger plan for street improvements as part of a deal struck between Yale-New Haven Hospital and the city for the construction of the Smilow Cancer Hospital. The model will be the intersection at Cedar Street and Congress Avenue, which has pedestrian crossing lights that flash and count down the seconds remaining for a safe crossing.

The hospital will also relocate a truck loading dock at South Frontage Road and York Street under the adjacent Air Rights Garage. Traffic that now leaves the garage onto South Frontage Road will leave through a roundabout to be built where the Route 34 Connector meets the garage.

In light of the planned improvements, the safety group is developing materials to promote pedestrian and cycling safety, petitioning the city government to enforce the city's 25 mile-per-hour speed limit, and calling for strict enforcement of traffic regulations governing stop lights and signs, cell phone use, bicycle lanes and crosswalks.

—J.C.



A few days before Commencement, students, faculty and staff at the medical school rallied at the intersection of York Street and South Frontage Road to urge drivers to respect traffic rules.

"Whenever she walked into a class or Marigolds, she was always smiling or had something nice to say," Zdanys said.

"If you asked people to think of a person in the class who always made people feel good ... she would be the first person," said Rachel Wattier, who has been leading a committee that has met with city and university officials to improve traffic safety.

A few days before Commencement, students, faculty and others gathered at the intersection where the accident occurred. Bearing signs that read "Yield 4 Walkers," and "No Turn on Red," the group asked drivers to slow down and respect the traffic lights.

"There was really no one to blame," Gregory L. Larkin, M.D., professor of surgery (emergency medicine), said at a meeting in The Anlyan Center the day after Rainof died. Larkin had been the attending in the emergency room when an ambulance delivered Rainof. The day before the accident, Larkin had been her teacher, instructing her in the use of ultrasound. Rainof was scheduled to begin a residency in emergency medicine in Oakland, Calif., after graduation.

On the morning of April 19 Rainof was on her way back to her York Street apartment after working out in the gym in Harkness Dormitory. A truck was leaving the loading dock of Yale-New Haven Hospital against a red light. As Rainof crossed South Frontage Road, also against the red light, the truck cleared the intersection and cars in the three oncoming lanes moved forward. Two swerved to avoid her, but a third struck her when she was just a yard away from the curb and safety. She died the next day of severe head injuries.

—John Curtis

## School of Medicine goes green as it aims for lower carbon emissions by 2020

The Yale School of Medicine's sustainability campaign is ambitious and costs a little extra, but it's perfectly willing to accept hand-me-down jeans—in fact, that's part of the point.

Denim discarded in the jean manufacturing process, which now helps insulate the Sterling Hall of Medicine's C wing, is one of many recycled materials that are lightening the university's carbon footprint. The building's recently renovated lab casework, ceiling tiles and wall insulation also come from such recycled materials as wheat straw board and soy-based spray foam. In total, the sustainability campaign squeezes more light from the sun, diverts trash from landfills and conserves water and heat.

Adding such features to previously planned renovations costs morebetween 1 and 2 percent of the \$8.2 million price tag of the Sterling renovations that were completed in 2006but Yale can't afford not to do it, said Virginia Chapman, director of construction and renovation for the School of Medicine's facilities office. "We're saving the university money as a by-product of reducing carbon emissions," she said. Still to come, Chapman added, are renovations to the second and third floors of Sterling's I wing, the Brady Memorial Laboratory, the Hunter Building, the sixth and seventh floors of the Laboratory for Epidemiology and Public Health and the Laboratory for Surgery, Obstetrics and Gynecology, all of which will incorporate green features.

Yale's overall sustainability strategy began with the student-initiated



"Yale Green Plan" in 1998. In 2002, the university's Advisory Committee on Environmental Management proposed a set of environmental principles, and in 2005 President Richard C. Levin committed the university to reducing greenhouse gases to 10 percent below 1990 levels by the year 2020.

Implementing a sustainable laboratory renovation that could be benchmarked and measured by a national standard would not come easily. Success is measured by the U.S. Green Building Council's Leadership in Energy and Environmental Design (LEED), but the organization had not set standards for lab renovations. "LEED was designed for new buildings or full-building renovations but not laboratories nor smallerscale renovations of the kind we do here at the medical school," Chapman said.

The work on the third floor of the C wing created a yardstick in 2006 when it became the first laboratory renovation project in the United States to gain LEED gold certification for its sustainable features. Among those features, said Robert Skolozdra, an associate at the architectural firm Svigals & Partners, which designed the renovations, are sensors that switch lights on only when a person is in the room. "Daylight harvesting"-adding windows-maximizes available light. The project eased the strain on landfills by recycling 85 percent of construction and demolition debris. Lab faucets have reduced their output from 2 to 1.5 gallons per minute, and low-flush toilets and urinals have been installed. Water use is now down 35 percent overall.

As green renovations continue at the medical school, officials know that the older buildings will pose a challenge, but The Anlyan Center, which opened in 2003, is also "a big energy user," Chapman said. When it was designed, "other concerns outweighed concerns for the environment." The building is undergoing an energy audit to determine how to address the high energy use, she said.

—John Dillon

## New financial aid policy geared toward middle-income families and students

Some students opening acceptance letters from the School of Medicine this spring had another reason to celebrate. While their colleagues in the Class of 2008 graduated with an average debt of \$115,000, a new financial aid formula should ease that burden for middleincome families.

Dean Robert J. Alpern, м.D., Ensign Professor of Medicine, announced the new policy in April. Formerly, parents with a combined income over \$45,000 were expected to help pay the costs of their child's medical education. Beginning this academic year, that threshold has been raised to \$100,000. The "base loan" (the amount students are expected to borrow before receiving scholarship funds) has been raised from \$17,000 to \$18,000, keeping it among the lowest in the country. The new formula applies to all current students.

"What we were expecting was not realistic," said Richard Belitsky, м.D., the Harold W. Jockers Associate Professor of Medical Education and deputy dean for education.

The change was made possible after Yale's endowment income added \$1.1 million to the medical school's financial aid budget. The school's financial aid committee then decided that students from middle-income families needed the extra funds most. Especially needy families did not need to borrow more than the base loan, as School of Medicine scholarships make up the difference, while affluent families were less burdened by tuition costs. The resources of students from middleincome families, though, consistently fell short of the old financial aid formula's estimate, and these students were forced to borrow above the base loan to pay what the school required.

"They should have been borrowing \$68,000—four times the unit loan but the average debt was \$115,000," said Alpern.



Another reason for the change, said Belitsky, was that high debt often influences specialty choice. For example, primary care physicians are in critically short supply nationwide, perhaps in part because they are less well reimbursed than their colleagues in some specialties. Of the 97 Yale students who matched this year, only four entered primary care, and another three entered family medicine. The American Medical Student Association has stated that the current American model of financing medical education harms efforts to improve physician diversity and patients' access to care.

Richard Silverman, director of admissions, speculates that the change may also affect the diversity of the applicant pool. "If another school is widely perceived to be generous or liberal in its financial aid policy, it might get more applications from candidates who assume that Yale, because of the name, is only for the wealthy," he said. Tuition, fees and expenses at the School of Medicine this year are expected to range from \$62,000 to \$69,000.

Other medical schools are also changing their financial aid policies. In March, citing concerns about debt and specialty choice, Harvard Medical School raised its parental-income threshold to \$120,000.

"If a student wants to be a neurosurgeon instead of going into primary care," said Alpern, "I'd hate for them to do it just because of the loans they had." -Jenny Blair



## **Online: Yale Netcasts**

Richard Belitsky: A Great Doctor Is Not What You Know but Who You Are.

# et cetera ...

## **PROVOST LEAVES FOR OXFORD**

Provost Andrew Hamilton, PH.D., is leaving Yale after 11 years to become the next vice chancellor of the University of Oxford in England.

"As a noted scientist, a successful department chair, university citizen and provost these past four years, Andy has had a remarkable impact on Yale since joining our faculty in 1997," said President Richard C. Levin.

Hamilton helped create the Yale Center for Genomics and Proteomics and the Yale Institute for Nanoscience and Ouantum Engineering. He has been instrumental in developing plans for research programs and core facilities for Yale's new West Campus. Hamilton also helped to create the new interdisciplinary Humanities Program and has supported Yale's investments in the arts.

After joining Yale, Hamilton became chair of the chemistry department in 1999. He became deputy provost for science and technology in 2003 and provost in 2004 after then-Provost Susan Hockfield, PH.D., was appointed president of MIT.

In September, Peter Salovey, PH.D., dean of Yale College was named provost. —John Curtis

**62 YMG MEMBERS IN TOP DOCS LIST** 

New York Magazine's 2008 list of the region's top physicians includes 62 physicians from Yale Medical Group (YMG). Yale's "top docs" are in 40 specialties and serve patients of all ages.

The list, which appeared in the magazine's June 16 issue, is based on the Top Doctors New York Metro Area guidebook, published annually by Castle Connolly Medical Ltd. The publishers ask doctors throughout the region which of their colleagues they would recommend to a friend or relative. The guidebook includes the top 10 percent of the metro area's physicians. New York Magazine publishes a shorter list—the top quarter of the top 10 percent.

"Our strong representation in the New York metro area highlights the fact that YMG is a regional and, in some cases, national practice," said David J. Leffell, M.D., CEO of YMG. "Patients throughout New York and New England are coming to see YMG as a medical destination of choice." —J.C.

## A stroke of luck saves New London patient

A new telemedicine initiative brought a potentially lifesaving drug to a patient 50 miles away.

When Jeanne Munnelly went for a swim at a high school in East Lyme one August morning, she could not have known she was about to have a stroke—and make medical history in Connecticut.

At about 8:15, as she swam in the school's pool, Munnelly became weak on her right side and unable to speak. Lifeguards pulled her out and emergency personnel based at the fire station across the street arrived within five minutes. She reached New London's Lawrence and Memorial Hospital in just 15 minutes.

That's when Munnelly, 67, became the first patient to benefit from the Yale-New Haven TeleStroke Network, a program modeled on a similar initiative at Massachusetts General Hospital. The TeleStroke Network allows area hospitals to call upon Yale neurologists' expertise in assessing stroke victims. Using high-speed network videoconferencing and image-sharing technology, neurologist Joseph Schindler, м.D., evaluated Munnelly via computer from Yale-New Haven Hospital (Үмнн), then gave the "green light" to physicians in New London to use the clot-busting drug tissue plasminogen activator (tpa). Munnelly received the drug only 37 minutes after reaching the hospitalmuch more quickly than if she had been transported to YNHH first.

Schindler said the process of evaluating a stroke patient via TeleStroke is the same as when he sees a patient in YNHH's emergency department. "It's no different; it's just the use of technology to do it remotely," he said.

Speed and decisiveness are critically important in treating stroke victims. Most blood clots that cause ischemic strokes can be dissolved by tPA, a thrombolytic agent. But this medication can also cause bleeding in the brain, and that risk increases beyond three hours after the onset of symptoms. To meet that three-hour deadline and try to prevent this complication, doctors must ensure that a patient is an appropriate candidate for tPA. Yet in most hospitals, neurologists are not always available to assist emergency physicians with the evaluation and treatment decision. As a result, many patients who might benefit from tPA do not receive it.

With telemedical technology, a neurologist need not be physically present. While seated at a computer 50

miles away from the patient, Schindler, the clinical director of the Yale-New Haven Stroke Center, used a high-speed Internet connection to speak with the patient, family and clinical staff and review Munnelly's medical history, blood tests and CT scan. He also examined her using a camera with a zoom feature. She was, he determined, a good candidate to receive tPA. Shortly after receiving the drug, Munnelly regained the use of her right leg as well as some ability to speak.

Schindler, who is optimistic that Munnelly's condition will continue to improve, was pleased not only that the technology worked but also that he and the team in New London could act so quickly. "We've done it at Yale when the entire team was already in the ED; we [assessed and treated the patient] in a similar time. But to have that done remotely, it's wonderful." (See related story, page 9.)

—Jenny Blair



From a console in New Haven, neurologist Joseph Schindler evaluated a stroke patient 50 miles away in New London.

## With virtual lives on the line, simulations help responders assess triage systems

Imagine being the first paramedic on the scene after a tanker truck has plowed into a city bus. Traffic is snarled, cars are honking and people are screaming. Who needs your attention most the man on the concrete holding his bloodied knee or the woman on her back with closed eyes? What about the people inside the overturned bus? And what is that white vapor drifting from the truck's tank?

In emergencies, prioritizing care for victims is called triage. The word comes from the French *trier*, "to select" or "to sift," a usage that goes back to Dominique Larrey, the chief surgeon of Napoleon's armies. A victim might be color-coded as red, meaning he needs help immediately; yellow, meaning he will need help soon; green, meaning he has minor injuries; or black, meaning he cannot be helped with available resources. But sorting human lives in this way is still more art than science.

This uncertainty persists because, although many rules exist to help rescuers, it is hard to evaluate whether those rules actually save lives. The decades-old Simple Triage and Rapid Treatment (START) system color-codes patients as described above. But like other such systems, said David C. Cone, M.D., associate professor of surgery (emergency medicine) and of epidemiology, "we have no idea if it works."

Cone has spent his career thinking about disasters and mass-casualty triage. He studies emergency medical services and plans for chemical, biological and nuclear terrorist incidents. He has run disaster simulations at Tweed-New Haven Airport complete with volunteers smeared with fake blood. But triage research is inherently difficult. For one thing, said Cone, "we don't even know what we want a mass-casualty triage system to do." Is the best system the one that's easiest to teach? Quickest to apply? Is the most important goal to get patients into ambulances as quickly as possible? Or to save the greatest number of lives? The complexities mount when one considers that every disaster is unique—it is almost impossible to compare triage systems in the real world. Now, though, Cone has begun working with a new tool to study START and other triage systems: a virtual-reality (VR) simulator.

While studying in Italy for a master's degree in disaster management in 2004, Cone saw a VR simulator used to train Dutch firefighters and realized that the software could be adapted for triage research. Developed by the Dutch company E-Semble, the simulator looks like the highly realistic video game Grand *Theft Auto*. Learners at a laptop "walk around" a vivid scene, assessing and triaging victims. Dangers and distractions, like toxic spills or television reporters, can be added to the scenario. The learners are timed and their actions exported into a database that can then be analyzed.

Working with emergency medicine resident John Serra, м.D., and supported by the Centers for Disease Control and Prevention and the Laerdal Foundation, Cone plans to teach paramedic students two different triage systems several months apart, then compare how they did with each system in identical VR scenarios. "Once we get the software tuned, then we can design the larger studies," said Cone. He plans eventually to use the tool to explore whether rules for triage are even necessary, or whether victims are better off being triaged by experienced rescuers who rely on clinical gestalt.

VR may one day allow researchers around the world to collaborate, exchange scenarios and compile "libraries" of standardized victims. Cone hopes the controlled VR environment will allow for real progress in triage research and ultimately save more lives during real disasters.

—Ј.В.

# et cetera ...

## CHOCOLATE AND PRE-ECLAMPSIA

Eating chocolate may lower the risk of preeclampsia, a dangerous condition in pregnancy characterized by increased blood pressure and proteinuria, according to a Yale study published in the journal *Epidemiology* in May. But the study is not a free pass for chocoholics. Eating too many sweets can cause health problems, said Elizabeth W. Triche, PH.D., of the Yale Center for Perinatal, Pediatric and Environmental Epidemiology, who led the study.

Triche's team wanted to find out whether chocolate—especially dark chocolate with antioxidants that confer cardiovascular benefits—would protect pregnant women against pre-eclampsia. The study found that women who had more than five servings a week had a lower risk of pre-eclampsia; those who had high levels of theobromine, a byproduct of chocolate consumption, were nearly 70 percent less likely to develop preeclampsia than women who had low levels.

"This looks promising, but we need to do more research into how much and what type of chocolate is the most beneficial," Triche said.

—John Curtis

## A VIPER'S VENOM AND STROKE

What does snake venom have to do with stroke? Depending on the results of a study in which Yale-New Haven Hospital (YNHH) is participating, possibly a lot.

Doctors at YNHH are administering ancrod, a drug derived from the venom of the Malayan pit viper, to eligible patients who enter the hospital with symptoms of acute ischemic stroke.

In such cases doctors may administer a clot-breaking agent—tissue plasminogen activator, or tPA—but it must be given no more than three hours after symptoms appear. Ancrod has an anticoagulant effect and can be administered up to six hours later. "If ancrod is safe and effective," said Joseph Schindler, M.D., assistant professor of neurology and neurosurgery and clinical director of the Stroke Center at YNHH, "it will double the time frame during which stroke patients can be treated."

YNHH is the only Connecticut hospital in the trial, which is expected to last one to two years.

-Charles Gershman



In this image of a developing embryonic rat spinal cord, the purple marks show growing commissural axons before they cross to opposing hemispheres. Yellow marks show a receptor called DSCAM, which is necessary to guide axons to their destinations.

# Biologists find molecule that guides axons

A receptor implicated in Down syndrome and fruit fly development also charts a path for nerve fibers.

Like a complex electronic device, the "wiring" of the nervous system has no tolerance for error. As an embryo develops, wirelike axons sprout from cells, elongating to form networks of neurons in the brain and spinal cord. Some axons cross the body from one side to the other, while others stay put. Neuroscientists have long wondered how axons migrate to form trillions of connections among neurons. How do they know where to travel and when to cross? Molecular signals are at the heart of the puzzle.

The first such signal, a guidance molecule called netrin-I, was identified about 20 years ago. Since then, researchers have found receptors on the axons that help them steer toward their targets. Now Yale researchers have found another molecule that guides axons on their intricate journey.

A team led by Elke Stein, PH.D., assistant professor of molecular, cellular and developmental biology and of cell biology, reported in June in the journal *Cell* that it had discovered that a gene linked to mental retardation in Down syndrome is also essential for axons in the spinal cord to cross from one side of the body to the other.

The protein made from that gene is a receptor called DSCAM, which stands for Down Syndrome Cell Adhesion Molecule. DSCAM is already familiar to researchers. Its genetic instructions are on chromosome 21, and people with Down syndrome have three copies of the chromosome rather than the normal two.

The Yale scientists found DSCAM through studies of nerve fibers called commissural axons that cross at the midline of the spinal cord, which divides the body into its right and left halves. Cells at the midline instruct axons by secreting attractive and repulsive molecules. Netrin-1, the guidance molecule identified 20 years ago, is one such molecule. It attracts and guides commissural axons over long distances to the midline of the central nervous system. Researchers had previously found that netrin-I signals DCC, a receptor that steers commissural axons to their targets. But they noted that some axons migrate even when DCC is absent. There had to be another receptor involved, and scientists searched for it for more than 10 years.

The missing receptor, Stein's lab found, was DSCAM, which was known to regulate nervous system development in fruit flies. But in humans it had only been known to help neural cells adhere to each other, and was thought to contribute to mental retardation in people with Down syndrome. In collaboration with scientists from Genentech. Stein and graduate student Alice Ly found that DSCAM at the tips of migrating axons is required in order to cross the midline in response to the attractant, netrin-I, which activates DSCAM and initiates directional growth of commissural axons in much the same way that a key turns the ignition and starts a car.

The researchers showed that commissural axons that lack DSCAM lose their "sense of direction," fail to grow and don't reach the midline. The Stein laboratory is now investigating whether DSCAM plays a key role in wiring other parts of the nervous system and its contributions to mental retardation in Down syndrome.

—Jenny Blair

## Bacteria disable immune cells by exploiting a genetic similarity

The bacteria that cause Legionnaires' disease and Q fever, both of which are linked to pneumonia, use a clever form of mimicry to survive inside host cells, according to a team of Yale scientists. Both bacteria use genes that have evolved in tandem with genes in their hosts and that disarm the immune system cells that are trying to kill them, the researchers reported in the journal *Science* in June.

"Because of their lifestyle, trying to identify how these organisms cause disease has been really difficult," said Craig R. Roy, PH.D., associate professor of microbial pathogenesis, referring to the fact that the bacteria live inside their host cells. Roy's team knew that some disease-causing bacteria inject proteins into human cells. What those proteins are and what they do, though, was unknown.

Previous research on the genomes of the bacteria, *Legionella* and *Coxiella*, had turned up many genes with areas called ANKS (ankyrin repeat homology domains). These genes bear a strong resemblance to important genes in eukaryotic cells, those cells with a nucleus that are found in humans and other advanced life forms. *Legionella* and *Coxiella* appear to have "hijacked" genes from their hosts in order to survive in the cell. In fact, some species of these bacteria cannot exist outside a eukaryotic cell.

Roy's lab showed that ANK proteins are secreted into macrophages immune system cells—and once inside, the proteins turn off mechanisms designed to destroy the bacteria. The macrophage ordinarily kills bacteria by exposing them to a destructive acidic environment, but the ANK proteins prevent the acidic compartment from being transported to the bacteria by mimicking a natural process that occurs during cell division.

Roy believes that more such survival tricks of gram-negative pathogens will be found, and that the diseases may one day be preventable with a vaccine that disables the ANK protein and allows macrophages to complete the job of destruction. "This study at least gives us a foothold," he said.

—J.B.



This image of a cell infected with *Legionella* shows host cell microtubules, which have been labeled using green fluorescent protein to show the bacterial compartments closely aligned on the microtubule network.

## et cetera ...

## METASTASIS AND A HYBRID CELL

Metastasis, the spread of cancer throughout the body, may be caused by a hybrid cell that takes on the most dangerous features of two different cell types, according to a review by Yale scientists in the May issue of *Nature Reviews Cancer*.

According to dermatology researchers John M. Pawelek, PH.D., and Ashok K. Chakraborty, PH.D., the natural hybrids take on both the white cell's migratory ability and the cancer cell's tendency to divide uncontrollably. The hybrid can travel to other organs and seed new cancer sites.

"This is a unifying explanation for metastasis," said Pawelek. "We expect this to open new areas for therapy based on the fusion process itself." So far, one case of fusion in humans and many cases in mice have been reported. Pawelek said more research is needed to be certain that fusion accounts for metastasis in humans. —1.B.

## A CLUE TO EVOLUTION

After 16 years of research, Yale scientists have produced the first images of a group II intron, a cellular molecule whose ancestor may have opened the door to the evolution of higher organisms.

Anna Marie Pyle, PH.D., professor of molecular biophysics and biochemistry, and her team crystallized the intron of a salttolerant bacterium that lives in the Sea of Japan. High-resolution images of the crystal, which appeared in *Science* in April, support the hypothesis that the intron shares a close evolutionary heritage with the human spliceosome, a complex molecular machine found in higher organisms that allows many proteins to be made from one stretch of the genome.

"The molecules showed us their structure, their active site and their activity," said Pyle. "We were even able to visualize their associated ions." Pyle hopes the introns may be developed into agents for gene therapy. —J.B.

## When the doctor is the patient

Robert Klitzman's resistance to his own depression led him to explore what happens when doctors get sick.

Robert L. Klitzman, M.D. '85, expected the grief that followed the death of his sister Karen, who died at the age of 38 in the World Trade Center on September II, 200I. But he did not expect that he would be unable to sleep and would suffer from persistent flu. Or that he would stop listening to music and take no pleasure in reading.

When friends told Klitzman that he was depressed, he rejected the idea. As a psychiatrist, of course, he knew that emotional depression often manifests itself in the body. "I'd read it in textbooks," he acknowledged. Eventually Klitzman did recognize that it was depression, not flu, that was making him feel that his body had "given way" beneath him. "Going through it myself made me realize how much I didn't know about what it was to be a patient," he said. That realization, he said, was "a defining moment."

Klitzman, a research scientist and associate professor of clinical psychiatry at the HIV Center for Clinical and Behavioral Studies at the New York State Psychiatric Institute and Columbia University, had already written five books. In fact, he'd gotten his start as a writer by reviewing books while a medical student at Yale—a starting point he recommends to students today. His role models included Richard A. Selzer, M.D., HS '61; Sherwin B. Nuland, M.D. '55, HS '61; and Howard M. Spiro, M.D.—Yale physicians who are also prominent authors. Klitzman had already contemplated writing a book about doctors as patients. Now, however, "It was no longer an academic question."

When Doctors Become Patients is the product of interviews with 70 physicians of all ages who were facing cancer, heart disease, Huntington disease, bipolar disorder, HIV and other illnesses. Klitzman analyzes such common themes as denial of illness, doctors choosing doctors, "self-doctoring," going public about one's disease, overworking, coping and the role of spiritual beliefs.

Klitzman found that the doctors viewed themselves either as patients or as doctors, "as if individuals had a zero-sum identity." In reality, Klitzman said, "They're not entirely doctors and they're not entirely patients." Klitzman called this "odd hybrid form" the "doctor-patient"—one doctor-patient with a foot infection brought his own bag of opiates to the hospital. And as patients, Klitzman's interviewees were often upset by the carelessness with which their doctors addressed their fears. A surgeon told one doctor-patient that a procedure carried a 5 percent chance of dying. The patient would rather have heard that he had a 95 percent chance of living.

Just as Klitzman resisted the notion of his own depression, his colleagues also denied that they were sick. They told him, "I feel like I have a magic white coat. Illness happens out there—not to me." Klitzman noted that magical thinking is part of our everyday lives: "When we blow out the birthday candles, we all make a wish." But doctors deny their irrationality, contending, "We do not engage in magical thinking. We're trained scientists."

Perhaps because doctors see themselves as scientists, they are reluctant to discuss religion or spirituality with their patients, as Klitzman's research suggests. Yet "when patients are lying in bed, that's what they're thinking about," he said. He advocates adding at least a lecture on the topic during medical school.

A reviewer wrote in the *New England Journal of Medicine* that Klitzman's book "goes to the very heart of the question of what a physician is." In addition, *When Doctors Become Patients* serves as a lasting memorial to Karen Klitzman.

—Cathy Shufro



Robert Klitzman's depression after the loss of his sister on 9/11 led him to explore what he calls the "odd hybrid" of doctors who become patients.

*Bookshelf* focuses on books and authors at the School of Medicine. Send suggestions to Cathy Shufro at cathy.shufro@yale.edu.

## **BOOK NOTES**











Polarities of Experiences: Relatedness and Self-Definition in Personality Development, Psychopathology and the Therapeutic Process

by Sidney J. Blatt, PH.D., professor of psychiatry and psychology (American Psychological Association) The author proposes that psychological development is a lifelong personal negotiation between two dimensions: relatedness, which he terms the anaclitic dimension; and selfdefinition, or the introjective dimension. He contends that emphasis on one developmental line at the expense of the other, however, can lead to a variety of mental disorders. Within this framework, Blatt sees mental disorders as compensatory exaggerations of the normal polarities of relatedness and self-definition rather than clusters of present or absent symptoms. Blatt discusses research indicating that anaclitic and introjective persons respond differently to psychotherapy. He then argues that this conceptualization of personality development has clear implications for refining approaches to therapy.

## The Kazdin Method for Parenting the Defiant Child: With No Pills, No Therapy, No Contest of Wills

by Alan E. Kazdin, PH.D., the John M. Musser Professor of Psychology, and director of the Yale Parenting Center and Child Conduct Clinic (Houghton Mifflin) In this book and DVD, Kazdin lays out his science-based program for using praise and rewards to alter children's behavior. Kazdin provides a step-by-step method that relies on positive reinforcement and a reward system for dealing with behavior problems. The book describes approaches for children of different ages; discusses ways to involve siblings; and provides scenarios for coping with such commonplace difficulties as tantrums, dawdling, resisting homework and delaying bedtime.

## Saving Sickly Children: The Tuberculosis Preventorium in American Life, 1909-1970

by Cynthia A. Connolly, R.N., PH.D., assistant professor of nursing and the history of medicine (Rutgers University Press) The author provides an analysis of public health and family welfare viewed through the institution of the tuberculosis preventorium of the early 20th century. This facility was intended to prevent TB in indigent children at risk for developing the disease or who came from families labeled as irresponsible. Connolly further explains how the child-saving themes embedded in the preventorium movement continue to shape contemporary pediatric health care delivery and family policy in the United States.

#### Attachment and Sexuality

edited by Sidney J. Blatt, PH.D., professor of psychiatry and psychology; Diana Diamond, PH.D., and Joseph D. Lichtenberg, M.D. (The Analytic Press) Each paper featured in this text forms a separate narrative strand that clarifies different configurations of the relationship between attachment and sexuality. The unifying thread is the notion that the attachment system, and particularly the degree of felt security—or lack thereof—in relation to early attachment figures, provides a paradigm for relationships that forms a scaffold for the developmental unfolding of sexuality in all its manifestations. These manifestations include infantile and adult, masturbatory and mutual, and normative and perverse sexuality.

## Apoptosis and Cancer: Methods and Protocols

edited by Gil Mor, м.D., PH.D., associate professor of obstetrics, gynecology and reproductive sciences, and Ayesha B. Alvero, м.D., associate research scientist in obstetrics, gynecology and reproductive sciences (Humana Press) This book, a collaboration between academics and industrybased scientists, describes the performance of contemporary techniques for studying the biology of apoptosis and its role in cancer. The protocols described within will aid both academic laboratory workers interested in further characterizing the mechanism of apoptosis and industry-based researchers concerned with identifying new target molecules or screening for new compounds with potential clinical use The text covers the newest methods as well as basic conventional techniques.

## The Future of Medicine: Megatrends in Health Care That Will Improve Your Quality of Life

by Stephen C. Schimpff, м.р. '67, нs '69 (Thomas Nelson Publisher) This book describes and evaluates health care innovations in areas including genomics, imaging, pharmaceuticals, the operating room, and alternative and complementary medicine. The author combines scientific fact with personal stories and experiences to describe the tools, techniques and treatments that are making a difference in health care. These innovations include vaccines that prevent cancer and chronic disease; surgery simulation and robots in the operating room; and smaller, more powerful medical devices that help a patient's heart beat, relieve depression and replace failing organs.

## Hip and Knee Surgery: A Patient's Guide to Hip Replacement, Hip Resurfacing, Knee Replacement and Knee Arthroscopy

by Robert E. Kennon, M.D., HS '04 (Lulu Publisher) This book contains information for patients considering treatment for hip or knee arthritis and related conditions. The author explains what to expect before, during and after hospitalization; describes postoperative exercises; and offers recommendations for rehabilitation. Illustrated sections discuss hip and knee surgeries; nonoperative treatment options; surgical approaches, the latest minimally invasive surgery techniques; implant materials and designs; and potential complications of joint surgery.

## **Books & Ideas** BOOK NOTES



## Neuroinformatics (Methods in Molecular Biology)

edited by Chiquito J. Crasto, PH.D., м.s., associate research scientist in neurobiology (Humana Press) This book describes advances in data sharing and the use of computational models in neuroscience. It provides expert summaries of specific computational models and simulations as well as approaches to data mining. The authors also discuss informatics representation and approaches to the structural complexity of the brain using a variety of both traditional and noninvasive imaging methods. The book's final section considers the value of using neuroinformatics to understand such complex mental disorders as dementia, schizophrenia and Alzheimer disease.

## Comfortably Numb: How Psychiatry Is Medicating a Nation

by Charles M. Barber, M.F.A., lecturer in psychiatry (Pantheon) The author argues that without an industry to promote them, nonpharmaceutical approaches to reducing emotional distress are overlooked by a nation that sees drugs as instant cure-alls. He argues that Americans are under increasing pressure to selfmedicate. In analyzing these influences, Barber cites directto-consumer advertising; the promise of the quick fix; and the blurring of the distinction between mental illness-for which medication might be appropriate—and everyday emotional problems. Barber then offers therapeutic alternatives to prescription antidepressants.

## Seldin and Giebisch's The Kidney: Physiology and Pathophysiology, 4th ed.

YOU TAKE THAT PILL

edited by Robert J. Alpern, м.р., dean of the School of Medicine and Ensign Professor of Medicine (nephrology), and the late Steven С. Hebert, м.D., former с.N.H. Long Professor of Cellular and Molecular Physiology and professor of medicine (nephrology) (Academic Press) This edition has more than 40 new chapters and 1,000 illustrations, providing comprehensive coverage of renal physiology and pathophysiology. The topics move from the molecular biology of the kidney and its cell physiology to clinical issues surrounding renal function and dysfunction.

## Before You Take That Pill: Why the Drug Industry May Be Bad for Your Health

by J. Douglas Bremner, м.D., former associate professor of diagnostic radiology and psychiatry (Avery of PenguinGroup) The author offers an inside look at the pharmaceutical industry as well as a scientifically backed assessment of the risks of more than 300 prescribed medications, vitamins and supplements. This book distinguishes between the pharmaceuticals that are essential to the health of consumers and those whose benefits may not outweigh their potential side effects.

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

## IN CIRCULATION

# A Yale librarian upgrades Internet access for physicians in Uganda

When librarian Mark Gentry, M.A., M.L.S., set out to expand Internet access at a hospital in Uganda, he experienced déjà vu. "The speed of the Internet took me back 15 years to the beginning of the Web, when we had dial-up modems," said Gentry, the clinical support librarian at the Cushing/ Whitney Medical Library.

Gentry learned about the idiosyncrasies of satellitebased Internet service in Uganda when he joined the Yale-Makerere collaboration, a partnership that includes the School of Medicine, Makerere University and Mulago Hospital in Kampala. Since 2006 Yale attendings and residents have traveled to Kampala for rotations at Mulago Hospital, and Ugandan residents are now coming to Yale for clinical training.

While visiting Mulago Hospital in the spring of 2008, Gentry streamlined Internet use for physicians by setting up a home page that links directly to such often-used functions as e-mail and online journals. "*Click*: you go right to it. Because every time you get an intermediate page, you have to wait from 10 to 30 seconds," said Gentry. Meanwhile a Yale resident compiled CDs that allow Ugandan colleagues to bypass the Internet—the disks contain copyright-free information on diseases such as HIV, tuberculosis and malaria.

Gentry next began building up the library for the Department of Medicine at Mulago Hospital, where the medical textbooks were 20 years old. Gentry collected 50 essential texts that were hand-delivered to Kampala. Up-to-date books are a godsend, said Ugandan resident Fred Okuku, M.D. During a five-month rotation at Yale last spring, Okuku discovered journal articles about research done in Uganda that he'd been unable to access at home.

While in Uganda, Gentry promoted a free Internet service called HINARI; sponsored by the World Health Organization for health care workers in developing countries, it provides links to nearly 4,000 journals.

Gentry said the Makerere collaboration has been a natural extension of his work on Cedar Street. "Part of my job as a clinical support librarian is to do what I can to support our people wherever they are."

—*Cathy* Shufro

*In Circulation* focuses on activities at the Cushing/Whitney Medical Library. Send suggestions to Cathy Shufro at cathy.shufro@yale.edu.

## ON CAMPUS



PAUL OFFIT Lawsuits could bankrupt vaccine program

A program that encourages childhood vaccinations could collapse under unproven allegations that the shots cause disease, an expert warned at grand rounds for the Department of Pediatrics in May.

Paul Offit, M.D., chief of infectious diseases at Children's Hospital of Philadelphia, said that the fallout from a 2008 court decision would discourage vaccine makers from continuing production. Since 1955, when a bad batch of polio vaccine killed 10 people, testing and regulation of vaccines have improved. But subsequent court rulings that vaccine makers could be held liable without being negligent led to "a flood of lawsuits" in the 1970s.

In 1986 Congress created the National Vaccine Injury Compensation Program to protect vaccine makers while compensating those harmed by faulty vaccines. But Offit said that the program took "a sad turn" in 2008 when a special "vaccine court" composed of epidemiologists and clinicians ruled that claims can be granted even if it's only possible—with no epidemiological evidence—that vaccines are responsible.

About 5,000 children who claim to be harmed as a result of vaccination await a decision that could bankrupt the vaccine program. If the decision allows for monetary compensation, "it could eliminate the program," Offit said.

—John Dillon



JOSEPH BERTINO A gene to protect bone marrow from chemotherapy

In a new approach to cancer treatment, researchers are studying a form of gene therapy that may make bone marrow more resistant to chemotherapy, allowing for higher doses and better outcomes.

"We are turning the tables," said Joseph R. Bertino, M.D., interim director and chief scientific officer of the Cancer Institute of New Jersey, at Yale Cancer Center grand rounds in May. "This therapy will allow for safer use of drugs and an increase in dosage. If we do this we can protect patients from a wide variety of chemotherapy drugs."

Bertino, who was director of the Yale Comprehensive Cancer Center from 1973 to 1975, said this approach calls for introducing a drug-resistant gene into hematopoietic progenitor cells. That could limit the drugs' toxicity and preserve the marrow's ability to produce infectionfighting white blood cells. Oncologists would then be able to prescribe higher doses of chemotherapy, potentially leading to improved outcomes.

Bertino said two clinical trials—one for lymphoma and another for pancreatic and breast cancer—are in the planning stages.

—John Curtis



CHARLES ZEANAH Children, foster care and orphanages

When Nicolae Ceauşescu took power in Romania in 1965, he believed that his country needed a larger work force. He decreed, said Charles H. Zeanah Jr., M.D., Sellars-Polchow Professor of Psychiatry at Tulane University, that all women must bear five children.

The economy didn't improve, Zeanah told an audience at pediatric grand rounds in May, but more children entered the country's orphanages. "Children with a history of institutional rearing have a high risk of psychological and social problems," Zeanah said. In 2000, Zeanah and Charles Nelson, PH.D., of Harvard and Nathan Fox, PH.D., of the University of Maryland began a four-year study of 136 children who ranged in age from 7 to 33 months, and found that their development lagged in most areas. Half of the 136 children were then placed in foster care, previously unavailable in Bucharest, and half remained in institutions

Foster care enhanced development in most areas, but complete recovery was rare. For cognitive development and attachment, recovery seemed to have more to do with the timing of interventions than their duration. Children who entered foster care before their second birthday, Zeanah said, were more likely to recover from the severe deprivations of Romanian orphanages.

—J.C.



SARAH JANICKI Bolero, dementia and the creative process

In 1930, when Maurice Ravel composed *Bolero*, his best-known work, he may have been in the throes of frontotemporal dementia (FTD), a neurodegenerative disease that usually affects people in their late 50s. Ravel's meticulous handwriting had become irregular, he had lost his bags and tickets on a concert tour and, while conducting one of his works, he had uncharacteristically skipped from the opening movement to the coda.

In a talk at neuroscience grand rounds in May, Sarah C. Janicki, M.D., M.P.H., HS '08, said Ravel's case is not unusual—FTD has been linked to strong bouts of creativity. "Over time a series of patients were coming to light, patients with FTD developing creative skills," she said.

Although the reasons for this connection are not clear. the brain's left temporal lobe appears to be involved. And the disorder appears to release artistic inhibitions—artists move from representational to more abstract forms of expression. But as the disease progresses, that process reverses itself. "As [the patients'] language skills declined, their art became fairly representational instead of a creative manipulation to generate new thought," Janicki said.

—J.C.

# A theory abandoned but still compelling



In 1977 readers were enthralled by *The Dragons of Eden*, a book by the astronomer Carl Sagan that explored the evolution of the human brain. *Dragons* won the 1978 Pulitzer Prize for general nonfiction and helped to launch Sagan's celebrity as a spokesman for science in the 1980s.

The real star of the book, however, was a theory of human neural organization that took root some 30 years earlier in writings by Paul D. MacLean, M.D. '40. MacLean, who died last December at age 94, was a highly original—some say eccentric—thinker whose model of the triune brain, though now discredited, has had a lasting cultural impact.

"Paul never traveled with the herd," said Thomas R. Insel, M.D., director of the National Institute of Mental Health, who worked alongside MacLean for 10 years at the Laboratory of Brain Evolution and Behavior in Poolesville, Md. Insel remembers his colleague as irreverent and uninhibited. MacLean once roamed through a room, Insel recalled, feeling the scalps of visiting scientists to ascertain the presence or absence of a skull protuberance he had deemed an important factor in the evolution of human intelligence.

The beginnings of MacLean's theory appeared in a 1949 paper just as he joined the faculty of the School of Medicine as an assistant professor of physiology with a joint appointment in psychiatry. After conducting electroencephalographic recordings in patients

**OPPOSITE** Paul MacLean believed that the neocortex was a relatively late development in the mammalian lineage, but there is now a consensus that homologues of this structure exist in simple fish, and even in insects.

**BELOW** In MacLean's triune brain (top), the neocortex has only partial dominion over the emotional responses of the more primitive limbic system (bottom). "This situation," he wrote, "provides a clue to understanding the difference between what we 'feel' and what we 'know.' "

In Paul MacLean's triune brain, primitive emotions overruled conscious thoughts.

with psychosomatic illnesses and epilepsy at Massachusetts General Hospital, MacLean had become convinced that the emotional components of these disorders were seated in deep brain structures that he called the visceral brain (and renamed the limbic system in 1952), which included the hippocampus, amygdala and cingulate gyrus.

Since all mammals possess variants of these structures, MacLean concluded that they are phylogenetically ancient and that the emotional responses they produce are only weakly regulated by such newer, human structures as the neocortex. "Our affective behavior continues to be dominated by a relatively crude and primitive system," he wrote. Twenty years later, MacLean rounded out his picture of the triune (three in one) brain by adding what he termed the R-complex (for "reptilian")-structures in the brain's core and brain stem that govern basic survival functionsto the neocortical and limbic systems he had defined previously.

The theory saw its fullest expression in MacLean's 1990 magnum opus, *The Triune Brain in Evolution*, which was based on wide-ranging anatomical studies of brains in animals as diverse as alligators and monkeys. In its casting of a cognitively sophisticated neocortex unable to fully restrain the primal emotional responses of the limbic system, MacLean's model was a neuroanatomical cousin to Freud's tripartite view of the mind, with its warring superego, ego and id. The theory's conceptual beauty and intuitive appeal lent it enormous staying power; it is still covered in many textbooks and course lectures in biological psychology.

But according to Terrence Deacon, PH.D., an expert on the evolution of human cognition at the University of California, Berkeley, subsequent research has revealed that MacLean's basic premise—his "thats on top of hats' view" that brain systems were added by accretion over the course of evolution—was mistaken. "Adding on is almost certainly not the way the brain has evolved," said Deacon. "Instead, the same structures have become modified in different ways in different lineages."

Nonetheless, Deacon said, the force of MacLean's personality gave his ideas a special resonance. "His death represents the passing of an era, because he was really the model of the move towards understanding the brain in evolutionary terms," said Deacon. "A lot of our contemporary advances ride on top of his work, even though in hindsight it was misleading. That happens a lot in the sciences, and we don't often give credit to the false starts that really push us along the way."

Peter Farley is the managing editor of the bimonthly newsletter *Medicine@Yale*.





S PRINGER (

# Mapping the future of medicine

Medical schools are relatively new to the game of large-scale clinical research; however, they are sponsoring studies to test new therapies with increasing frequency. With its largest grant ever, Yale is plunging headlong into human trials and assembling resources to help clinical scientists focus on ideas—and leave the red tape to others.

By Jill Max Illustrations by Jeffrey Fisher

About six years ago, Thomas O. Carpenter, M.D., professor of pediatrics (endocrinology), wondered why he was seeing an increasing number of infants with nutritional rickets. He examined some of the infants' medical records and found that although rickets is presumed to be caused by a vitamin D deficiency, fewer than half of the infants had low levels of the vitamin. Many appeared to be calcium-deficient as a result of being weaned from breast milk to juices and soda. With funding from the Gerber Foundation, Carpenter began a largescale three-year study in 2005 that involved 800 babies from inner-city New Haven health clinics and the Primary Care Center at Yale-New Haven Hospital. By screening infants at their well-child visits, Carpenter aims to define the prevalence of early rickets in New Haven, determine how much of it is due to vitamin D deficiency versus calcium deficiency and look for changes in biomarkers that can be spotted before bone disease is evident. The study is already showing results: Carpenter found that elevated levels of parathyroid hormone, which is used to diagnose rickets, can also be used to predict who may eventually develop the disease, so that doctors can begin to treat children to ward off the disorder before symptoms are present. He is also searching for other genetic factors that may represent an increased susceptibility to the disease.

Such clinical research is not a novelty at Yale. But these efforts are now being organized and supported on a much broader scale under the umbrella of the Yale Center for Clinical Investigation (YCCI). The center was launched in early 2006 to coordinate research programs among Yale's health science schools and the surrounding community. It is also intended to support faculty research efforts while at the same time ensuring that patients are protected and receive high-quality care. YCCI's mission dovetails with the National Institutes of Health (NIH) Roadmap for Medical Research, which was implemented in 2002 near the end of a five-year period in which Congress doubled the NIH budget. The Roadmap helped garner public support for NIH-supported research and provided a framework for bringing medical knowledge from the laboratory to the patient. In October 2006 the School of Medicine was one of 12 institutions around the country to receive a Clinical and Translational Science Award (CTSA); at \$57.3 million the five-year award is by far the largest NIH research grant in the school's history (see related story, page 24). When fully implemented in 2012, the CTSA initiative is expected to provide \$500 million annually to 60 academic health centers working in concert. NIH Director Elias A. Zerhouni, M.D., said that CTSA will "transform how clinical and translational research is conducted."

Yale has traditionally been strong in basic science and has been successful in identifying drug targets and such other methods of combating disease as tissue engineering or large-scale public health interventions aimed at disease prevention. But until recently a center for translating basic science discoveries into clinical practice had never taken hold.





"We just never had the necessary resources to set up the infrastructure we're able to have now," said Robert S. Sherwin, M.D., the C.N.H. Long Professor of Medicine and director of YCCI. The center is a one-stop shop that provides the support investigators need to translate their work from the bench to the bedside. YCCI is accomplishing this task through a mix of such initiatives as helping investigators implement their own clinical trials, nurturing a new generation of physician-scientists and clinical investigators, and supporting collaborations with local organizations to promote public health.

## Expertise and an online database

No one is more cognizant of the difficulties of negotiating the clinical trial maze than Christopher K. Breuer, м.D., assistant professor of surgery (pediatrics) and pediatrics. Breuer and Toshiharu Shinoka, M.D., PH.D., director of pediatric cardiac surgery at Yale-New Haven Children's Hospital, have developed a technique for engineering blood vessels to connect the inferior vena cava to the pulmonary artery. Known as Fontan surgery, the technique corrects a single-ventricle anomaly-a heart defect in which a patient has a weakened or single ventricle instead of the usual two. Breuer starts by seeding mononuclear cells isolated from a patient's bone marrow onto a tube made from a synthetic material similar to that used to make absorbable sutures. The cells attach to the synthetic scaffold and form new tissue; as the tissue forms the scaffold degrades, leaving a purely biological vessel. Blood vessels grown from a patient's own cells are less prone to infection than the artificial vessels that have traditionally been used in this surgery. The natural vessels are biocompatible and—perhaps most important for pediatric applications-they grow with the child, precluding the need for further surgery.

When Breuer began experimenting with tissue engineering in the early 1990s, he broke down a blood vessel into its cellular components in order to grow a new one. But this approach required additional surgery to procure the blood vessel and up to four months to grow the cells in culture and allow them to attach to the scaffold. He can now perform a bone marrow aspiration, isolate a special fraction of stem cells, seed them onto the scaffold, and implant the engineered vessel into the patient in a single procedure that lasts about six hours.

Breuer is about to begin a Phase I study to test the procedure's safety. He plans to try it in six patients over the next three years, staggering enrollment so that each patient can benefit from the one before. Although Shinoka has successfully performed the procedure on 23 patients in Japan, the regulatory requirements in the United States are more demanding. "One of the biggest challenges is the regulatory requirements," said Breuer. "YCCI has offered a lot of help and expertise."

Breuer is now well versed in running a clinical trial. For other researchers who lack the experience to put together an effective study, however, YCCI offers expertise in trial design, regulatory issues, protocol development, biostatistics and epidemiology, budget and recruitment. The center also offers research nursing support, data management, laboratory services, and both inpatient and outpatient facilities to conduct trials. A new online database at yaletrials.org provides detailed information about all clinical trials at Yale, so that patients interested in a specific disease can search for a trial related to it. YCCI also integrates the efforts of Yale's institutional review boards (IRBS) into the process. These panels, comprising clinicians, faculty, students and members of the community, must approve every research project that involves humans, even a paper-and-pencil survey. The medical school's two IRBS meet weekly to discuss the several hundred new proposals and more than 1,500 requests to renew ongoing studies that come their way each year.

In the world of clinical trials, some studies, such as Breuer's work, attempt to treat an existing condition, while others try to answer basic questions about the course of diseases or ways to prevent them. Carpenter's work does both. His nutritional rickets study is helping doctors treat the disease before it can do damage, but he also conducts research on X-linked hypophosphatemia (XLH), the most common form of inherited rickets in the United States. XLH can lead to deformed bones and debilitating arthritis. Carpenter established the Yale Center for XLH, an NIH-sponsored Center of Research Translation (CORT), one of eight in the country that serve as a model of translational research in academic medical centers. Some of the center's projects interface with CTSA, such as clinical trials studying the effect of a medication specifically aiming to suppress the hyperparathyroidism that occurs with XLH. Carpenter is also conducting an observational study to characterize the disease in patients past childhood and he is trying to determine the chemical and skeletal features of XLH in older patients. "Understanding the disease has opened up a whole new mechanism of how minerals are regulated in the body," said Carpenter. That area of research includes new therapies applicable not only to XLH but also to other disorders in which the body's handling of phosphate has gone amiss, such as chronic renal failure.

## Focus on training

Perhaps the single most important aspect of the CTSA—and by extension YCCI—is training young researchers to conduct clinical studies. "In the past, most physicians learned on the job, sort of like an apprenticeship," said YCCI Director Sherwin. "But the kind of sophistication that's now required to do clinical research and the kind of mentorship background you need to do research today are much more involved than a simple apprenticeship." The Investigative Medicine Program, which serves as the administrative home for the educational component of YCCI, was developed at the School of Medicine in 1999 to award the PH.D. to physicians training in clinical research. Under the CTSA it has expanded to offer courses to medical, nursing and public health students. In addition, 20 junior faculty members and senior fellows who are committed to careers in clinical or translational research have received 18-month grants for salary and research support through YCCI'S Scholar program. Drawn from the three Yale health schools, the grant recipients are pursuing research projects under the guidance of individualized mentorship committees. "We're investing in them like we invest in training a PH.D., which involves having people from diverse backgrounds looking at their work from different perspectives," said Sherwin.

The work of Mary E. Tinetti, M.D., director of the Yale Program on Aging, serves as an example of the kind of research the program strives to advance. While training in geriatrics more than 20 years ago, she recognized that a slew of health conditions—such as incontinence, delirium and injuries caused by falls—were neglected by the health care system yet have a major impact on quality of life and functioning.

Tinetti identified characteristics linked to an increased risk of falls and conducted a study to determine whether interventions targeting these risk factors would prevent falls and injuries. Until that time, most clinical trials focused on a single intervention; however, Tinetti and her colleagues developed a new multifactorial trial design in which patients receive a combination of interventions tailored to their particular risk factors. For example, the intervention for patients who experience a drop in blood pressure when moving from lying or sitting to standing consists of increased hydration, specific exercises to do before getting up, and a reduction in medications likely to affect blood pressure changes on standing. In the mid-1990s, Tinetti and colleagues followed a group of 320 patients and controls for two years and found that patients who received such interventions reduced their risk of falling by about 30 percent. The next step was to see whether this reduction in falls would also occur when real-world clinicians, rather than investigators, were responsible for carrying out the interventions. For the past eight years, she and colleagues have been conducting a study in the greater Hartford area to train health care practitioners to incorporate components of fall prevention into their practice. The real-world trial was funded by the West Hartford-based Donaghue Medical Research Foundation, said Tinetti, the Gladys Phillips Crofoot Professor of Medicine (geriatrics) and professor of epidemiology (chronic diseases) and investigative medicine.

In an article published in the *New England Journal of Medicine* in July, Tinetti and her colleagues reported that the fall prevention programs resulted in an 11 percent reduction in falls compared to the control group, and 10 percent fewer



fall-related hip fractures and head injuries. The reduced injury rate translated into some 1,800 fewer emergency room visits over a two-year period and health care savings estimated at \$21 million.

"The research is done," Tinetti said. "The next step is to put it into practice, by making physicians, nurses and physical therapists everywhere more conscious of fall risks among their patients and what can be done to prevent falls."

## From bedside to community

Tinetti's application of her research to clinical practice ties in with another major goal of YCCI-forging research relationships with the local community to improve public health. The Community Alliance for Research & Engagement (CARE), supported in part by YCCI, fosters community-based research and translates these findings for the benefit of New Havenarea residents. "The specific goal of CARE is to go from bedside to the community," said Jeannette R. Ickovics, PH.D., deputy director of CARE and professor of epidemiology (chronic diseases) and public health and of psychology. The first major initiative of CARE was to sponsor a consensus conference in 2007 with more than 70 leaders from New Haven and Yale. CARE has awarded five grants totaling \$110,000 for pilot research projects—including childhood obesity and violence prevention. CARE also publishes a quarterly newsletter highlighting community-based health information about how research is conducted, and "CAREtips"—easily accessible recommendations based on faculty findings. "There are so many important discoveries at Yale that land in the major medical journals but never benefit our neighbors right here in New Haven," said Ickovics. "We're looking to take the work of excellent Yale scientists and really give the science away. Our goal is to improve health in New Haven."

Even when investigators reach the point where they are conducting trials with study participants, they often continue working in the lab. For example, as Breuer prepares for the clinical trial to implant tissue-engineered blood vessels in children, he is experimenting with mice to discover the mechanism that forms the new tissue. Working with colleagues in biomedical engineering, he has isolated the protein responsible for maintaining the vessel's lumen (inner cavity), a finding that may eliminate the need for bone marrow aspiration in the next generation of tissue-engineered grafts for humans. Every investigation has the potential to advance the prevention and treatment of disease. The structure provided by YCCI is helping clinical investigators from different disciplines to pool their efforts, learn from one another, and take advantage of their collective expertise. "That's how progress is," said Breuer. "Everyone adds their own tiny step, and in the end you've gone a long way." YM Jill Max is a freelance writer in Trumbull, Conn.

## Patient-volunteers help find cures on medicine's front lines

Every day at the medical school, patients and control subjects undergo imaging tests, hop on treadmills and swallow medications in the name of advancing knowledge. Some do it to contribute to society and research, some are lured by the payments offered, and some hope to help find a cure and ease a loved one's suffering or that of future patients.

That last consideration is what motivated Kriste Gill to enroll her newborn twins in a study on early indications of autism. A speech pathologist with a professional interest in the study, Gill also has a 22-year-old brother with autism. "I get to give back to research for a disability that's very near to us," she said. For the past two years, Gill's babies have undergone developmental assessments. The exams are not physically invasive, and Gill has learned much about the twins' development. And if any signs of autism should surface, she's confident the research team would flag them and recommend next steps for further evaluation.

A different concern brought Jan Davey into the Kronos Early Estrogen Prevention Study (KEEPS), a study to determine whether early menopausal hormone therapy prevents or delays heart disease. Davey, 61, has a 27-year-old daughter and sees the need for research that may benefit future generations of women. Participants commit to taking hormones or a placebo as well as undergoing periodic lipid profile tests and vaginal ultrasounds for four years. As a clinical research nurse in Cardiovascular Medicine and at Yale **Cancer Center. Davey understands** the demands and rewards of clinical trials but had never before participated in one. "It's a very

important part of what we do in health care," she said.

Some participate in hopes of obtaining treatment for a disease from which they or a loved one suffer. Terri Rathbun's 16-year-old daughter, Molly, has childhood absence epilepsy—short seizures in which the person appears to blank out. Her condition has not responded to medication. To assess Molly's brain function, she underwent MRI scans while performing cognitive tasks. Her mother is hoping the study will benefit other children; in the meantime, it has helped her recognize how well Molly has coped while living with seizures. According to her mother, Molly hopes that participating in this study "will open up opportunities for other kids so that seizures don't define their lives."

For cancer patients Kathy Willie and Geralyn Spollett, a trial for treatment of HER2-positive breast cancer was a chance to receive chemotherapy that might have reduced or eliminated their tumors before surgery. Willie initially didn't want to undergo chemotherapy, but her decision paid off; during a partial mastectomy her surgeon found no trace of the tumor. Although the treatment didn't change the course of Spollett's treatment—she ended up needing a mastectomy as well as chemotherapy and radiation—she believes it was a positive experience. "I felt lucky to be in the trial because of the consultation and support," said Spollett, who will have follow-up blood work in September.

Social responsibility also motivates patients. Jean O'Brien, 65, and her daughter Stephanie, 32, have X-linked hypophosphatemia (XLH), the most common form of inherited rickets in the United States. They joined in a study designed to define the features of the disease in adults. "It's a few days out of my life that could change someone else's life," said Stephanie, referring to two days of bone scans, X-rays and ultrasounds at Yale-New Haven Hospital. "My generation is writing the textbook on this disease," said Jean, who hopes the study will benefit her grandson and future grandchildren.

**Clinical trials require not only** sick but also healthy subjects. One 76-year-old woman participates in the Alzheimer Disease **Neuro-imaging Initiative even** though she is healthy. As part of the three-year study she gets MRI and PET scans every six months so that researchers can compare the mental changes that occur in normal aging, mild cognitive impairment and Alzheimer disease. She hopes that the trial will lead to a cure that will help family members and friends who have the disease.

Because he has a family history of heart disease, 27-year-old Niall McComiskey agreed to a stress test on a treadmill, administration of adenosine to increase his heart rate and a PET scan. McComiskey also said that the \$200 he was paid didn't hurt, and for some people, financial compensation is reward enough. For others, it's a combination of factors that spur them to participate. One 40-year-old veteran, a recovering alcoholic and addict who suffers from post-traumatic stress disorder, had two reasons for undergoing PET scans as part of a study to measure the levels of neurotransmitters in brain tissue. He wanted to understand the chemical imbalances in his brain; he was also paid about \$700 to participate in the study. Thomas O. Carpenter, M.D., professor of pediatrics (endocrinology), offers a \$25 grocery card to participants in his nutritional study, which he said is an effective incentive.

Such are the rewards of clinical studies that patients often repeat the experience. Jan Davey, who is participating in the KEEPS study, has also signed up for three ancillary studies. "We wouldn't be where we are in health care if we hadn't been doing clinical research all these years," she said.

—Jill Max



# Is the straight road too narrow?

Congressional demands for cures and accountability—combined with a flat NIH budget—have increased pressure on scientists to produce findings with direct application to disease. Nonetheless, there's great value in cultivating the art of finding what you're not looking for.

## By Pat McCaffrey Illustrations by Jeffrey Fisher

The stereotype of the basic researcher—driven by curiosity, absorbed in the arcane, immune to practical considerations is only half right. The need to unravel a puzzle, to uncover the beauty and order in biological systems, or simply to follow one's nose, asking and answering questions, is both the initial impulse and sustaining force for many a career in basic research. Yet these scientists are not indifferent to the practical applications of their work. They are just not starting out with that particular end in mind.

Take structural biologist Thomas A. Steitz, PH.D., Sterling Professor of Molecular Biophysics and Biochemistry. Beginning with his doctoral work more than 40 years ago, Steitz has fixated on one question: How do proteins and nucleic acids carry out their diverse jobs in cells? For Steitz, that question is best answered by looking at the macromolecule's shape; he is a leader in charting the topology of proteins and nucleic acids at the atomic level.

Steitz and his team were the first to see one particularly important biological machine eight years ago when they solved the molecular structure of the large subunit of the ribosome, the protein-making factory inside all cells. That discovery, coming after five years of effort, a few dead ends and a little luck, has turned out to have practical benefits. Many antibiotics work by interfering with the functions of bacterial ribosomes. Steitz's lab was soon busy looking at the ways in which antibiotics recognize and bind to the bacterial large ribosomal subunit and shut it down. Hard data about molecular interactions are like gold to scientists looking to design new antibiotics—as they are now doing in a company that Steitz helped found.

"When I started solving protein structures as a graduate student, I had no idea, nor did anyone else, that this would ever be of any practical benefit whatsoever," Steitz says. "We just wanted to know, how does this machine work? ... Our work has led to translational research, but it wasn't the goal. I never thought that I would end up building a pharmaceutical company around the study of the structure of the ribosome."

It is a cliché of scientific exploration that even the most esoteric work can yield unexpected benefits. From synthetic insulin, the first biotech drug (a result of studies of bacteria) to the latest frontier of RNA-based therapies (started by work in worms), Steitz posits that every single medical discovery of major importance made over the last 30 years has its roots in basic research. "If you trace back through the history of molecular biology, which made biotechnology possible, you find that it all came from basic research," he says.

So why are Steitz and his colleagues so worried about the future of creative, idea-driven biological research? He

and researchers like him are proof that investments in ideas and individuals can and do pay off handsomely for human health. Nonetheless, these days a combination of painfully lean budgets at the government agencies that fund basic research, coupled with a current fashion for applied, diseaseoriented studies (see related story, page 18) have basic researchers asking where their next grant—not to mention the next generation of like-minded scientists—will come from.

## **Risk management**

"What really gets me excited is a brand new project," says fruit fly researcher Lynn Cooley, PH.D., professor of genetics and cell biology.

Cooley is fascinated by egg production in female fruit flies, a process that reveals the ways in which the flies' cells communicate and cooperate in order to form nurturing environments for developing eggs. Although her work has some application to the growth and spread of human cancers, Cooley's research is guided by her team's latest experiments. "When a set of experiments opens doors to unexplored areas of biology, that's the fun part," she says. "That's what makes it exciting to go into the lab every day."

The harder part is finding the funding to support her quest. The bedrock of basic biomedical research in the United States has long been the investigator-initiated research grant from the National Institutes of Health (NIH), known as an ROI. These grants cover salaries and laboratory expenses for an investigator and a few junior scientists to work on projects of their own design. ROI grant applications are 25-page proposals that are reviewed by committees of researcher's peers, who judge their merits and recommend the best for funding. The system has worked well for years to cull out the most promising new research for NIH support.

And that research has been well supported. With a total NIH budget of \$29.5 billion in 2008, the United States leads the world in its funding of basic research in the biological sciences. Half of all federal funds devoted to scientific research are funneled to biomedical research through the NIH. That money pays for 80 percent of biomedical research done in the United States. Support for basic research boomed during the years between 1998 and 2003, when Congress oversaw the doubling of the NIH budget. The ROI program was a major beneficiary of the increase. "The fact is that the NIH has put us far ahead of the curve in biomedical research," says Cooley. "And we have seen a huge payoff from research at the extremely basic level. Look at the examples of therapeutic RNAS or stem cells. In both cases, the researchers were driven by curiosity as to how organisms develop from single cells to complicated systems. Who would have known that their work would become the underpinnings of some of the biggest therapeutic advances we'll see over the next decades?"

But what Congress gives, it can also take away. Since peaking in 2004, NIH funding has flatlined at \$29.5 billion, and next year's proposed budget looks to be more of the same. While Congress often kicks in a little more money to keep programs from further cuts, the effects of inflation mean that the NIH is operating with 13 percent less buying power than it had in 2004.

On top of that, the demand for ROI funding is higher than ever. During the doubling period, the whole research enterprise grew as universities and academic medical centers expanded basic research facilities and faculties. That expansion takes time, so the NIH saw only modest growth in the number of grant applications received during the doubling years. As a result, a larger proportion of grant applications were funded. In the first two years of flat budgets, however, the number of grant applications doubled as new researchers came on line, and success rates in obtaining grants plummeted.

There is no relief in sight. According to a budgetary analysis by the American Association for the Advancement of Science, under the proposed 2009 NIH budget, the number of new grants, the average size of a grant, and the expected success rate for grant applications are all expected to fall.

"I have two new projects I'm really excited about but also kind of nervous," admits Cooley. "The most exciting projects are the ones that are hardest to fund because they tend to be the risky ones—ones where our lab has no track record—and there's not a big field of established work to point to and show where we fit in."

Lean times force funding agencies like the NIH to be more conservative and favor surefire bets. That means that finding support for innovative science can go from difficult to impossible as budgets shrink, says Richard A. Flavell, PH.D., chair and Sterling Professor of Immunobiology, professor of biology and an HHMI investigator. "Grant reviewers still recognize research that is new and exciting and worth taking a chance on. But in a super-competitive environment, those off-the-wall, risky, creative projects lose out," he says.

## **Enter the Roadmap**

Money, or lack of it, is not the only threat basic researchers perceive. Many report a growing unease with the wider world's view of their work, and with what some think is a mistaken assessment of its value. Among researchers, there is a palpable feeling that a recent and highly visible growth in support for clinically oriented translational research programs means less funding for basic research. In this regard, some re-searchers blame a set of programs collec(YCCI), under the direction of Robert S. Sherwin, M.D., the C.N.H. Long Professor of Medicine, received a \$57.3 million grant in 2006—the largest single NIH grant ever given to Yale. That grant included existing grants to Yale of \$25.8 million, so the net increase to Yale was \$31.5 million. Another recent NIH award supports the training of medical students to carry out clinical research.

No matter the merit of those programs, they create a perception problem, says Carolyn W. Slayman, PH.D., Sterling Professor of Genetics and deputy dean for academic and scientific affairs. Compared to an average ROI grant of about \$1 million over four years, the new awards were eye-popping. "To starving scientists who are worrying about

## "The NIH is not the Academic Scientist Employment Act. It's a mandate from Congress to create a phological basis for improved therapies and for improving health care." "Immunologist Jordan Pober

tively called the NIH Roadmap for Medical Research for draining support from their labs.

The Roadmap had its start at the end of the period of rapid budget growth. Anticipating that the public and its representatives in Congress would be looking for payoff on their investment, the then-new NIH director, Elias Zerhouni, M.D., initiated a mass consultation in 2002 with hundreds of scientists to identify gaps in NIH programs. Over the course of a year, Zerhouni identified areas in which the NIH might do a better job of supporting multidisciplinary teams as well as translational and clinical research. The process was dubbed the Roadmap; its first projects began in 2004.

There was controversy about the Roadmap from the beginning. Just as ROI funding was tightening, basic researchers watched money flow to translational research, multi-investigator grants and clinical research.

The School of Medicine has certainly benefited from that funding stream. The Yale Center for Clinical Investigation

their own ROI, it's hard to see Roadmap grants awarded in huge and very visible chunks of \$20 or \$40 or \$50 million," Slayman says. "Their immediate reaction is, how many laboratories like mine could be kept going very happily for years with that money?"

Even so, the idea that the Roadmap is a drag on basic science funding is exaggerated, says Jordan S. Pober, M.D., PH.D., professor of immunobiology, pathology and dermatology and vice chair of the Section of Human and Translational Immunology.

The numbers support his view. Taken together, Road-map projects account for less than 2 percent of the total NIH budget; moreover, fully half of Roadmap funding goes to individual researchers in the form of ROI or similar grants. The real culprit, Pober says, is the stagnation of the overall budget. His message: "There is pain, to be sure. But don't blame the Roadmap, blame the budget." Moreover, the activities championed by the Roadmap are necessary for the NIH to fulfill its goal to improve people's health, Pober says. "The NIH is not the Academic Scientist Employment Act. It's a mandate from Congress to create a biological basis for improved therapies and for improving health care."

The Roadmap initiative just happened to come at the same time as the NIH budget stagnated and the chances to obtain ROI funding decreased dramatically, says Jeremy M. Berg, PH.D., the director of the NIH's National Institute of General Medical Sciences, which primarily supports basic, nondisease-targeted research and is heavily involved in over the rocks in the field of biology and see what is underneath. And that means an investigator in a lab working steadily over years and decades. That means Steitz tinkering with the ribosome. It means Cooley finding out how flies make eggs.

That theme—the long and winding road from disease to cure—was echoed in a recent editorial in the journal *Science*. Editor in chief Bruce Alberts, PH.D., argued eloquently for the importance of basic research in spurring medical progress.

"We have all been taught that the shortest distance between two points is a straight line," Alberts writes. "But

## We have all been taught that the shortest distance between two points is a straight line But the same idea has repeatedly proven not to be true for progress in medical research. -*Secence* eddor Brace Alberts

Roadmap activities. "That does not mean those events are causally related."

On the contrary, Berg says, the Roadmap has been a very good thing for basic research. The idea of setting aside a relatively small amount of money for new kinds of programs and approaches was a key provision of the Roadmap and has paid off by becoming quite popular in Congress. "In my opinion the Roadmap has been quite successful with Congress in terms of their seeing the value in what we're doing. My sense is that the NIH would have been substantially worse off than we are right now if we had not had the Roadmap."

## Shortest distance between two points

Money talk aside, researchers still worry that the hoopla surrounding new clinical and applied programs that began under the Roadmap may divert attention from the fact that successful medical research relies on a foundation of basic knowledge about the functioning of healthy cells and organisms. The only way to get that information is to turn the same idea has repeatedly proven not to be true for progress in medical research." The reason, he says, is that we understand so little of what there is to know about the basic functions of cells that researchers tracing a path from disease to cure must navigate largely uncharted terrain. Scientists continue to rely on lessons learned from simple organisms—yeast, bacteria, plants, fruit flies, worms—to guide progress through the terra incognita of human disease.

John Carlson, PH.D., the Eugene Higgins Professor of Molecular, Cellular and Developmental Biology, has been looking for answers in the fruit fly's sense of smell for 20 years. Carlson has spent that time figuring out the workings of odor receptors and the olfactory system of flies, which use their sense of smell primarily to navigate the world. He and his colleagues mapped out the chemical receptors and brain pathways involved in the uncanny ability of these pests to appear out of nowhere in response to the aroma of a banana left outside to ripen on a warm day. On the way, he has found both beauty and some unanticipated applications. "The same way that fruit flies find bananas, mosquitoes find humans," Carlson explains. "They both depend on their sense of smell." That insight propelled him into the field of malaria, a disease that infects hundreds of millions of people around the world each year. Carlson is working with European and African colleagues to find chemical compounds that confuse the sensory receptors on a mosquito's nose and prevent them from finding humans. In the future, he foresees using a similar approach to keep crops free of agricultural pests. Carlson says the work may also be adapted to use odor receptors as detection devices for explosives.

For two decades, Carlson has been able to keep his research program on track with an uninterrupted stream of funding from NIH. His applied research draws support from private foundations, including the Bill and Melinda Gates Foundation for the malaria work. Nonetheless, he says, "I do worry about the NIH dropping support for individual labs exploring questions that excite their curiosity about basic science."

## The long view

The Nobel Prize-winning biologist Arthur Kornberg, M.D., liked to tell a story that starts with a surgeon out for his morning jog. While passing a lake, the doctor sees a man in the water about to drown. So he dives in, pulls the man out, resuscitates him and continues running.

A bit farther down the path, another man is flailing in the water in another part of the lake. The surgeon saves him, and no sooner sets off jogging again than he sees two more people in trouble in the water. He notices his friend, a neuroscience professor, loitering nearby and calls out for him to save one person while the surgeon rescues the other. When the neuroscientist does not move, the exasperated surgeon shouts at him, "Why aren't you doing something?"

The neuroscientist answers calmly, "I am doing something. I'm desperately trying to figure out who's throwing all these people in the lake."

The point is, of course, that the fight against human disease occurs on several fronts. Someone has to rush in and save today's victims. Solving fundamental problems, however, requires other people with different skills and interests. Neither group is more important than the other. That is one message that researchers fear is being lost on lawmakers and the public, and even on budding young scientists as the funding freeze continues.

Pietro De Camilli, M.D., Eugene Higgins Professor of Cell Biology and co-director of the program for Cellular Neuroscience, Neurodegeneration and Repair, sees this loss of perspective in his experience with up-and-coming researchers. "There is a perception I see in young people that if they want to be a scientist and successfully compete for funding, they have to work on applied problems. A career in basic research seems less and less attractive."

The boom-and-bust cycle of congressional appropriations to NIH over the last decade has left some senior researchers struggling to maintain long-term projects. When young investigators see their mentors not being funded, they get the message, says stem cell researcher Diane Krause, M.D., PH.D., professor of laboratory medicine and cell biology and associate director of the Yale Stem Cell Center. "This is dissuading people from trying to succeed as academic researchers. We certainly make it look difficult to our students and postdoctoral fellows."

At current levels, the NIH budget overall is a prescription for slowing medical progress in the future, not speeding it up, according to immunologist Flavell. He supports the Roadmap but cautions that any success depends on maintaining a healthy basic research environment and pushing forward with applied and clinical programs. One without the other makes no sense, yet increasingly he sees outstanding researchers unable to win grants. Unless something changes soon, he says, we may find ourselves 20 years down the road with an impressive clinical and translational infrastructure but few new basic findings to translate. YM

Pat McCaffrey is a freelance writer in Boston.



Online: Yale Netcasts THOMAS STEITZ: Mapping the Ribosome. RICHARD FLAVELL: Mouse With a Human Immune System Could Revolutionize Research. PIETRO DE CAMILLI: Getting the Message.

# A life's work in Indonesia

By Jill Max Photographs by Erick Danzer Kinari Webb came to medical school knowing how and where she wanted to practice medicine. Now, she and her ecologist husband are working to bring health care to a remote corner of Borneo while preserving the rain forest.



Kinari Webb, a 2002 graduate of the School of Medicine, visits with a family in the town of Sukadana in a remote corner of the Indonesian island of Borneo. Webb has opened a clinic that serves the local population. She and her husband are also working to preserve the rain forest of nearby Gunung Palung National Park. Webb spent a year traveling throughout Indonesia to find the right place to launch her clinic. Sukadana is next to a national park with a rain forest under siege from logging, and the region's three clinics and 60,000 people shared a single physician.



Pak Rudi, a 40-year-old from a remote corner of the island of Borneo, Indonesia, was in bad shape. Walking even a few steps left him short of breath. In the fall of 2007, with his wife and several family members, he traveled for eight hours by motorboat and motorcycle taxi to reach the coastal town of Sukadana, where he had relatives who urged him to seek help at the local clinic. By the time his

family carried him into the Alam Sehat Lestari clinic, known as ASRI, Pak Rudi was close to death. Although the clinic lacks an X-ray machine, the medical staff diagnosed Pak Rudi based on a physical exam and the medical history he and his family provided. Dilated cardiomyopathy due to a viral infection a decade earlier was causing his heart to fill almost his entire chest cavity—it was only later, after the doctors saw an old X-ray, that they realized how swollen the heart had been.

In Indonesia, which has 16 physicians per 100,000 people, 12 times lower than the ratio in the United States, medical care is a scarce commodity. In rural areas, the ratio is even worse: where Pak Rudi lived—in West Kalimantan three clinics and 60,000 residents shared one doctor. That changed when ASRI opened in June 2007 as the newest clinic in the area. A small house with three exam rooms and a lab for basic tests, the clinic is run by Kinari Webb, M.D. '02, who also led Pak Rudi's medical team.

"I figure there are not very many humans on the planet who are crazy enough to do something like this," says Webb, who spent a decade preparing to open her clinic in the rain forest. "Something like this" refers to her dual dreams of bringing health care to Borneo and promoting forest conservation. It's no accident that her clinic is next to Gunung Palung National Park—558 square miles of forest, swamps and mountains that contain 5,000 species of trees, wild orangutans, sun bears, agile gibbons, proboscis monkeys, wild boars and hundreds of bird species. This pristine habitat is in danger from logging companies and poachers who eke out a living by harvesting lumber. In the 1960s, rain forest covered 82 percent of Indonesia—now it covers 49 percent. Since the 1980s more than half the rain forest in Borneo, one of the largest of Indonesia's 17,500 islands, has been destroyed.

Webb first visited the island as an undergraduate at Reed College in Portland, Ore., and was both entranced by the beauty of Gunung Palung, with its mangrove forests and verdant mountains shrouded in gentle mists, and horrified by the extent of the region's illegal logging. While the government has tried to protect the rain forests through mass tree plantings and international carbon-trading schemes, villagers have few ways to earn a living. Some work on rubber and oil palm farms. Others earn a few dollars a week breaking boulders and selling the rocks to roadbuilding crews. More than 7 percent of the former Dutch colony's 245 million people live on less than a dollar a day. In ASRI's catchment area, many households survive on about \$15 a month, and for many families, a shared weekly egg is the sole source of protein. Tree poaching, although it pays less than \$2 a day, remains an attractive option.

## A life-changing experience

In a sense, Webb's journey to Indonesia began during her childhood in Dixon, N.M., a small town about an hour from Santa Fe. Her parents, both of whom have PH.D.s in psychology, were hippies who had joined the back-to-theland movement and taught Webb and her sister a love of animals and nature. Webb majored in biology at Reed, where she focused on orangutans. She pursued her studies with a determination that would serve her well later: she went to the library, looked up articles on orangutans and asked every author for a job. In 1993, between her junior and senior years, she worked at a research station in Gunung Palung National Park, one of the world's few remaining orangutan habitats.

One day a research assistant approached her with a cut on the palm of his hand, and although the wound was not serious, he acted as if it were life-threatening. It dawned on Webb that for people living in remote areas a seemingly routine injury could have dire consequences. Since she had no medical training, Webb whipped out her copy of the health care manual *Where There Is No Doctor*, by David Werner, cleaned the cut and closed it with improvised butterfly

**BELOW** Webb examines a woman in Sukadana. With limited resources and frequent power failures, Webb often improvises her treatment. She has used honey to treat a diabetic ulcer; cardboard to make inserts for shoes; and mucuna beans, with their high L-dopa concentration, to treat Parkinson disease. **MIDDLE** A family relaxes on their front porch in Sukadana. Webb has engaged the townspeople in a dialogue about conservation and offers health care credits at her clinic for those who promise not to engage in illegal logging.



bandages made of adhesive tape. The cut healed and Webb was hooked; she knew that she wanted to become a physician and that she wanted to help people in rural Indonesia.

Her experience at Gunung Palung was life-changing for other reasons as well. She met Campbell Webb, PH.D., a biologist and ecologist who was pursuing his doctorate at Harvard. At first they resisted romance in an isolated setting under the scrutiny of their colleagues. But candlelit dinners (there was no electricity), bathing in waterfalls (there was no plumbing) and two months alone at their camp weakened their resolve. They were married as soon as Kinari graduated from Reed.

In Gunung Palung the idea of the interconnectedness of living things took hold in Kinari Webb's mind. For several species of trees, for example, propagation depends on orangutans that eat their fruit and defecate the seeds. On a more global level, Webb realized that timbering not only reduced rainfall and lengthened the dry season, but also contributed to global warming. Webb decided to focus her energy on a new project: she would provide health care to a population in desperate need, but she would also use it as an incentive for villagers to stop cutting down trees.



**RIGHT** Webb and her husband, Cam, make their home in Sukadana, but the couple spend as many as five months of each year apart. Campbell Webb, a Harvard ecologist, travels throughout Indonesia and Malaysia for his work with the Arnold Arboretum.



## A decade of preparation

More than 10 years passed before she could bring her vision to life. During that time she laid the groundwork for ASRI, whose name means "beautiful and harmoniously balanced." She came to Yale knowing exactly where she wanted to practice medicine. When it was time to apply for her residency, Webb looked for a family medicine program that would provide the best training for practicing medicine in a developing nation. At Contra Costa Regional Medical Center in Martinez, Calif., she delivered more than 250 babies and performed enough C-sections to qualify for privileges at any hospital in the United States. "She got this incredible preparation to be out in the middle of nowhere

and be the first person to do whatever has to be done," said Nancy R. Angoff, M.P.H. '81, M.D. '90, HS '93, associate dean for student affairs.

In early 2005, just before completing her residency, Webb returned to Indonesia to help in the aftermath of the tsunami that devastated coastal areas of more than a dozen countries on the Indian Ocean in December 2004. She was distressed to see that the efforts of many of the agencies and organizations were ineffective and little of the aid was reaching those who needed it most. This only fueled her determination to open her own clinic. After her residency, she set up Health in Harmony (healthinharmony.org), a nonprofit organization to manage fundraising. Cam Webb moved to Bogor, West Java, which his wife used as a base while she searched for a location that was both close to a rain forest and in an area with few health care resources. "The whole process was like stepping off a cliff," she said.

After almost a year of searching, Kinari Webb realized that Sukadana, just outside Gunung Palung, was the perfect spot. It's two airplane flights and a two-hour drive through mangrove swamps from Jakarta, Indonesia's capital. The heart of the park's forest is still uncut, so there is conservation work to be done, and the local population has unmet medical needs. The location also worked for Cam Webb, who got a job as a senior research scientist with Harvard and is working with the Center for Tropical Forest Science, the world's largest tropical forest research program. His work takes him from his home base in Sukadana to his office in Bogor, and to sites throughout Indonesia and Malaysia where he does research in plant biodiversity and teaches a Harvard field course on Bornean ecology.

Before she set up shop, Webb recruited college and medical school classmates to help raise start-up money through a combination of Indonesian and American grants and private donations. Despite support from the Indonesian government, Webb faced innumerable delays in securing permits to open her clinic. Every time she produced a document, bureaucrats demanded yet another. Even worse, officials had their hands out for bribes, which she refused to give.

On June 12, 2007, ASRI opened its doors. A fiveminute walk from an undeveloped beach, ASRI is on the outskirts of Sukadana (population 12,000), a sleepy town with a pungent fish market and several stores packed with flipflops, rattan baskets and plastic buckets. A forest stretches up the hills surrounding the village, and gibbons can be heard calling through the trees. Orange with a bright blue roof, the six-room clinic is surrounded by houses, rice fields and gardens. It has three exam rooms, a dental exam room and a room for patients to sleep overnight, plus a lab for malaria and TB smears, blood work and urinalysis. There is a small pharmacy with a refrigerator, but Webb would like to have a solar-powered model since the electricity blacks out as often as five times a day. When that happens Webb lights candles, and if an emergency requires electricity she turns on a generator. She would like to add an X-ray machine to the ultrasound, EKG machine and other equipment on hand.

The staff of 15 includes two Indonesian doctors, a dentist, three nurses, a pharmacy assistant, a conservation director and an organic farm manager. "Kinari has surrounded herself with a system that can support this project and she's sort of the spark in the middle, the lifeblood of the project," said Roger Barrow, M.D., associate clinical professor of family medicine at the University of California, Davis, who Gunung Palung National Park is one of the world's last habitats for orangutans, but logging, legal and illegal, has led to deforestation of more than 70 percent of Borneo's rain forest since 1980.



worked with Webb in the aftermath of the tsunami and visited ASRI in April 2007.

"What they were able to accomplish in four months is almost impossible to imagine in a country that moves that slowly," said Jeremy Sussman, M.D., who spent a few weeks at ASRI in November 2007 as part of the Johnson & Johnson Physician Scholars in International Health Program at Yale, which sends residents to underserved areas around the world. Webb appreciates the opportunity to tap into the expertise of volunteers like Sussman. "It's good for my doctors to have someone else teaching them besides me," she said. "It helps to have a wider variety of opinions and ways of doing medicine."

The clinic is already bursting at the seams—ASRI treated 3,000 patients in its first nine months and is booked three weeks in advance. Webb has started to think about a new building and plans to open a hospital. The nearest hospital is two hours away and anything more than minor surgery requires a seven-hour journey to Pontianak, the regional capital.

Because her resources are limited, Webb finds innovative ways to treat her patients, some of which she has picked up from visitors like Werner. Webb has used honey to treat a diabetic ulcer on a hand, fashioned cardboard shoe inserts for a boy who had trouble walking, and used mucuna beans from the clinic's organic garden (they have a high concentration of L-dopa, which increases dopamine levels) to treat Parkinson disease. She and her staff treated Pak Rudi with aspirin, diuretics and blood pressure medications. In June 2008, Webb learned that Pak Rudi had died; he went 34



With donations from the United States, Webb has been able to offer eyeglasses to villagers in Borneo. On a single day last year she handed out 93 pairs in one village.

off his medicines for a month, in part because of the difficulties of transportation from his village.

Patients with cancer, diabetes, high blood pressure, severe diarrhea and a variety of other ills come to ASRI, but the area's biggest health problem is tuberculosis. More than 20 percent of the local population has TB, Webb estimates, and she has trained and hired workers to institute a Directly Observed Therapy program, in which they visit patients to monitor them while they take their medications.

Poverty plays a major role in many of the diseases Webb treats and is also a barrier in receiving treatment, but Webb doesn't believe in free health care. "It's reasonable that you pay for it, but it's also reasonable that you pay for it in a way you can actually afford," she said. "It gives patients dignity." That's why health care credits are a key component of her program. Patients and their families can pay for their treatment by cleaning the clinic, doing laundry, washing equipment or providing manure for the organic garden. They can also undertake conservation work, as Pak Rudi's family did. During the month he spent recuperating at a nearby relative's house, his family worked in the organic garden next door to the clinic. Area villagers are learning organic farming, and vegetables from the garden feed the clinic staff and patients. Webb expects to have produce to sell in the local market to help pay for medicine and other supplies.

## Linking health care to ecology

Getting the local population to understand why they should worry about the environment pervades almost everything Webb does. When asked why she and her colleagues bicycle instead of driving to the clinic, she says, "Because biking is healthier, cheaper and better for the environment." The clinic's staff held a series of meetings in villages surrounding Gunung Palung to discuss the connection between health and the environment and identify incentives that would motivate the villagers to protect the park from logging. It is here that Webb's effervescent yet soft-spoken demeanor works its charm. Indonesia is the largest Muslim nation in the world, but in West Kalimantan there are no restrictions on women's social liberties, and she engages villagers in lively discussions. ASRI's staff and local residents came up with a plan: communities would work toward a "green" conservation status, meaning no illegal logging in the previous month. In return, they receive one month of free ambulance service, mobile clinic visits and clinic discounts. No one is ever denied health care, but Webb would like to provide incentives for the long-term health of both the community and the environment. "We don't know yet whether the incentive is strong enough on an individual level or on a community level for people to actually change their behaviors," said Cam Webb, "but even if it doesn't work we're doing a lot of education. If we get even a portion of forest restored, then it's having a positive effect."

Although the program is still in its infancy, its reputation is spreading. The managers of an elephant conservation project on the Indonesian island of Sumatra have approached Webb about replicating the ASRI model. She hopes that other organizations around the world will also recognize its potential. Meanwhile, each day brings satisfaction that her vision is working. "I'm feeling kind of like a parent whose child has just started to toddle around," she said.

At the end of a long day treating patients, Webb will sometimes provide an evening meal to village children who stop by her thatched-roof house. Many of their neighbors consider the Webbs' house, with its cement floor and no plumbing, quite modest, but the couple finds it charming. A pump from their well fills a water tank on a hill that drains to a sink and they use a squat toilet which they flush with water from a bucket.

When Cam Webb is home, the two often paddle their dugout canoe to a small island, where they watch the sunset or go for a swim. When she's on her own, Kinari writes thank-you notes to donors and answers e-mail before falling into bed, where she may be awakened by a raucous serenade from gibbons camped out in the trees behind her house.

If she had any doubts about the course her life was taking, a recent boat ride into the park, where miles of grassland have replaced the once-majestic forests, convinced her that this is exactly where she wants to be and where her future lies. She plans on spending the next few decades in this remote corner of the world, but her patients hope the clinic will be around even longer, so that they won't have to worry whether a simple cut on the hand might end in tragedy. As one village leader put it, "We hope that ASRI will be forever and ever." **YM** 

Jill Max is a freelance writer in Trumbull, Conn. Erick Danzer is a freelance photographer based in Indonesia.

## Faculty



**James Rothman** 

# Leading cell biologist to head department

JAMES E. ROTHMAN, PH.D. '71, one of the world's leading cell biologists, has been named chair of the Department of Cell Biology and the Fergus F. Wallace Professor of Biomedical Sciences. Rothman will also launch the new Center for High-Throughput Cell Biology at Yale's West Campus, formerly the site of Baver HealthCare.

Rothman came to Yale from Columbia University's College of Physicians and Surgeons, where he was a professor in the Department of Physiology and Biophysics, the Clyde and Helen Wu Professor of Chemical Biology and director of the Columbia Genome Center. Under Rothman's leadership Yale's Department of Cell Biology will be significantly expanded and will be co-located at the West Campus along with its present location at the main campus of the School of Medicine.

At the Yale Center for High-Throughput Cell Biology, Rothman will lead multidisciplinary teams of scientists to develop tools and techniques to rapidly decipher the cellular functions of the 25,000 known protein-coding genes in the human genome, providing fresh insights into disease and identifying new molecular targets for therapy. For more than two decades, Rothman has performed seminal research on membrane trafficking.

Rothman graduated summa cum laude from Yale College in 1971 with a degree in physics. His research interests were inspired by cell biologist and Nobel laureate George E. Palade, M.D., who founded Yale's Department of Cell Biology.



Joan Steitz

Rothman earned a PH.D. in

biological chemistry from Harvard

Medical School in 1976. He then spent two years as a postdoctoral

associate in the laboratory of

Harvey F. Lodish, PH.D., a pre-

eminent biochemist at the Massa-

chusetts Institute of Technology.

In 1978, Rothman moved to the

Department of Biochemistry at

Stanford School of Medicine as an

assistant professor. He continued

his research at Princeton Univer-

he became the founding chair of

sity from 1988 until 1991, when

**Biochemistry and Biophysics at** 

Memorial Sloan-Kettering Cancer

Center in New York and vice chair

Rothman succeeds cell biolo-

of the Sloan-Kettering Institute.

gist and immunologist Ira S.

and Sterling Professor of Cell

Mellman, PH.D., who was chair

**Biology at the School of Medicine** 

until 2007, when he joined the

Genentech as vice president for

Jamieson, M.D., professor of cell

biology and director of the medi-

cal school's M.D./PH.D. program,

served as interim chair of the

department.

oncology research. James D.

biotechnology company

the Department of Cellular

## Yale professor receives Albany prize

JOAN A. STEITZ, PH.D., Sterling **Professor of Molecular Biophysics** and Biochemistry, is one of the first two women scientists to receive the Albany Medical Center **Prize in Medicine and Biomedical** Research, America's top award in medicine. She shared the award with Elizabeth H. Blackburn, PH.D., FW '77, SC.D.H. '91, the Morris Herzstein Professor of Biology and Physiology at the University of California, San Francisco. The two will share the \$500,000 award. Now in its eighth year, the prize is the largest in medicine in the United States and the second largest in the world outside of the Nobel Prize.

Steitz is best known for her pioneering work in RNA. She discovered and defined the function of small ribonucleoproteins (snRNPs) in pre-messenger RNAthe earliest product of DNA transcription-and was the first to learn that these cellular complexes (snRNPs) play a key role in processing messenger RNA by excising noncoding regions and splicing together the resulting segments. Her breakthroughs into the previously mysterious splicing process have clarified the science behind the formation of proteins and other biological processes, including the intricate changes that occur as the immune system and brain develop.

Steitz earned her PH.D. from Harvard in 1967. After completing postdoctoral work in Cambridge, England, she joined the Department of Molecular Biophysics and Biochemistry at Yale as an assistant professor and later became an associate and full professor, as well as chair of the department.



Pasko Rakic

## Kavli Prize for a Yale neuroscientist

PASKO RAKIC, M.D., PH.D., chair and the Doris McConnell Duberg Professor of Neurobiology, professor of neurology and director of the Kavli Institute of Neuroscience at Yale, was named one of the inaugural recipients of the Kavli Prize, given for the first time this year. The 2008 laureates were selected for groundbreaking research that has significantly advanced understanding of the unusual properties of matter on an ultra-small scale, the basic circuitry of the human brain and the nature of quasars. Rakic, one of seven scientists to receive the \$1 million prize, was honored for a pioneering series of anatomical studies carried out over the past three decades that revealed how neurons in the developing cerebral cortex are generated and how they assemble themselves into interconnected circuits that direct higher-order sensory and motor functions. The seven winners will receive a scroll, a medal and a share of the overall prize for each area.

## Faculty NOTES



Jack Elias



Andrew

Hamilton





R

Harlan Krumholz

Michael Snyder



Mary Tinetti





Amy Arnsten

**Henry Cabin** 

Seven faculty members of the School of Medicine were elected to the Connecticut Academy of Science and Engineering. They are Jack A. Elias, M.D., Waldemar von Zedtwitz Professor of Medicine and chair of the Department of Internal Medicine; Andrew D. Hamilton, PH.D., provost of the university and the Benjamin Silliman Professor of Chemistry; Diane S. Krause, M.D., PH.D., professor of laboratory medicine and cell biology; Harlan M. Krumholz, M.D., the Harold H. Hines Jr. Professor of Medicine and professor of epidemiology and public health and investigative medicine; Nancy H. Ruddle, PH.D., the John Rodman Paul Professor of Epidemiology and Public Health and professor of immunobiology; Michael P. Snyder, PH.D., the Lewis B. Cullman Professor of Molecular, Cellular and Developmental Biology and professor of molecular biophysics and biochemistry; and Mary E. Tinetti, M.D., the Gladys Phillips Crofoot Professor of Medicine and professor of epidemiology (chronic diseases) and investigative medicine.

Amy F.T. Arnsten, PH.D., professor of neurobiology, was selected by NARSAD in April to receive its prestigious Distinguished Investigator Award. NARSAD will provide a one-year grant of \$100,000 to advance her research on schizophrenia. Arnsten's past work on prefrontal cortex and executive function has contributed to the development of new treatments for attention deficit disorder.

In April two faculty members were awarded 2008 Young Investigator Awards from NARSAD, the world's leading charity dedicated to funding research on psychiatric disorders. They are among 220 earlycareer scientists in the United States and 11 other countries who will receive funds this year from NARSAD to advance their research on mental illnesses. Each will receive \$60,000 over the next two years. Savita G. Bhakta, M.B.B.S., plans to gain a better understanding of how cannabinoids (chemical compounds found in marijuana) induce schizophrenia-like behavioral and cognitive effects in healthy people and exacerbate symptoms in patients with schizophrenia. Fei Wang, PH.D., will use multimodal MRI technology to study adolescents with bipolar disorder. The study will identify abnormalities in the structural integrity of connections in brain circuitry serving the emotional processing that are implicated in the illness, as well as associated disruptions in circuitry function.

Henry S. Cabin, M.D., professor of medicine (cardiology), has been named medical director of the Yale-New Haven Hospital (YNHH) Heart and Vascular Center. Cabin will be responsible for day-to-day operations associated with the cardiovascular service line. including inpatient services, and diagnostic and interventional catheterization laboratories. In addition, Cabin will participate on an executive council and work collaboratively with other multidisciplinary physician leaders in medicine, radiology and surgery to build a comprehensive cardiac and vascular center. Since 1994,

Cabin has been associate section chief of cardiology at YNHH and associate chair, Department of Internal Medicine.

David C. Cone, M.D., associate professor of surgery (emergency medicine) and of epidemiology, has been appointed editor in chief of *Academic Emergency Medicine*, the journal of the Society of Academic Emergency Medicine.

Stephen C. Edberg, PH.D., professor of laboratory medicine and director of the Yale-New Haven Hospital microbiology laboratory, has been awarded the American Society for Microbiology's BD Award for Research in Clinical Microbiology. This award honors a clinical microbiologist for outstanding research accomplishments leading to or forming the foundation of important applications in clinical microbiology. Edberg's contributions to clinical microbiology range from basic science, through applications and technology transfer, to critical analysis of current microbiologic findings and principles as applied within the context of public health problems. His research has resulted in more than 180 publications.

**Richard L. Edelson**, M.D., director of Yale Cancer Center, has been named the inaugural Aaron B. and Marguerite Lerner Professor



Christine Jacobs-Wagner, PH.D., the Maxine Singer Associate Professor of Molecular, Cellular and Developmental Biology, has been designated a Howard Hughes Medical Institute investigator. She is one of 17 Yale scientists who now hold the prestigious appointment. Jacobs-Wagner is one of the world's leading experts on the internal cellular workings of bacteria. Her descriptions of the inner mechanisms of bacteria have led to an appreciation of the survival strategies of these ancient organisms and new insights into how to study modern human illnesses.



David Cone







**Brian Smith** Jacobs-Wagner

Ruslan Medzhitov, PH.D., received the Howard Taylor Ricketts Award from the University of Chicago in May. The Howard Taylor Ricketts Award is given in memory of Ricketts, the scientist for whom the Rickettsia genus of microorganisms is named. The award recognizes an individual who has made an outstanding contribution in a field of the medical sciences.

Curtis L. Patton, PH.D., professor emeritus in the School of Public Health, was one of 13 people to receive a Seton Elm/Ivy Award this spring. Patton was honored for bringing previously unrecognized African-Americans to public light. Yale's recognition of Edward A. Bouchet, a distinguished New Havener, Yale College's first African-American graduate and the first African-American to earn a PH.D. anywhere in the nation, is due in part to Patton. He also celebrated the work and legacy of Cortlandt Van Rensselaer Creed, M.D., another distinguished New Havener and the first African-American graduate of Yale University. In 2007, on the occasion of the 150th anniversary of Creed's graduation from the School of Medicine, Patton and his colleagues organized a series of events culminating in the dedication of a new memorial to Creed at the Grove Street Cemetery.

Joel L. Rosenbaum, PH.D., professor of cellular and molecular biology, received an honorary degree from the University of Siena in Italy, in May. Rosenbaum has been studying the ultra-structure of the intraflagellar transport (IFT) process at the University of Siena with his colleagues there. IFT was discovered in the Rosenbaum laboratory in 1992 and was shown to be responsible for the formation and maintenance of almost all cilia and flagella. Analysis of the genes underlying the IFT process have led to new insights into the role of cilia and flagella in polycystic kidney disease and other human diseases.

Brian R. Smith, M.D., professor and chair of laboratory medicine, has been elected president of the Academy of Clinical Laboratory Physicians and Scientists, the major academic society for laboratory medicine.

Edward L. Snyder, M.D., professor and associate chair for clinical affairs in the Department of Laboratory Medicine, has been voted president-elect of the National Marrow Donor Program. He will begin his twoyear term in January.

Scott A. Strobel, PH.D., professor of molecular biophysics and biochemistry, has been awarded the Schering-Plough Research Institute Award. The award is given by the American Society of Biochemistry and Molecular Biology to recognize outstanding scientific contributions made by young researchers early in their careers. Strobel gave the award lecture, "Three Views of RNA Catalysis: Ribozymes, Ribosomes and Riboswitches," at the society's annual meeting in San Diego in April.



**Ronald Vender** 

Ronald J. Vender, M.D., '77, HS '80, FW '82, a nationally recognized gastroenterologist who specializes in therapeutic endoscopy and inflammatory bowel disease, started on June 1 as chief medical officer (CMO) for Yale Medical Group (YMG) and associate dean for clinical affairs at the School of Medicine. He reports to David J. Leffell, M.D., chief executive officer of YMG and deputy dean for clinical affairs. Vender, a clinical professor of medicine, built a clinical practice in the New Haven area and has held leadership and teaching roles at Yale-New Haven Hospital, the Hospital of Saint Raphael and Milford Hospital. He chaired the National Affairs Committee of the American College of Gastroenterology and currently serves on the board of trustees. He has published numerous research papers with colleagues on the Yale faculty. One of the appeals of his new position is the chance to return to his alma mater and work with colleagues he's known since he was a student. "There are a number of people with whom I was a resident who are on the faculty. Some of my teachers and mentors are still here," Vender says. "I am being very warmly and generously received by my colleagues and former mentors. I feel that I am coming back to a place I never left."

## SEND FACULTY NEWS TO

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# The Class of '08



Liza Goldman Huertas, James Troy, Amy Meadows and Alexander Diaz de Villalvilla before the Commencement ceremony at Old Campus.



**ABOVE** Class co-president Kristina Zdanys received her degree from Dean Robert Alpern.

**RIGHT** Zofia Piotrowska, Karl Laskowski, Lu Anne Dinglasan and Kevin Lau on their way to Old Campus.



# Celebration, loss and an exhortation to dream

Marking their own graduation, students in the Class of 2008 remembered a fallen classmate.

Commencement was a day of mixed emotions for graduates in the Class of 2008. As they celebrated their own passage from students to physicians, they also mourned the loss of their classmate Mila Rainof, who died on April 20 after being struck by a car. (See related story, page 4).

Rainof's absence was palpable throughout the day's events. As the medical and public health students marched to Old Campus, each left a carnation at the site of the accident at York Street and South Frontage Road. During the ceremony on Harkness Lawn, Merle Waxman, M.A., associate dean, ombudsperson and director of the Office of Women in Medicine, accepted Rainof's posthumous medical degree. And the class gift was a donation to a scholarship fund in Rainof's memory.

Maggie Samuels-Kalow and Ellen House took the podium to offer their reflections. They recalled Rainof's commitment to her friends and patients as well as her seemingly boundless warmth and compassion. Samuels-Kalow urged her classmates to find other ways to remember Rainof. "We honor her memory in less tangible ways, in the ways we treat each other and our patients," she said.

"Let's celebrate today, as Mila would have wanted us to," said House.

Commencement speaker Alfredo Quiñones-Hinojosa, M.D., offered as inspiration his own life story, recounting how he packed his few possessions into a bag 20 years ago and, with \$65 to his name, crossed the border illegally from Mexico to California. The same hands that now probe "the most beautiful organ in the human body the brain" were once bloody and raw from pulling weeds on the farms of the San Joaquin Valley. After an industrial accident almost killed him, Quiñones-Hinojosa's father told him, "You have been given a gift. Life is short."

Quiñones-Hinojosa went on to graduate from a California community

college and Harvard Medical School. While at Harvard he became a U.S. citizen. He is now a neurosurgeon at the Johns Hopkins School of Medicine. (For the full text of the address, visit medicine.yale.edu/ysminfo/top\_story/ 2008/05/commencement\_speech.html)

## **Commencement awards**

This year's Bohmfalk Prizes for excellence in teaching went to Leigh V. Evans, M.D., HS '02, assistant professor of surgery (emergency medicine), for clinical sciences, and to Aldo J. Peixoto, M.D., associate professor of medicine (nephrology), for basic science.

Thomas P. Duffy, M.D., professor of medicine (hematology), received the Leonard Tow Humanism in Medicine Award. The Leah M. Lowenstein Awards went to Nina Horowitz, M.D., assistant clinical professor of surgery, and to Andres S. Martin, M.D., M.P.H. '02, associate professor in the Child Study Center and of psychiatry.

Eve R. Colson, M.D. '89, associate professor of pediatrics, received the Alvan R. Feinstein Award. Lynn D. Wilson, M.D., M.P.H. '86, professor of therapeutic radiology and of dermatology, received the Francis Gilman Blake Award. And the Betsy Winters House Staff Award went to Vikram Reddy, M.D.

—John Curtis





**ABOVE** Deans Nancy Angoff and Richard Belitsky before the procession to Old Campus.

LEFT Former Beatle Sir Paul McCartney was among those who received an honorary doctorate from Yale this year.

## Public health grads urged to develop skills beyond science as leaders and advocates

The 108 graduates of the School of Public Health's Class of 2008 have their work cut out for them: defeating the AIDS virus, reducing obesity and eliminating health care disparitiesto name just a few of the tasks cited by Dean Paul D. Cleary, рн.р. And they'll face one more challenge, said Commencement speaker Georges C. Benjamin, м.D., director of the American Public Health Association: "Nobody's going to know what you do," he told the graduates gathered in Battell Chapel on May 26.

Benjamin offered an analogy: Two people rescue a drowning person who drifts by their picnic spot. The next day they save two more people; and as the numbers steadily increase, they establish an elaborate rescue system using boats, ambulances and helicopters. When the rescuers finally address the

cause of the problem-a curve in an upstream road—and solve it with a guardrail and speed limit, the flow of victims ends.

To achieve this sort of prevention, Benjamin told the graduates they'd need skills as leaders, administrators and advocates and good relationships with policy-makers. "Science is necessary but not sufficient," Cleary said, noting that students on the medical campus are pressing New Haven officials to improve traffic safety at nearby intersections. In April a medical student was killed (see related story, page 39); in October 2006 a public health student was seriously injured. Both were struck by cars.

## Public health awards

This year's excellence in teaching award went to Annette M. Molinaro, PH.D., assistant professor of public health (biostatistics). "If you can generate enthusiasm for core biostatistics, you are some teacher," Cleary guipped.



Sharing the Dean's Prize for Outstanding м.р.н. Thesis were Rupak Datta, Ling-I Hsu, Diane Martinez and Stephanie Smith. The Henry J. (Sam) Chauncey Jr. Inspiration Award went to Heather McPheron, and Ashley Fields won the Cortlandt Van Rensselaer Creed Award. Student speaker Rebecca Boulos offered warm memories of her classmates.

-Cathy Shufro



ABOVE Graduate Daina Barauskas with faculty member Annette Molinaro.

**RIGHT** Public health students proceed to Old Campus.



## PA students don white coats in new ceremony marking their entry to medicine

Second-year students in the Physician Associate (PA) program helped their 37 first-year colleagues in the Class of 2009 don the white coats that symbolize the medical profession on the afternoon of March 20. Medical students have long participated in this tradition, but it is only the second time that Yale PA students have joined in the ritual. And unlike their medical colleagues, they celebrated not the beginning of their training, but a different milestone. The donning of the white coat in the Medical Historical Library marked the transition from learning in the classroom to learning on the wards from real patients.

"We wanted to incorporate into a ceremony the idea of trying to instill in the students the ethical responsibility of being health care providers and the reverence with which they should practice," said Mary L. Warner, M.M.Sc., PA-C, director of the PA program.

"The White Coat Ceremony is a rite of passage, serving as a reminder of your need to balance excellence in the medical sciences with demonstrated compassionate care," said keynote speaker Cynthia B. Lord, PA '91, director of the Quinnipiac University PA program and president-elect of the American Academy of Physician Assistants. "The white coat should never be a symbol of status, hierarchy or power."

—Melinda Tuhus





**ABOVE** At the White Coat Ceremony for students in the Physician Associate Program, second-year students helped first-years don the coats that symbolize their entry into clinical medicine. In turn, the first-year students placed School of Medicine pins on the coats of the second-years. Thea Cogan-Drew, president of the first-year class, right, put a pin on Karen Edwards' coat.



**TOP** Michelle Smith smiled as she got help from Tamara Brining.

**ABOVE** Jason Fleury helped Megan Dieterich don her white coat.

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## Students present their findings at 22nd Student Research Day

At this year's Student Research Day, the 22nd Annual Scientific Poster Session featuring research by students in medicine and public health, 58 students presented their findings on topics ranging from the soon-to-be-personal (Depression and Resilience During the First Six Months of Internship) to the practical (Educational and Behavioral Interventions to Reduce Exposure to Isocyanates in Auto Body Shops) to the profound (Beyond Patient Satisfaction: Physician Ambivalence, Authenticity





**TOP** Jennifer Dominguez, center, with colleagues from the Yale Program for Women's Reproductive Behavioral Health, where Dominguez did her thesis research.

**ABOVE** Amanika Kumar, a student from Stony Brook University Health Sciences Center School of Medicine, who was at Yale on a fellowship, with David G. Nathan, who delivered the Farr Lecture. and The Challenges to Patient-Centered Medicine).

Some projects reflected the notion that the most common expression in science is not "Eureka!," but "Huh?" As medical student Kiera S. Levine analyzed her findings—patients expressed satisfaction with physicians whose manner was cold and impersonal—she asked, "That's interesting. What's going on?" Her conclusion: "The idea of satisfaction is complicated and tremendously ambivalent. Looking for simple assessments doesn't reflect the patient's circumstances."

Medical student Ayal Aizer-Radical Prostatectomy Versus Intensity-Modulated Radiation Therapy in the Management of Localized Prostate Adenocarcinoma—reviewed the records of about 800 patients treated for prostate cancer at Yale over a 10-year period to see whether they fared better with surgery or radiation therapy. For patients with a favorable prognosis, there was no difference in outcomes between patients who had surgery and those who had radiation. Patients with a poor prognosis tended to do better with the radiation therapy, as did patients with the most advanced cancers.

Allison Arwady, who graduated with a degree in medicine this year, studied an old disease that is on the rise again in New Haven and elsewhere. In her project, *The Uses of Rickets: Race, Technology and the Politics of Preventive Medicine in The Early 20th Century*, she found that in the century's early decades, as higher rates of the disease were observed in people with darker skin, it was erroneously concluded that the disease must be the result of poor sanitation. A large-scale study in New Haven in the 1920s found that the disease, now known to be caused by a vitamin D deficiency, was widespread and afflicted people of all races and ethnic groups. Only then, Arwady said, did the public stop blaming the victims.

She believes there's a lesson to be learned from this rush to judge and stereotype, as she sees that reaction reflected in the response to some public health issues we face today, such as HIV/AIDS.

Following the poster session, five students who won prizes for their research gave oral presentations. Lu Anne Dinglasan discussed "The role of matrix metalloproteinases in axon guidance and neurite outgrowth"; Ryan Kaple wrote his thesis on "The axial distribution of lesion-site atherosclerotic plaque components: An in vivo volumetric intravascular ultrasound radiofrequency analysis"; Jason Roh's talk was "The chemokine MCP-I is an essential mediator in tissue engineered blood vessel development"; Andrew Simpson researched "The utility of plain radiography in the evaluation of degenerative spine disease"; and Nandakumar Narayanan's paper was titled "While they wait: Rodent frontal cortex and delayed-response performance."

The day ended with the annual Farr Lecture, delivered this year by David G. Nathan, M.D., president emeritus of the Dana-Farber Cancer Institute. His talk, "A voyage in clinical research," focused on his pioneering investigations into blood disorders.

—Jennifer Kaylin

Sarah Frasure, right, got a congratulatory hug from classmate Lindsay McGuire at Match Day in March.

## Match Day 2008

Nationally, this year's match was the largest ever—more than 28,000 applicants competed for 22,240 slots as firstyear residents. At Yale, 97 students matched. And for the third time in the last four years, all students found a match. "I couldn't be happier," said Nancy R. Angoff, M.P.H. '81, M.D. '90, HS '93, associate dean for student affairs. This year's match also saw a high number of students entering psychiatry—nine chose the field, the most ever at Yale.

## California

#### Alameda County Medical Center, Oakland

Mary Hatcher, emergency medicine Mila Rainof, emergency medicine

California Pacific Medical Center, San Francisco Sean McBride, medicine-preliminary

## Santa Clara Valley Medical Center, San Jose

Jenelle Jindal, medicine-preliminary Maulik Shah, medicine-preliminary

Stanford University Programs Louis Salamone, general surgery

Sutter Medical Center of Santa Rosa Rachel Friedman, family medicine

UCLA Medical Center, Los Angeles Anne Ackerman, surgery-preliminary, urology

University of California, San Francisco Jessica Beard, general surgery Tina Dasgupta, radiation oncology Rasha Khoury, obstetrics and gynecology Yunie Kim, internal medicine/primary Kiera Levine, psychiatry Maulik Shah, neurology Krishan Soni, internal medicine Michael Swetye, psychiatry James Troy, internal medicine Pavithra Venkat, obstetrics and gynecology

## Connecticut

preliminary

**Greenwich Hospital** Claudia Castiblanco, medicine-

## Griffin Hospital, Derby

Louvonia Boone, medicine-preliminary

Hospital of Saint Raphael, New Haven Jennifer Dominguez, medicinepreliminary

Keith Gipson, transitional Nandakumar Narayanan, medicine-

preliminary Karen Shoebotham, transitional Hannah Yu, medicine-preliminary

St. Vincent's Medical Center, Bridgeport

Scott Kennedy, transitional

## **University of Connecticut Program, Farmington** Keith Gipson, anesthesiology

Jeannine Ruby, general surgery

## Yale-New Haven Hospital

Mary Allison Arwady, medicine/ pediatrics

Eric Arzubi, psychiatry Erik Carlson, orthopaedic surgery Claudia Castiblanco, ophthalmology

Douglas Davis, medicine/primarypreliminary, diagnostic radiology Jennifer Dominguez, anesthesiology Ryan Hebert, surgery-preliminary,

neurosurgery Kristin Hoffmann, medicine/primarypreliminary, dermatology Lily Horng, internal medicine

Rasika Jayasekera, psychiatry Kimberly Johung, medicinepreliminary, radiation oncology

Rachel Laff, Internal medicine/primary Tamara Lazic, medicine/primary-

preliminary Nandakumar Narayanan, neurology David Peaper, clinical pathology Elizabeth Wahl, internal medicine/ primary

#### **District of Columbia**

Children's Nat'l Medical Center/ George Washington University Ephat Russcol, pediatrics

Uniformed Services University of the Health Sciences

Melissa Wollan, obstetrics and gynecology

Walter Reed Army Medical Center Amanda Sandoval, psychiatry Indy Wilkinson, anesthesiology Kimberly Schinnerer, medicine-

preliminary

Corinna Levine, left, shared the good news with classmate Zofia Piotrowska.



#### Florida

Jackson Memorial Hospital, Miami Gabriel Widi, neurosurgery-preliminary

Mount Sinai Medical Center of Florida Program, Miami Beach Roger Goldberg, medicine-preliminary

**University of Miami** Gabriel Widi, neurosurgery

University of Miami/Bascom Palmer Eye Institute Roger Goldberg, ophthalmology

#### Illinois

University of Chicago Medical Center Jason Griffith, internal medicine/ M.D. scientist

#### lowa

**University of Iowa Hospitals and Clinics, Iowa City** Paul Walker, otolaryngology

## **Maryland** Johns Hopkins Hospital, Baltimore

Mohamad Bydon, surgerypreliminary, neurosurgery Julia Marsh, internal medicine Kimberly Schinnerer, anesthesiology

Johns Hopkins University Alison Norris, social science postdoctoral fellow

Johns Hopkins University/Bayview Medical Center Elizabeth Houle, medicine-preliminary

Johns Hopkins University/Wilmer Eye Institute

Elizabeth Houle, ophthalmology

#### Massachusetts

Brigham and Women's Hospital, Boston

Candace Feldman, internal medicine/ primary

Sarah Frasure, emergency medicine Sanaz Ghazal, obstetrics and

gynecology Karl Laskowski, internal medicine Sean McBride, radiation oncology Zofia Piotrowska, internal medicine Jason Roh, internal medicine Margaret Samuels-Kalow, emergency medicine

#### Massachusetts General Hospital, Boston

Argyro Caminis, psychiatry Sharmin Ghaznavi, psychiatry Ellen House, psychiatry Jenelle Jindal, neurology Ryan Kaple, internal medicine Jeffrey Winer, pediatrics

#### Massachusetts General Hospital/ Harvard Combined Program

Dania Magri, orthopaedic surgery Andrew Simpson, orthopaedic surgery

Mount Auburn Hospital Program, Cambridge

Karen Shoebotham, diagnostic radiology

## Minnesota

Regions Hospital/HealthPartners Institute, St. Paul

Timothy Sullivan, emergency medicine

#### Missouri

**Barnes-Jewish Hospital, St. Louis** Gregory Nelson, orthopaedic surgery

#### **New York**

Albert Einstein College of Medicine (Jacobi/Montefiore), Bronx Kurtland Ma, emergency medicine

Albert Einstein College/Montefiore Medical Center, Bronx Liza Goldman Huertas, family medicine

Hospital for Special Surgery/Cornell Medical Center, New York City Peter Fabricant, orthopaedic surgery

Memorial Sloan-Kettering Cancer Center, New York City Tina Dasgupta, transitional Carolyn Graeber, transitional Sophia Liu, transitional

Mount Sinai Hospital, New York City Leon Boudourakis, general surgery Lindsay McGuire, medicine-preliminary

#### New York-Presbyterian Hospital– Columbia University Medical Center, New York City

Louvonia Boone, anesthesiology Cynthia Correll, medicine-preliminary, neurology

Sophia Liu, anesthesiology Christopher Winterbottom, internal medicine

Hannah Yu, anesthesiology

#### New York-Presbyterian Hospital– Weill Cornell Medical Center, New York City

Scott Kennedy, diagnostic radiology Lindsay McGuire, dermatology Lori Spoozak, obstetrics and gynecology

#### New York University School of Medicine, New York City

Benjamin Bowling, internal medicine Carolyn Graeber, ophthalmology Mark McRae, plastic surgery Kristina Zdanys, psychiatry

#### St. Luke's-Roosevelt Hospital Center Program

Barbara Wexelman, general surgery

**BELOW LEFT** Gene-Fu Liu and Julia Marsh, right, celebrated.

**BELOW RIGHT** Kristin Hoffman will stay in New Haven for a dermatology residency. **BOTTOM** Yunie Kim discussed the Match with faculty member Cyrus Kapadia.





#### Ohio

**Cleveland Clinic Foundation** Al Makkouk, orthopaedic surgery

#### Pennsylvania

**Children's Hospital of Philadelphia** Kevin Lau, pediatrics Tamara Miller, pediatrics Ashley Neal, pediatrics

Drexel University College of Medicine, Philadelphia Abby Hochberg, medicinepreliminary, dermatology

## Hospital of the University of Pennsylvania, Philadelphia Lu Anne Dinglasan, diagnostic radiology

Pennsylvania Hospital, Philadelphia Lu Anne Dinglasan, medicinepreliminary

University of Pittsburgh Medical Center

Misaki Kiguchi, vascular surgery Amy Meadows, pediatrics/psychiatryadult and child Danielle Smith, obstetrics and gynecology

## Rhode Island Rhode Island Hospital/Brown University, Providence Alexander Diaz de Villalvilla, medicine/pediatrics

Roger Williams Medical Center Program, Providence Tamara Lazic, dermatology

#### Tennessee Vanderbilt University Medical Center

Jennifer Giltnane, pathology

Washington Swedish Medical Center Program, Seattle Soledad Ayres, family medicine

University of Washington Affiliated Hospitals, Seattle Corinna Levine, otolaryngology/

research Natalya Lopushnyan, surgery-

preliminary, urology



# Reunion 2008

The big news and main attraction of this year's alumni gathering was the university's new West Campus, which could transform research at Yale.



of West Haven and Orange and that will provide the university with 1.5 million square feet of new office, storage and laboratory space. This year's reunion was a jaw-dropping experience for the scores of alumni who toured Yale University's new West Campus during the weekend. On the three buses shuttling alumni to the 136-acre campus in neighboring West Haven and Orange and in the corridors of one of the site's research buildings, alumni marveled at the new space, its pristine laboratories and the low price. When Dean Robert J. Alpern, м.D., Ensign Professor of Medicine, led alumni down a hallway past a chemistry lab that seemed to stretch forever, the possibilities for research seemed equally endless.

After a brief tour of the lab and its 12-foot chemistry hoods followed by a lunch in the facility's cafeteria, Alpern described the process that led to the university's \$109 million purchase of the site and its 1.5 million square feet of office, storage and research space, as well as some of the medical school's plans for its use. "We don't see this as a site for classroom teaching," Alpern said, "but we do see this as a site for research, some of which will include student participation."

The first research program to be based at West Campus will be the new Center for High-Throughput Cell Biology, headed by the new chair of cell biology, James E. Rothman, PH.D. '71, the Fergus F. Wallace Professor of Biomedical Sciences. The center will focus on developing tools and techniques for analyzing the cellular functions of the 25,000 known proteincoding genes in the human genome.

West Campus, Alpern said, may also be a site for clinical use. Yale-New Haven Hospital sees potential for building an emergency room, and Yale Medical Group could open clinical practices at West Campus, which has parking for 3,000 cars. "For people coming up from southern Connecticut, the thing they hate most is the last 10 minutes, driving into New Haven and trying to find parking," Alpern said.

Baver HealthCare, which had owned the site for decades, decided to close it down in 2006 after a corporate merger. The company put the property on the market hoping to sell it to another pharmaceutical firm, but the only bids came from developers interested in the land. "When it became clear that no pharmaceutical company was going to come into the bidding process ... they told us they would love to get a bid from us," Alpern said. "The developers were getting land. We were getting research buildings, office buildings and land. The biggest bonus is the time. If I convince [Yale President Richard C. Levin] that we need to start today on a new research building, it is a six-year time frame. ... We have gotten something that would have taken six years."

West Campus was also a central theme in Alpern's State of the School address earlier that day at the Association of Yale Alumni in Medicine's business meeting. "We want to establish programs of exceptional quality that greatly enrich science at Yale and outside of Yale," Alpern said, explaining the vision for the new campus. "This needs to transform science at Yale."

West Campus was not the only topic, however, in Alpern's discussion of the state of the school. The School of Medicine, he said, remains one of the best in the world. "It has become absolutely impossible to get into the School of Medicine. We get over 4,000 applications for 100 spaces," he said. "The top 1,000 applicants are indistinguishable, they are so fantastic."

Among the new educational initiatives is a program for clinical clerkships in global health, which relies on established and ongoing programs with universities and hospitals abroad. "We used to let students pick a place in Africa and go there," Alpern said. "Now we really try to have organized rotations."

The medical school is moving away from the traditional "see one, do one, teach one" methodology through the use of such computerized models that mimic the human body as SimMan, a portable manikin that allows students to practice emergency treatment techniques and decision-making skills. "It is completely real," Alpern said. "You see EKG, you see vital signs, you give medications. You don't know that the patient isn't real." The medical school has also adjusted its financial aid policy (see related story, page 7), in order to ease the burden on middleincome families.

The clinical practice, Alpern said, is the fastest-growing area of the medical school. The partnership with Yale-New Haven Hospital, he said, "has never been better." The new liver transplant program had performed 33 procedures since the summer of 2007; in September 2007 the program completed the first split-liver transplant in the state. "We have overnight become a center for liver transplants," he said.

At the alumni meeting that morning Christine A. Walsh, M.D. '73, a professor of clinical pediatrics at Albert Einstein College of Medicine in New York, received the Distinguished Alumni 48

Service Award in recognition of her service to her profession, patients and family. "It is icing on the cake to receive an award for something you absolutely love to do," Walsh said.

## Improved outcomes for autism

Diagnosing autism these days, said Fred R. Volkmar, M.D., director of the Yale Child Study Center, is something like filling out a form to diagnose deafness. "You'd say 'I want a hearing test!" ... We're trying to make the diagnosis [of autism] ... more like a hearing test."

Although researchers have found some genetic markers for autism, diagnosis is still a complex process requiring far more than a simple hearing exam. The current diagnostic gold standard requires the judgment of an experienced clinician who looks for certain behaviors in a child and discusses the child's developmental history with his or her caregiver. Most cases aren't diagnosed until the child is between the ages of 3 and 5; however, recent advances have allowed clinicians to diagnose the disorder in children as young as 2. Clinicians and researchers at Yale are now developing ways to spot autism even earlier.

Formal diagnostic criteria became available only in 1980, and research and interventions developed since then have led to improved outcomes. Autistic children now apply for college, Volkmar said—something unthinkable 25 years ago. "In a university setting," Volkmar joked, the odd social behaviors typical of people with autism "are often more easily tolerated and people can fit right in."

Volkmar and his colleague Ami Klin, PH.D., director of the Yale Autism Program, described new diagnostic techniques at this year's reunion symposium. The new approaches allow clinicians to deduce what a child is thinking by tracking what she looks at. Klin's team recently found that toddlers who were later diagnosed with autism, when shown a video of a woman speaking tenderly into the camera, pay attention mostly to her mouth or to background objects. Other children typically watch the woman's eyes.

The eye-tracking technology that led to this discovery has been central to research at the Child Study Center since 2000, when Warren Jones, now a graduate student in neuroscience, proposed its use to Klin. Using this technique, researchers found that autistic adults watch actors' mouths or background objects during emotional movie scenes rather than the actors' faces. Brain imaging studies confirmed that people with autism see human faces the way normal people see objects.

The youngest subjects of eye-tracking technology, though, are infants. The team created a video of a human figure rendered as a series of moving dots along with a spoken soundtrack; they then showed the video to babies. Infants later diagnosed with autism tended to look at both upright and upside-down figures, while normal babies preferred the upright figures. The autistic group, though, were more interested in



figures that move in time with the soundtrack. This preference for audiovisual synchrony may be part of the reason that autistic people watch lips so intently—they're drawn to the synchronous occurrence of lip movements and speech sounds. The team showed that mouth-looking exceeds eyelooking as early as 5 months of age in at-risk infants.

Volkmar and Klin hope that in the near future babies held on a parent's lap can watch a video while eye-tracking technology monitors their gaze and offers an early diagnosis of autism. But little research on effective treatments has been done in children under the age of 3. Klin told the audience that a task force for extending therapies to babies has been formed. "We need a rapidresponse system for the very young children who can't wait."

## Telemedicine's global reach

At \$10,000 per hour for analog satellite time, said Ronald C. Merrell, M.D., the world's first telemedical surgery "was a little bit, well, unwieldy."

The former chair of surgery at Yale referred to a pioneering open-heart operation in Houston in 1965, when a satellite linkup connected legendary surgeon Michael E. DeBakey, M.D., to viewers in Geneva. More recently, a surgeon in New York performed the first fully remote surgery on a patient in France. The momentous event was underreported, said Merrell, because the press conference was scheduled for September 11, 2001.

Merrell, who left Yale in 1999 to become chair of surgery at Virginia Commonwealth University (vcu), discussed the past, present and future of telemedicine at the Yale Surgical Society Spring Reunion, which was held this year in his honor. He now leads the Medical Informatics and Technology Applications Consortium at vcu. Telemedicine, he said, is "the application of telecommunications and information science to support the delivery of health care at a distance."

Telemedicine is already with us in many ways, he said. Picture archiving and communication systems, now common, allow radiologists to diagnose patients from thousands of miles away. Preoperative clearance can also be done remotely, as Merrell and a team of surgeons demonstrated when they cleared the way for patients in the Dominican Republic to undergo surgery before the surgeons had arrived. A satellite dish installed on the roof of an outbuilding provided the link for low-bandwidth video.

In medical education, Merrell said, telemedicine can be as simple as Internet access in Kenya from solarpowered laptops, or as sophisticated as the class he once taught from the operating room for a group of medical students in Russia. "Education can be distributed in virtual reality in ways that really do work," Merrell said, adding that he hoped such techniques would reduce our "separation and alienation from the developing world." Telemedical techniques might one day beam top-quality medical education into medical classrooms around the world.

"I would make this integral to the training of medical students internationally," he said. "As long as it's interactive, I think we can do as well as we could in a classroom."



Former chair of surgery Ronald Merrell was honored at the Yale Surgical Society Spring Reunion. In his address, Merrell described telemedical techniques that bring medical education around the world.

#### A focus on ethics in public health

As Lawrence O. Gostin, J.D., associate dean and the O'Neill Professor of Global Health Law at the Georgetown University Law Center, surveys the health landscape around the world, he comes to an obvious yet troubling conclusion. "Rich countries just don't care enough," he said, calling the response of the United States and other affluent countries to health inequalities "limited and quite pathetic."

Gostin, the keynote speaker at the School of Public Health's Alumni Day symposium, said that government leaders need to pay closer attention to health threats in other parts of the world. "Infectious diseases don't respect national borders," he said, noting that health issues pose serious ramifications for international commerce, trade, tourism and government stability. "States with unhealthy populations provide a great opportunity to harbor terrorists." Even the CIA, he said, uses infant mortality as a marker of political stability.

While such headline-grabbing events as the recent China earthquake and the East Asian tsunami of December 2004 are typically followed by a "powerful humanitarian response," Gostin said that help to meet such basic necessities as sanitation, clean air and water, pest abatement and vaccines is more urgently needed in developing countries. "It's disarmingly simple and inexpensive," he said. "They don't need state-of-the-art facilities or foreign aid workers parachuting in to rescue them; they just need basic stuff they can run themselves."

Noting that governments currently exist in a state of "global health anarchy,"

Gostin proposed the creation of an international framework convention on global health modeled on the Kyoto Protocol, which raised the visibility of climate change as a global threat. The framework convention, an idea that is already being discussed by the World Health Organization and other international agencies, would convene key stakeholders for the purpose of addressing health disparities and developing global health solutions.

When it comes to health, "the poor suffer much more than the rich," Gostin said. "Health disparities are no less important than global warming and other issues of the times."

The panel that followed Gostin's talk also pursued the subject of ethics and public health. On the panel was Stewart D. Smith, M.A., M.P.H. '96, a former Navy officer, who served in the first Gulf War and was in the Pentagon on September 11. Since leaving the military, Smith has made a career as a consultant who helps organizations prepare for disaster. However, he has yet to see a company disaster plan that includes an ethics analysis. "Everybody assumes that ethics is common sense, that they intuitively know the right thing to do, and-guess what-they really don't. They need to be taught; and the time to do it is before disaster strikes," he said. For example, a recent government survey found that 73 percent of its employees would not come to work during a flu outbreak. Would it be ethical to require them to? "Get real," said Smith. "Ethics is real."



Curtis Patton presented posthumously the Award for Excellence in Public Health to the late Virginia Alexander. Her great-niece, Virginia Brown, and niece, Rae Alexander-Minter, accepted the award.

Smith was one of four panelists to discuss the importance of ethics in emergency planning and public health. Speaking from their own experienceswhich range from military action to anthrax attacks-the panelists made a strong case for ethics training in public health education and decision making.

James L. Hadler, м.D., Fw '80, м.р.н. '82, who recently retired as chief of the infectious diseases section at the Connecticut Department of Public Health, often juggles benefits to the community and individual rights. (See related story, page 58.) He usually favors the welfare of the community "when the individual can't predictably be harmed." But determining the chances of harm isn't always easy. During a meningitis outbreak on college campuses just a few days before the end of a semester, for example, Hadler had to decide whether to vaccinate more than 12,000 students with jet-injector guns that carried a small risk of cross-contamination with bloodborne pathogens or with injections that would take much longer to administer, thereby putting students at risk of meningitis infections. After consulting with an ethicist and the Centers for Disease Control and Prevention, and researching different brands, Hadler authorized the use of jet-injector guns.

On a smaller scale, there are the problems of running an inner-city clinic. "Do we rob Peter to pay Paul?" asked Thomas J. Krause, м.р.н. '81. For Krause, that question isn't just hypothetical. Krause is chief operations officer at Southwest Community Health Center in Bridgeport, where most of his patients are self-pay or have Medicaid, and every year he faces budget cuts. He

is responsible for delivering health care to poor people, many of them immigrants who have never encountered Western medicine. And he must maintain the morale of a staff that is hamstrung by scarcity and the difficulty of caring for this patient population. In the face of such pressures, it would be easy to think of ways to trim and skimp, Krause said. "But we never go there."

Bruce Jennings, м.А., a lecturer in ethics at the School of Public Health. explored the philosophical underpinnings of the others' real-world stories. The idea that society serves the individual and not the other way around, he said, sometimes "butts heads" with public health when officials must weigh an individual's liberty against the greater public good. Debates from the early days of AIDS provide an example. As the epidemic silently spread, public health officials pushed for greater tracking and surveillance of cases, while others argued that to do so would infringe on privacy rights. Since the AIDS era began, he said, "it has been impossible to take a purely libertarian [standpoint] and it has been impossible to be purely utilitarian." But, he added, "We have to figure out how to get respect for persons and liberty-and outcomes and health-together."

## Awards and the state of the school

Dean Paul D. Cleary, PH.D., delivered good news to those gathered at Alumni Day 2008 at the New Haven Lawn Club-the School of Public Health has gone through a successful reaccreditation process. And, Cleary said, changes are in the works for the school, including a revamping of the global health program.







TOP Christine Walsh received the Distinguished Alumni Service Award, for her contributions to the school and the profession, from Dean Robert Alpern.

ABOVE Tobias Carling, Vikram Reddy and Walter Longo at the Yale Surgical Society Spring Reunion.

"We stopped admitting students to global health last year," Cleary said. "We dissolved the division of global health and created a schoolwide global health program."

In addition, he said, Elizabeth H. Bradley, PH.D., professor of public health (health policy), is developing a global health leadership initiative that will bring practitioners from around the world to Yale. The school has also created an office of community health, led by Elaine O'Keefe, former head of the New Haven Health Department's AIDS division and former health director for the town of Stratford. The new office will oversee student internships, Cleary said. "We will move from a less-thanoptimal approach to a better-focused, more-managed program," he said.

The Association of Yale Alumni in Public Health (AYAPH) presented several awards this year.

Robert E. Steele, M.P.H. '71, PH.D. '75, M.DIV., received the Distinguished Alumni Award for his contributions to the school and the profession. Steele has been on the AYAPH board since 2001 and served as president from 2004 to 2007. He is a founder and benefactor of the Creed/Patton/Steele Endowed Scholarship Fund, which supports future public health professionals. "It is important to support the institutions that have supported us," Steele said as he accepted the award.

The Eric W. Mood New Professionals Award went to Keshia M. Pollack, M.P.H. '02, PH.D., who teaches at Johns Hopkins Bloomberg School of Public Health. She also works for a member of the Maryland General Assembly and advises a Baltimore community coalition seeking to alleviate childhood obesity.

The Award for Excellence in Public Health Practice was given posthumously to Virginia Alexander, M.D., M.P.H. '41. Alexander received her medical degree from Woman's College of Pennsylvania in 1925, but no Philadelphia hospital would accept Alexander, who was African-American, for training. Instead she completed her internship at Kansas City General Hospital, in Missouri, the designated hospital for people of color in that city. After receiving her public health degree from Yale, she became physician-in-charge of women students at Howard University in Washington, D.C. Her niece, Rae Alexander-Minter, ED.D., and great-niece, Virginia Brown, accepted the award on her behalf.

# HN CURTS

## PHYSICIAN ASSOCIATE ALUMNI HOLD REUNION

About two dozen alumni of the Physician Associate Program gathered in June for their fourth annual reunion. The tradition started in 2005, as graduates from the program's 35 years reunited over dinner at the Graduate Club on Elm Street. With program director Mary L. Warner, PA-C (third from left), were, from left, Gary Spinner, PA-C '83; Kenneth Watkins, PA-C '98; and John Cassidy, PA-C '73.

#### 1948

## **60th Reunion**

The 6oth reunion of the Class of 1948 was a great success. As of June this year 31 of the 55 of us who graduated in 1948 were still around, and 15 attended the reunion along with nine of the wives. They were a pretty vigorous bunch of 80-somethings.

Three of our five living women members were there. The prize for vigor has to go to Elizabeth Fuller Elsner, who spends the winter in Alaska where she is addicted to cross-country skiing. She had to take time off this past year to get a new hip but she is now back to her old sport. She spends the summer in Massachusetts and came down on Saturday morning with Nan Godley. Nan still does some volunteer work at Harvard. Sylvia Preston Griffiths also does volunteer work at Columbia.

The prize for the longest trip goes to Al and Ruth Fisk who came from California. They live in the Sonoma valley and until recently had a small vineyard. They also won a gold medal in 2003 at the Cal State Fair for their pinot noir. They have now given up the vineyard and keep busy with duplicate bridge, gardening and leading environmental walks. Next longest was Jock **Bishop**, who is retired from an academic career at Minnesota in internal medicine and research in the physiology and biochemistry of diabetes. He now pursues a hobby in creating rustic furniture from buckhorn wood. In listing our longer travelers I overlooked Dick Buker who is the last member of our class still seeing patients. He is the county health officer of Chester, Mont., and is in charge of disaster planning for his area. He attended with Candace Chang.

**Bob** and Mary **Lempke** joined the group on Friday from Indiana. The OR at the Richard L. Roudebush Indianapolis VA Medical Center was named in Bob's honor. He was chief of surgery there for many years. He has taken up oil paintinglandscapes and some portraits and has had a showing of his works in Indianapolis. **Dave** and Kayoke **Morton** came from Pueblo, Colo. They have been doing a lot of traveling, including trips to Japan to see Kayoke's relatives.

Bud and Esther Rowland, Jack and Ann Strominger and Paul Talalay came from Columbia, Harvard and Johns Hopkins respectively. I mention them together because they probably represent the most successful of our academicians. Paul is the John Jacob Abel Professor of Molecular Pharmacology at Hopkins. He is widely known for his studies of vegetables like broccoli that induce protective enzymes in the body and help prevent cancer. In 2005 he was awarded the prestigious Linus Pauling Award in recognition of his work. Jack is a professor at the Dana Farber institute at Harvard. He has studied histo-compatibility in man and other vertebrates leading to the understanding of mechanisms of immune recognition. In 1999 he received the Japan Prize, the largest monetary reward for scientific investigation. Bud was chief of the department of neurology at Columbia's Neurological Institute and was widely known for his work on stroke.

Paul and Betty Goldstein, Paul and Margaret Koehler, and Dick Richardson represent our clinicians who remained in the Northeast. Paul is the only member of the class who remained in New Haven and has been an anchor for returning alumni. He now spends winters in Florida. When he is in New Haven he spends one day a week in his clinic. Dick Peterson is now retired. He drove down from Southbury, Conn., with his daughter Melanie Barry. Paul and Margaret drove down from Newbury, N.H. Paul served us for 50 years as class secretary. He's still pretty active despite acquiring four artificial joints.

During the spring I contacted almost everyone in our class. I'd like to mention three of our achievers who couldn't come. They are **Herold Griffith**, **Tom Frei**  and Betty McCleary Hamburg. Herold spent eight years as chief of plastic surgery at the University of Illinois medical school. He was made an honorary member of British Association of Plastic Reconstructive and Aesthetic Surgeons, of which there are only eight in the United States. Tom is the Richard and Susan Smith Distinguished Professor of Medicine at Harvard and a member of the Dana Farber Cancer Institute. In 1972 he was given the Albert Lasker Medical Research Award for demonstrating that a combination of chemotherapeutic agents could result in long-term survival and even cures in some leukemias and lymphomas. This award is often a prelude to the Nobel Prize. Betty reports having two careers, first as a professor at Harvard and then as the first director of child psychiatry at The Mount Sinai Medical Center in New York City. After retiring from Mount Sinai, she began a second career as president of the William T. Grant Foundation. Herold couldn't come because his wife is so frail. Tom couldn't make it for health reasons. Betty thought she could come in on Saturday but something must have interfered. Looking forward to seeing all

of you on our 65th. Ben Rush

## 1953

## 55th Reunion

Our 55th class reunion welcomed 10 of our members, who had lively discussions in many venues. Two of our married sets. Ed and Rhoda Powsner and Ora and Howie Smith, added greatly to the pleasure of the weekend. Attending some of the reunion activities were Claude Bloch, Fred Lane and José Ramírez-Rivera. Tom Gentsch was accompanied by wife Betty. Hyla and Bob Melnick had to leave early Sunday to welcome a new grandchild who had arrived on Saturday. Maureen was with Hal Bornstein. Many of our regular attendees had excused absences for a variety of reasons from knee replacement











to family conflicts. Excellent weather enhanced the reunion program, especially the tour of Yale's new West Campus.

Harold D. Bornstein

## 1958

## 50th Reunion

Thirty-two members of our class of 72 graduates were in attendance. Many with their wives or significant others were there to partake of the festivities. George and Anne Aghajanian, Joe and Ann Angelo, John and Trudy Arnot, Gerry and Ann Burrow, Dave and Helen Carlson, Joe Cillo and Tina Callahan, John and Sheila Creatura, Bob and Ellen Donohue, Larry and Reggie Dubin, Don and Helen Duncan, Michael and Liz Fishman, Marcia Kraft Goin, Bill and Sue Gould, Stan and Debbie Harris, Ernie Hartmann, Dick Hinckley, Mike and Jean Kashgarian, Jay and Barbara Kislak, Ted and Dora Lieberman, Tom and Karen Mauro, Bill McClanahan and Anne Bourne, Andy and Lois McGowan, Richard and Eva Miller. Al and Judie Muggia, Bob Neuwirth, Carol Phillips, Bill and Dorothy Radcliffe, Paul and Sandra Rudnick, Bruce Sklarew and Margaret Meyer, Ray and Maria Turner, Jack and Pauli Wood. We missed Bill Schlaepfer who could not attend and were sorry to hear that Chuck Kashima was not doing well. Our Friday night class dinner was held at the old Fulton Mansion on Deepwood Drive. We were fortunate to enlist the Union League Café as our caterers since they produce the best French cuisine in Connecticut. Dean Robert Alpern joined us and assured us that the Yale system, although somewhat modified by external influences, is still alive and well and is attracting the very best students. We started dinner with a toast to honor the 10 members of our graduating class who have passed on over the years. John **Carlston**, Jake Gallagher, Dick Gershon, Jim Greenwald, Ken Jimenez, Mike Lotz, Pat McKegney, Al Phillips, Dave Pugh, Tom Shea, and Bob Wroblewski. Alumni

Day began with a symposium on autism that fascinated and enthralled all who attended. The afternoon was occupied by some with a visit to the new West Campus, where new programs in biotechnology, chemistry, physics, environmental sciences and art preservation will take place, while others had some moments of nostalgia by having pizza at Pepe's on Wooster Street. The weekend ended with dinner with the Friends of the 50th at the Graduate Club, where old friendships were renewed. Mike McCabe did not attend and is still surfing in Hawaii and sends this message "I miss all of you guys. But I love surfing my Hawaiian waves. So, come visit me in Hawaii!"

Mike Kashgarian Gerry Burrow

## 1963

## 45th Reunion

Eleven members of the Class of 1963, many accompanied by their spouses, made their way back to the mother ship for the 45th Reunion. Sending regrets but unable to attend because of illnesses, prior commitments, unavoidable conflicts or intractable lethargy were Wayne Brenckman, Bill Friedewald, Bill Lehmann, Bob Mueller, Bob Grummon, Seth Weingarten, Steve Joseph, Lee Talner, Peter Gregory, Judy Davis, John Mahoney, Rick Back, Dudley Danoff, Allen Flaxman, Ben Harris, Pete Tishler, Larry Tremonti, Jim Dalsimer, Gordon Cohen, John Conte, Bill Porter and Gene Profant. Many commitments were offered for attendance at our 50th in 2013.

Our small but very congenial and talkative group lingered through extensive conversation and reminiscing at Friday's clambake and a marvelous Saturday dinner at the Q-Club. **Art Ackerman**, who has been bringing Western medicine to the backwaters of developing countries over many decades, continues to do so, most recently in Africa (Tanzania and Rwanda) and the Caribbean (Antigua). Colonel **Craig Llewellyn**, fully career, splits his time between Florida and Vermont, while teaching and assisting in the establishment of emergency preparedness teams and procedures at universities. Sheldon Pinnell, a Duke faculty guy since 1973 and self-confessed workaholic, sold his SkinCeuticals Company (for which he developed research-based sunscreen and antioxidant skin protection and restoration products) to L'Oréal, and continues to spend full days in his lab at Durham, having a good time. Dave Fulmer, on the other hand, has his good times at the front end of a fishing rod. Back at the turn of the millennium, Dave decided that he had had enough of managed care and other regulatory baloney and would retire from his internal medicine practice in Princeton, N.J., and start enjoying his seven grandkids. Alex Gaudio continues his full-time retinal disease practice in Hartford, Conn., now with his son, Paul, and spends one day every week maintaining his academic connection at Mass Eye and Ear in Boston. Hal Kaplan finally retired from his gastroenterology practice in July 2007, but continues in his "part-time" medical affairs consulting slot at his old hospital in Meriden, Conn., while finding more time to enjoy his 10 (and still counting?) grandchildren. Mike Fessel, also still hanging out in the New Haven area, practices internal medicine, and, along with Hal, enjoys a clinical appointment to the med school faculty, trying to teach the art of effective communication with patients and family. Andy Edin continues his active internal medicine practice in Minnesota. Part of a large multi-specialty group, he now arranges his patient schedule on his own terms, allowing him time to enjoy his longtime hobby of hunting in Minnesota (these days, without shooting), as well as in any number of remote locations. Alan Shapiro remains happy in an active urology practice in Tinseltown. Helen Walsh, long since moved on from a career in anesthesia to one in psychiatry,

retired from his longtime Army

is quite active and happy with a part-time Massachusetts practice limited to geriatric psychiatry. Also still engaged in a part-time psychiatric practice is **Jay Pomeranz**, who in his free time wields a very competitive tennis racquet in Springfield, Mass.

Twenty-nine classmates contributed to the 45th Reunion Booklet, providing a variety of long and short glimpses of their personal lives, with fascinating details beyond the limited scope of this article. Copies will be distributed by mail to all members of the Class of 1963. This mailing will be the first phase of an intensive campaign to encourage maximum attendance at our 50th reunion, scheduled for June 7–8, 2013. SAVE THE DATES!

Harold Kaplan

## 1968

## **40th Reunion**

Seventeen members of the Class of 1968 came to New Haven for our 40th reunion. Elizabeth Short provided the star attraction with the 2008 edition of the Class Roster, a 139-page summary of the class that will be mailed to all who did not attend. Grace Jordison Boxer came with husband Larry from Michigan. Bob Dillard, who came with wife Laura, reminded us of his passions for treating sick babies and for fly fishing. Alan Finesilver, who came with wife Cindy, is also an avid fly fisherman (Wisconsin and Montana) and works as a volunteer to help find housing for homeless people. Bill Flynn Jr. is still working as a general surgeon with no intention of retiring any time soon. Gil Grand revels in his "perpetual immaturity." Len Grauer, who came with wife Betsy, was "delighted to see everyone." Ralph Greco came with wife Irene Wapnir. Peter Jokl was excused from the fête due to aortic valve surgery a few weeks earlier. Marc Lippman was happy "just to be here." Frank Lucente, who came with partner Stephen Saikin, tells us he is now enjoying "minimal work." Allen McCutchan and wife Emily are anticipating

semiretirement soon. Richard Morehead invites us all to Santa Fe, N.M., for next year's West Coast reunion-a necessary location due to global warming (i.e., no more West Coast). Jim Ogilvie is happy to "see a happy and productive Class of '68. We're not done yet!" Jerry Rauch and wife Nancy have been traveling internationally, rebuilding their house and volunteering at an animal shelter. Peter Kirkpatrick says this event brings back good memories. And Chuck Post has been semiretired for 8 years, sailing along the East Coast and the Caribbean, doing surgery in the Third World and bicycling in various countries.

Donald Lyman

## 1973 35th reunion

Among those who made the pilgrimage were Marv Chassin and wife Barbara. now in Phoenix. where Marv practices oncology. Marvin Miller is the class geneticist; he came from Dayton, Ohio, with wife and children. Sesh Cole and wife Pat came from St. Louis, where Sesh is in pediatrics at Washington University. They left the next day for Dartmouth's graduation. John Brown has retired from his surgical practice in Vancouver, Washington, and spends time in Mexico and Florida; he noted that John Jr. has presented him with grandchildren. Chris (Kull) Walsh arrived from New York with husband Sean. Chris is a pediatric cardiologist at Einstein and has a daughter in her own training program. Harry Romanowitz and wife Sheila drove up from Stamford, Conn., where Harry practices pediatrics. Doug Maddox and wife Kathryn flew in from Atlanta, where Doug is ENT chair at Emory.

On Saturday, Joe Eichenbaum, who practices ophthalmology at Mt. Sinai, and wife Ingrid joined us. Randy Zusman came from Boston; he has been at Mass. General since graduation. Tom Sweeney and Jim Sullivan were both in attendance, representing surgery and medicine in the New Haven community. **Rick** Young attended, fresh from his third tour of duty in Iraq. **Rick** is a pediatric neurologist and chair of pediatrics at the Hospital of Saint Raphael in New Haven. **Neil Handel** attended by phone, unable to make it from Los Angeles where he is a plastic surgeon and the proud father of three young children. I am a gastroenterologist in Dallas, run a colon cancer research laboratory, and still work on my medical school thesis.

We swapped tales about family and professional activities, tried to exchange information about those who weren't there, and made up what we didn't know for certain. We have produced two deans (Lee Goldman at Columbia and Dave **Bailey** at UC Irvine); several department chairs (George Lister in pediatrics at Southwestern Medical Center, Bob Buchholz, who just stepped down from orthopaedics at Southwestern, Jerry Rosenbaum in psychiatry at Mass. General, and probably more); and many division chiefs and other academic leaders. We look forward to seeing more of you at future reunions.

**Richard Boland** 

## 1978

## **30th Reunion**

The Class of 1978 reconvened in New Haven this June for their 30th reunion. Sightings included Rich Baron, Duke and Claudia Cameron. Howard Chase and Claudia McNamara, Stuart and Amy Forman, Bob Gelfand and Susan Boulware, Ken Lee and Ruth Daniel, Yvette Piovanetti and Jose Martinez, Barb and Jordan Pober, Seth Powsner and Elizabeth Yen, Mike Rogawski, Bern Shen, Tom Smith and Joann Bodurtha, Marcia Wade and David Officer, John Wagner and Julie Budd, Jonathan Weinberg, and Susan Wong. Dean Alpern joined our class for dinner at the Graduate Club, either because of our illustrious record of charitable giving to Yale or our legacy of mischief ... you decide. It was a heartwarming and spirited evening. Those not in attendance were missed but also well represented in embarrassing vignettes. Remember this when you consider your plans to attend the 35th! Seth and I will get to work on a class survey to provide a little more detail on everyone's lives. Have a great summer.

Duke Cameron Seth Powsner

## 1983

## 25th Reunion

"Spectacular" describes our reunion. As we gathered on Harkness lawn, at the 333 Cedar St. rotunda, and in the Historical Library, it seemed as though just yesterday we were students.

Attendees included: Mark Boytim and Anne Boytim, Nancy Crocker, Dianne Edgar, Gerri Goodman, Linda Grais and John Freund, Tammy Harris, Rob Homer, Ana Lamas, Judy Melin, Elizabeth Nolan, David Norton, Dan Oren and Jeanette Kuvin Oren, Alan Reznik and Elizabeth Reznik, David Schwartz, Susan Seward and David Seward, Steven Sockin and Susan Sockin, Michael Silverberg, Michael Tom.

Among us are expert clinicians, educators, chiefs, chairs, partners, directors, trustees, researchers and administrators throughout the country. We discussed our residencies, fellowship training, current or prior practice experiences in allergy (Ana, Steve), ENT (Mike T.), ER Med (Elizabeth), ophthalmology (Gerri), orthopaedics (Alan, Mark), primary care specialties (Tammy-FP; Judy, Sue-IM; Dave N., Nancy-pedi). We talked of teaching, research and practice at Yale and in New Haven (Alan, Dan, Rob). We talked of clinical leadership roles in anesthesia (Dave S., Mike S.), of management/VC work in life sciences (Linda), in pharmaceutical research (Dan). of health care administration and policy work (Dave N., Judy, Nancy et al). Most talked of educating medical students and residents (Ana, Dan, Dave S., Gerri, Judy, Rob, Sue et al.).











Our dinner on a sunny summer day at Sage's, formerly Chart House, was the ideal setting for our class photo on the ocean deck. We reviewed **Alan's** copy of our Class Yearbook, **Judy's** copy of our first-year Facesheet, and were proud to learn that it's our class that revived the Yearbook tradition at the School of Medicine.

Other classmates heard from recently include Alan Bloom (ophthalmology), April Hang-Miller (rheumatology), David Helfgott (ID), and Eric Winer (oncology). Tina Young Pouissant and Valerie Stone led the establishment of the memorial fund honoring Yvedt Matory, M.D. '81. We thank Michael Tom, for his leadership role in the Yale Tomorrow School of Medicine alumni fund campaign, our reunion gift volunteers David Schwartz and Eric Winer. and reunion co-chair David Helfgott. We also extend our thanks to Joan Peck of the Association of Yale Alumni in Medicine for organizing our reunion, and to Mary Meehan, director of alumni affairs, and Claire Bessinger of Yale Medicine.

For classmates not here for the reunion, know we talked of your research advances, publications, teaching, leadership, and outstanding care you provide. When we next convene, we'll again prove accurate the refrain from our fourth-year show theme song, that we're "one singular sensation, Yale Med Class of '83." We'll be holding a place for each classmate at our next reunion. Do join us.

Judy Melin

#### 1988

### 20th Reunion

It is hard to believe that it has been 20 years since we left New Haven, especially since everyone who attended looked unchanged from our medical school days. Five of us took a break from chauffeuring our children to their various activities and returned for this year's reunion.

**Dave Chelmow** arrived for the Saturday night dinner. He is the

director of the ob/gyn residency program and the IRB chair at Tufts Medical Center in Boston. He and wife Fay, a hospice nurse, live in Newton, Mass. They have two children, Ben, 15, and Jenny, 11.

Nicole Davis and Alex Vukasin also attended the Saturday night dinner after driving up from Princeton, N.J. Nicole is a gynecologist in solo private practice and Alex is a urologist in a group practice. They have two children, Gabrielle, 16, and Alex, 13.

Irene Freeman attended most of the reunion festivities. She is a pediatrician in a group practice in Chicago. She lives with husband Bob McDonald, an economist at Northwestern University, in Evanston, Ill. They have three children, Claire, 15, David, 13, and Henry, 11.

Rhonda Karol attended the Saturday night dinner with husband Gordon Berger, a managing director of the Bank of New York Mellon (and a very good sport as he was the only non-alum and non-physician present). She continues working as a dermatologist in Forest Hills, N.Y., in the solo private practice she started 13 years ago. They live in Roslyn, N.Y., with their two children, Elizabeth, 13, and William, 10.

We reminisced about absent classmates and exchanged stories about our last sightings of various class members. We also very much missed **Martha Brochin**, who passed away since our last reunion. We hope that more of you will return to New Haven for our next reunion.

Rhonda Karol

## 1998

## 10th Reunion

The Class of 1998 set another reunion attendance record, this time for our 10th. Friday night brought the traditional clambake and overtired children. Saturday was filled with official Yale lectures and touring, capped off by a dinner at the New Haven Lawn Club with dancing to the DJ'ed music of **Richard Lyn-Cook** and his perennial roadie/sidekick, **Steven**  **Williams**. Along the way we got updates from many of our classmates who were there.

Senai Asefaw lives in New Haven, where he works as a hospitalist at Yale-New Haven Hospital and does part-time consulting work. Kristen Aversa lives with her husband and children in Woodbridge, Conn., and continues to practice ob-gyn locally. Tamar Braverman and husband Michael brought their daughters Yael and Talya on Friday night. Tamar is an internist in Branford, Conn. Sydney Butts lives in Syracuse, N.Y., where she works as an ENT surgeon and volunteers her time reconstructing the faces of domestic violence victims. Kent and Shelley Chou flew in from Phoenix, where Kent is an orthopaedic surgeon.

Pediatricians Dan Coghlin and Barb McGee brought children Molly and Henry, who look like clones of their parents. Dan and Barb work in the same practice in Rhode Island. Psychiatrist Caroline **Dumont** lives with psychiatrist husband Brian Tobin and their three mentally healthy children in the New Haven area. Lawrence (Lori) Etter is a dermatologist in Durham, N.C. Husband Jeff Welty and daughter Caroline were barely recognizable beneath layers of sunscreen, hats, and longsleeved shirts. ENT Mark Homicz and Pam Loman came in from California wine country, where they live with their two children. Russ Huang is married, lives in New York and is a spine surgeon. Unfortunately, he has not had much time to play guitar, perhaps explaining the absence of class band Haploid Floyd at our reunion. Or Scott Floyd, for that matter, who wasn't at the reunion but who is a radiation oncologist in Boston.

One of our longest-in-training classmates, neurosurgeon Hahnah Kasowski and husband Robert Seminara live in New York with their son Nathaniel. Lisa Lipschitz practices obstetrics and gynecology in San Diego, where she lives with husband Steve Montal and their two children. Rich Lyn-Cook treats adults and kids, he spins tunes as a DJ, and he can impersonate any human born in the 19th or 20th centuries! The versatile **Rich** lives in Houston with his wife Monica, who is a surgeon but was too busy operating to join us.

After several years on faculty as a hospitalist at the University of Vermont, Ursula McVeigh recently moved to Boston to start a palliative care fellowship. Matt Mealiffe works as the director of clinical research at Perlegen Sciences in the South Bay. Ali Portnoy lives in Villanova, Penn., with husband Raphael Crawford; Ali works for GlaxoSmithKline as medical director of early phase clinical drug development in infectious disease. Ruth Potee lives in western Massachusetts with her husband Steve Martin and three kids; Ruth commutes once weekly to Boston, where she is on the family practice faculty at Boston Medical Center. Ruth is probably our only classmate who still sleeps in a call room once a week. Paul **Pottinger** lives in Seattle with wife Julie and children Zoe and Matthew. Paul is an infectious disease specialist, especially now that he has two children. Nikki Rabidou and her husband have a new baby boy; Nikki practices rheumatology in Torrington, Conn.

**Greg Raskin** lives in New York City and works at Alliance-Bernstein. **Greg** occasionally practices medicine on his wife Jackie Weiss and on his children Daphne and Morris.

Lisa Gale Suter, husband Lindsay and children Fenn and Halvor live near Yale, where Lisa is on faculty in rheumatology. They still have a sluice gate. Kimara Targoff and Josh live in New York with their three children. Kim is an instructor at Columbia in pediatric cardiology, and is also doing research on the regulation of cardiac development. Meena Thayu and husband Eric Keuffel have a year-old daughter Anna and live in Philadelphia, where Meena is a pediatric gastroenterologist at the Children's Hospital of Philadelphia. Ricky Torres isn't even in our class, but he gamely

showed up on Saturday night and danced some salsa. He's on faculty at Yale. **Sus Waikar** is a nephrologist at the Brigham in Boston and lives with his wife and kids in Brookline, Mass.

Steven Williams is a plastic surgeon in San Ramon, Calif., where he lives with his wife. Steve occasionally goes to Honduras on medical missions. Ashley Wivel lives with son Jackson in Philadelphia, where she works for GlaxoSmithKline as a pharmacovigilance specialist. Say that 10 times fast!

Lori Etter

## 2003

#### **5th Reunion**

If there had been one thing the 20 of us in attendance agreed upon, it was that everyone looked the same and no one seemed to have changed a bit. On the other hand, words cannot adequately capture all we have been through since graduating, so I will not attempt the impossible. Instead here are brief updates on those who made it to the reunion:

Severine Chavel Greenspan is finishing her dermatology residency at Yale and will begin private practice in Stamford, Conn., while remaining a volunteer attending at Yale. Severine and husband Mike have a 10month-old girl—Sophie! Mike Greenspan, one of several "Yale lifers" in attendance, is finishing his psych residency after winning the "world's strongest man competition." He will pursue a forensics fellowship at Yale, of all places.

Sean Christensen is beginning a four-year derm residency at Yale and proudly acknowledges his and Elin's official status as "lifers." Elin Lisska Christensen is now a partner in an internal medicine private practice in Madison, Conn. Elin and Sean just bought a house in Guilford. They are also celebrating their second wedding anniversary.

**Doug Davis** has "finally" graduated from the M.D./PH.D. program and is beginning his intern year in Yale's primary care internal medicine program.

**Nataliya Uboha** is beginning her second year of an internal medicine residency at Yale. She and husband Doug have bought a home in New Haven.

**Danny Kanada** had "two more weeks" of Yale radiology residency on reunion day. He's headed to UCSF for a crosssectional fellowship.

**Pramita Kuruvilla** is in the San Francisco Bay Area working as a hospitalist and teaching family medicine residents at Contra Costa Regional Medical Center.

Matt Goldenberg is an emergency psych attending and consultant/liaison at Dartmouth. He is contemplating focusing on refugee mental health and forecasts "liberation" in the near future.

Namita Seth Mohta lives in Cambridge, Mass., with husband Vinay and 10-month-old daughter Aanika. She is a clinical strategy consultant at Partners Health Care and a hospitalist at Brigham and Women's Hospital.

Kyeen Mesesan Andersson met husband Richard during her three years in South Africa completing her M.D./PH.D. She is now starting a postdoc at Yale.

Ada Emuwa, a family medicine physician, is moving with | husband Chi to Nashville, Tenn., and will practice in United Neighborhoods-Health Service Core Clinics for the underserved.

Satish Nagula finished an IM residency at Penn and is now living in NYC with wife Shreya, where he is completing his final year of a GI fellowship at Memorial Sloan-Kettering.

Marta Rivera is a hospitalist at Yale-New Haven Hospital after enjoying a highly recommended seven-month primary care stint in Hawaii post-residency. She has accepted a position in primary care in Virginia Beach, Va.

Dave Ross is finishing his third year in the Yale adult psychneuroscience research training program, where he continues researching his passion—music and the brain. **Rebecca Seekamp** is excitedly moving from Boston, where she is a practicing family doc, to San Francisco, where she will become a clinician-educator in Stanford's family medicine department.

Joahd Toure was found moonlighting in the Yale-New Haven MICU. He is finishing up a Robert Wood Johnson Clinical Scholars fellowship, moving to "the city" for a health care consulting position and still marveling at the recent purchase of a washer and dryer with wife Viviana.

Sunny Ramchandani is now a primary care internist with the U.S. Navy in Bethesda, Md. He is looking forward to seeing his fellow classmates at the next reunion!

Susan Rushing worked as an attorney before returning to medicine. She has two years left in psychiatry training at U Penn, where she assists with health law lectures at the med and law schools. She and husband Karl Richter have two children, Elizabeth, age 2, and Kaitlyn, age 2 months.

As for me, I am working on childhood obesity prevention as a special assistant to the president of the Robert Wood Johnson Foundation and as an obesity medicine consultant to Harvard Health Publications. I dream of resuming clinical work in obesity treatment and lifestyle medicine in the Promised Land (San Francisco).

Our goal is to have the entire class show up for the 10-year reunion. In the meantime, join our soon-to-be-created Facebook group to keep in touch and share news of the many bundles of joy brought into the world thus far as well as other life transitions.

Mark Berman













James Hadler began his career as a physician, but switched to public health. He retired recently after almost 25 years as Connecticut's state epidemiologist and chief of the state health department's Section of Infectious Diseases.

# A career fighting infectious disease

Physician and Connecticut state epidemiologist James Hadler sees the public as his patient.

James L. Hadler, M.D., FW '80, M.P.H. '82, said that his relatives, many of whom are physicians, sometimes tease him for not working at the bedside. "They ask me, 'When are you going to be a *real* doctor?'" But, he said laughingly, "The public is my patient."

Hadler, who retired in June after almost 25 years as Connecticut's state epidemiologist and chief of the state health department's Section of Infectious Diseases, has steered the state through a plethora of public health crises, from AIDS to Lyme disease to anthrax. Although he started his career as a physician while working on the Navajo reservation for the Indian Health Service and the Centers for Disease Control (CDC), Hadler found he liked looking at health from the perspective of populations. The experience, he said, "sold me on a career in public health."

He came to the state health department in 1984, just as the AIDS epidemic was picking up speed. For the first four or five years, "HIV became my life." High-profile debates kept him in the public eye. For example, Connecticut had one of the first cases of a schoolaged child with AIDS, and under national media attention, Hadler developed safety guidelines to allow the child to return to school.

The mid-1990s saw a dramatic shift in emphasis after the Institute of Medicine published a paper stating that the country was unprepared to combat emerging infectious diseases. In 1995, the Emerging Infections Program, affiliated with the CDC, was established in partnership with the state health department and the Yale School of Public Health. It was soon busy with outbreaks of Eastern equine encephalitis and West Nile virus and the re-emergence of the then rare tick-borne diseases babesiosis and ehrlichiosis.

After September 11, 2001, bioterrorism preparedness became a priority. Hadler was on the front lines during that year's anthrax attacks (he still attends an annual symposium in honor of victim Ottilie Lundgren, a Connecticut resident and one of five people who died from exposure to anthrax), and later faced a crisis of conscience when he was instructed to prepare mass smallpox vaccinations prior to the invasion of Iraq, which he strongly opposed. Reasoning that to do so might embolden the Bush administration's threat to invade, he considered resigning. In the end, he decided that to quit or go on strike would not stop the war, and chose to stay, "although uneasily."

While in office, Hadler also oversaw an increase in childhood vaccinations against preventable diseases, the elimination of race-based disparities in childhood vaccination rates and the reduction of the rates of tuberculosis and several sexually transmitted diseases.

Hadler said that what has motivated him, in large part, is the combination of Connecticut's small size and its great population diversity. Its problems come in manageable "little packets." "New Haven has its down-and-out side, Hartford does, but ... they're all small compared to New York or Chicago," he said. "To me, [Connecticut] is a perfect laboratory to try to take on the challenges of diversity and health disparities."

Hadler grew up in Bethesda, Md., where his father worked as a naval architect and international consultant. The family hosted exchange students and had friends from other countries, and Hadler says those experiences—and his stint in Pakistan as an exchange student—gave him and his three siblings a global perspective.

He attended McGill University in Montreal, then went to Columbia University's College of Physicians and Surgeons. After an internship at Roosevelt Hospital in Manhattan, Hadler joined the Indian Health Service in a position supported by the CDC as a tuberculosis control officer. He completed his residency at Waterbury Hospital in Connecticut, did an infectious diseases fellowship at Yale-New Haven Hospital and then earned an м.р.н. Finally, he and his wife and two children spent a year in China as part of a School of Medicine exchange with Hunan Medical College. He began as Connecticut's state epidemiologist the following year.

The job, he said, has allowed him to combine diverse interests and to work with people from all walks of life. "Public health is dynamic," he said. "I love that aspect of the job."

Hadler lives in New Haven with his wife, Alice, who speaks several languages and whose experiences with adult education on the Navajo reservation with her husband grew into a teaching career; she is now an associate dean at Wesleyan. They have three grown children.

Hadler plans to work as a public health consultant to the state and to New York City. He will also write scientific papers, deliver talks and continue to teach at the School of Public Health. —Jenny Blair

## A primary care physician finds peace of mind in concierge medicine

On a typical day two years ago, Steven Fugaro, M.D. '81, saw a patient in his solo primary care practice every 10 to 15 minutes. Onerous paperwork and economic difficulties made it hard for the San Francisco-based physician to provide the quality of care he felt his 3,000 patients deserved. "I was becoming increasingly dissatisfied with what I was doing," he said, "although I was probably too busy to be reflective of it at that point."

Then MD<sup>2</sup>, a concierge medicine group, based in Bellevue, Wash., approached him. Would he like to join them as a concierge physician and gain the time and resources to provide extraordinary care for a small number of patients? His decision to do so changed his life and made him part of a controversial trend in primary care.

Fugaro had opened a private practice after an internal medicine residency at the University of California, San Francisco, and eight years in academic medicine. Although he loved primary care, physicians in that field are under tremendous pressure to see patients in great numbers-time is tight, reimbursement rates are stagnant and preventive care must take a back seat to immediate problems. Few medical students choose the field, and many weary primary care physicians are retiring early or taking jobs in industry or administration. These doctors are in short supply.

Enter concierge medicine. In this model, introduced in 1996 by MD<sup>2</sup> founder Howard Maron, M.D., patients

## **Alumni** FACES

Steven Fugaro traded a solo primary care practice for a career in concierge medicine.



pay a yearly fee ranging from \$15,000 for an individual to \$25,000 for a family of four. In return, physicians make themselves readily available, offering prompt appointments, house calls and other extras.

Critics of the practice, also known as "boutique medicine" or "retainerbased medicine," call it unethical. The retainer is beyond the means of many people and because concierge physicians care for fewer patients than other primary care doctors, the practice increases colleagues' burdens and may endanger access to care. But many concierge doctors say that they would have quit practicing altogether if not for this option. Fugaro agonized for months over his decision. "I was worried about what my colleagues would think. I was worried about ... leaving patients. I wondered if I would be intellectually stimulated," he said. "On the plus side [was] being able ... to have basically unlimited time with

[patients], to be able to care for them in a very holistic way and to have balance back in my life." For Fugaro that meant more time for such pursuits as mountain biking and spending time with his wife of 22 years and their son, who studies theater at Northwestern University.

In 2007, Fugaro arranged for the patients in his primary care practice to be cared for by a successor, Allan Treadwell, м.D., relinquishing the practice free of charge. Then Fugaro ioined  $MD^2$ .

He cares for just 50 families now, and on a typical day sees or speaks to six to 10 of his patients. The office does many of its own tests, with results available on the spot. He makes regular house calls. Many of his patients have complex medical conditions and he is better able to anticipate problems before they arise. "I was juggling so many things before," Fugaro said, "it was clearly possible for something to fall through the cracks, and that's far less likely now." He also accompanies patients to specialty appointments and the ER, and enjoys learning from subspecialty colleagues at such times, "as opposed to just communicating through a consult letter." For about 5 percent of his patients, the retainer fee is waived.

Fugaro is partnered with another physician; neither leaves town unless the other can stay. Though always "on call," Fugaro said he has more time now for nonclinical professional pursuits. In 2007, he was elected president of the San Francisco Medical Society, where he pushes for such public health measures as restrictions on secondhand smoke, and partners with the

California Medical Association to battle Medicaid cuts. He also has volunteered at a clinic in Mexico.

Fugaro says his colleagues' reactions have been mostly positive. Indeed, several are opening retainer-based practices of their own, including Treadwell, the physician who took over his old practice. Fugaro acknowledged that access to primary care is a tremendous problem in American medicine. "We need to create a better model for primary care doctors to continue doing what they're doing and be emotionally rewarded for it, as well as deriving reasonable economic compensation. And right now our system is broken in that regard." -Jenny Blair

## Familiar Faces

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

## NOTES



1960s



Arthur Beaudet John Patti

Jonathan Lewin

1980s



vin Paul Rothman



Lu Anne Dinglasan Kevin Lau

Steven I. Rosenfeld, M.D. '80, is an assistant clinical professor of ophthalmology at the Bascom Palmer Eye Institute in Miami. He received two awards from the American Academy of Ophthalmology at its annual meeting in November 2007: the Senior Achievement Award and the Secretariat Award for "exceptional leadership and enthusiastic service." He serves on the editorial boards of EyeNet Magazine, Focal Points, and the Basic and Clinical Science Course, Section 13: Refractive Surgery, and is an associate examiner for the American Board of Ophthalmology.

Paul Rothman, M.D. '84, was named dean of the University of Iowa's Roy J. and Lucille A. Carver College of Medicine, effective June 1. Rothman has served as head and professor of internal medicine at the UI Carver College of Medicine and UI Hospitals and Clinics since 2004. An expert in rheumatology, he has provided clinical care for more than 20 years, trained medical students, fellows, and residents, and published extensively. Rothman's research on cytokines focuses on their role in the development of white blood cells, the abnormal development of which can lead to leukemia.

## 2000S

Elizabeth K. Arleo, M.D. '04, and her husband, Joshua W. Thompson, J.D., announce the birth of their first child. Sophia Arleo Thompson was born on May 31 and weighed in at 8 lbs., 3 oz. Arleo is in the final year of a radiology residency at New York Presbyterian Hospital-Weill



Carolyn Graeber Robert Jahn

Cornell Medical Center, where she plans to stay for a year-long fellowship in women's imaging. Thompson is a partner at the New York City law office of Proskauer Rose.

Lu Anne V. Dinglasan, M.D. '08, and Kevin C. Lau, M.P.H., M.D. '08, were married on May 31 at the Yale Club in Manhattan. Dinglasan began an internship in June at Pennsylvania Hospital in Philadelphia and Lau began his internship at the Children's Hospital of Philadelphia.

**Carolyn P. Graeber**, M.D. '08, was married on April 26 to Robert E. Jahn at St. Thomas Episcopal Church in Manhattan. Graeber began an internship in June at the Memorial Sloan-Kettering Cancer Center in New York. Jahn is completing an M.B.A. at the University of Pennsylvania.

Mona Kotecha, M.D. '04, was married on April 5 to Nikhil Shanbhag, J.D. '03, in Saratoga, Calif. Kotecha is a fourth-year anesthesiology resident at the University of California, San Francisco. Shanbhag is an intellectual property lawyer at Google in Mountain View, Calif.

## 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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Arthur L. Beaudet, M.D. '67, the Henry and Emma Meyer Professor and chair of the Department of Human and Molecular Genetics at Baylor College of Medicine, has been elected to the Johns Hopkins University Society of Scholars. Beaudet and 14 other esteemed scientists and clinicians were honored during the society's 39th induction ceremony in May. His accomplishments include key discoveries in several genetic disorders, including Angelman syndrome, Prader-Willi syndrome and autism. Beaudet's many honors include the March of **Dimes/Colonel Harland Sanders** Award for lifetime achievement in genetic sciences.

## 1**97**05

Harvey Berger, M.D. '77, and his wife, Chrysanthi, are ecstatic about the latest addition to their family, Isabella Grace Berger, born on March 6. Berger is the founder, chair and CEO of ARIAD Pharmaceuticals, Inc., in Cambridge, Mass., an oncology company developing molecularly targeted cancer drugs.

John A. Patti, M.D. '71, was elected vice chair of the American College of Radiology (ACR) Board of Chancellors at the ACR annual meeting in Washington, D.C., in May. Patti, a member of the radiology staff at the North Shore Medical Center in Salem, Mass., since 1975, is the immediate past chair of the ACR Commission on Economics, current chair of the Task Force on Value Added and vice chair of the Commission on Government Relations.

Josef Bohm, M.P.H. '89, will be joining the faculty of City University's New York City College of Technology as an assistant professor within their Health Services Administration program. Bohm is a former deputy principal to the Anglo-**European College of Chiropractic** in Bournemouth, England. He is a member of the adjunct faculty at the State University of New York at Stony Brook. His academic interests include behavioral economics, health policy and finance.

Jonathan S. Lewin, M.D. '85, has been inducted as a fellow in the American College of Radiology. Lewin is the Martin W. Donner Professor and chair of the Department of Radiology at the Johns Hopkins University School of Medicine. He holds leadership positions in such medical societies as the Academy of Radiology Research, Association of University Radiologists and the International Society for Strategic Studies in Radiology.

**Troy Pappas**, M.P.H. '86, has been appointed to the faculty of the Fox School of Business at Temple University in Philadelphia. He has a dual appointment with Temple's School of Tourism and Hospitality and will be teaching entrepreneurship and business strategy. This fall, he will teach entrepreneurism at Temple's College of Health Professions. He is the founder and president of World Athlete, a sports and fitness management company specializing in track and field.

Rex B. Conn Jr. M.D. '53, died of Parkinson disease on March 2 in Philadelphia. He was 8o. Born in Cedar Rapids, Iowa, Conn taught at West Virginia University in Morgantown, where he established the pathology department and clinical laboratory. He served as a radar specialist in the Navy Reserve during World War II. Conn was subsequently named to advisory committees at the National Institutes of Health, Walter Reed Army Medical Center and the Armed Forces Institute of Pathology. From 1968 to 1977 he taught at Johns Hopkins University School of Medicine. Conn ran clinical labs both there and at Emory University, where he also taught. In 1987 he moved to Philadelphia, where he taught at Thomas Jefferson Medical College until his retirement in 2003.

Alfred Robert Cordell, M.D., H.S. '50, died on April 9 in Winston-Salem, N.C. He was 83. After receiving his medical degree and completing an internship at Johns Hopkins University, Cordell came to the Yale VA Surgical Services for an assistant residency in surgery from 1948 to 1950. Following a stint as a surgeon with the Medical Corps, U.S. Navy Reserve, training in general and thoracic surgery at Wake Forest University, and a year as a visiting instructor in the Department of Surgery at the University of Buffalo, he returned in 1970 to Wake Forest, where he became a professor of surgery. From 1979 to 1991 he served as the Howard Holt Bradshaw Professor of Surgery and chair of Wake Forest's Department of Cardiothoracic Surgery. Cordell developed

techniques in myocardial preservation and blood conservation and established an open-heart program at Wake Forest's Baptist Medical Center. He served on the board of governors of the American College of Surgeons from 1983 to 1989. In September 1995, he was named professor emeritus at Wake Forest; the A. Robert Cordell Chair in Cardiothoracic Surgery was established in his honor.

Roger W. Davis Jr., M.D. '43, died on March 16 in Springfield, Vt. He was 90. After graduation from medical school, Davis completed internships at Hartford Hospital in 1943 and 1946. From 1944 to 1946 he served with the U.S. Army's 174th Engineer Combat Battalion. He completed residencies in orthopaedic surgery at the Hospital for Special Surgery in New York City from 1947 to 1949 and at Boston City Hospital in 1950. He opened a private practice in orthopaedic surgery in Hartford and worked as assistant medical director of the Aetna Life and Casualty Co. From 1974 until his retirement in 1981, he served as a part-time physician in Springfield Hospital's emergency room.

**D. Joseph Demis**, PH.D., M.D. '57, died on March 8 in Clifton Park, N.Y. He was 78. After interning in Seattle, Demis took a fellowship in biochemistry at Oxford University. There he explained the biosynthetic pathway of adrenaline in mammalian tissue and performed pioneering studies that showed the effectiveness of antimetabolites as treatment for psoriasis and similar skin conditions. He received further training in dermatology at Walter Reed Army Hospital in Washington, D.C. His interest in tropical diseases, and especially pinta, a bacterial skin disease endemic to Central and South America, led him to the U.S. Public Health Service. Working with the Brazilian government, Demis helped to eliminate pinta in that country. Demis subsequently served as professor and chair of dermatology at Washington University in St. Louis from 1964 to 1966; at that time he was the youngest chair of a major dermatology department in the United States. After accepting an appointment as professor and chair of dermatology at Albany Medical College, he collaborated to produce the text *Clinical Dermatology*. He also maintained a private dermatology practice.

Frederick James Finseth, M.D., died in February in San Francisco. He was 67. A graduate of Harvard Medical School, Finseth completed a residency in surgery at Massachusetts General Hospital. He was assistant professor in reconstructive and plastic surgery at the School of Medicine from 1974 to 1977. He published several papers on the impairment of blood flow in the hand from cigarette smoking during his years at Yale. From 1977 to 1979 Finseth was an assistant professor in plastic and reconstructive surgery at Stanford University School of Medicine, specializing in reconstructive surgery of the hand. He traveled widely and made annual trips to teach at Tata Memorial Hospital in Mumbai, India. He also taught in South America, Singapore, China and South Asia.

**Steven C. Hebert**, M.D., chair and C.N.H. Long Professor of Cellular

and Molecular Physiology and professor of medicine, died of cardiovascular disease in New Haven on April 15. He was 61.

Hebert was a board-certified nephrologist who devoted his career to the science of renal fluid and electrolyte regulation. He made major contributions to medicine, notably in the cloning of genes that mediate or regulate the transport of sodium, potassium and calcium across cell membranes. His work won him election to the National Academy of Sciences in 2005, and his research was the basis for a new class of drugs used to treat hyperparathyroidism, a hormonal disorder that affects many of the more than 1 million patients worldwide with endstage kidney disease.

Hebert was born in 1946 in Rockford, Ill., and lived for part of his childhood on the island of Great Inagua in the Bahamas, where his father was a contractor for the Morton Salt Co. In a profile published in 2006 in the Proceedings of the National Academies of Sciences, he recalled watching bulldozers pile dried sea salt into mountains 150 feet high and speculated that his interest in metabolic salts may have had its genesis there. He entered Florida State University at age 15 and graduated after three years.

Hebert received his medical degree from the University of Florida in 1970. Following training in internal medicine and nephrology at the University of Alabama at Birmingham (UAB), he served on the faculty at UAB, Eastern Virginia Medical School, the University of Texas Medical School in Houston, Harvard Medical School, and Brigham and Women's Hospital. In 1997



he joined Vanderbilt University as director of the Division of Nephrology and the Ann and Roscoe R. Robinson Professor of Medicine. In 2000 he was offered the chair at Yale, which gave him the opportunity to lead a world-class department and continue his close collaboration with Gerhard Giebisch, M.D., a longtime friend and mentor.

In the early 1990s, Hebert's laboratory made three fundamental discoveries about the kidney's processing of potassium, sodium and calcium. His group identified a channel that regulates potassium excretion and is involved in Bartter syndrome type II, an inherited disorder that causes loss of sodium and potassium through the urine. He and his colleagues also identified two sodium chloride transporters that are target sites for important diuretic drugs. His subsequent discovery of a calcium-sensing receptor known as CASR led to the development of a new class of drugs that modulate calciumreceptor activity.

Most recently, with John Geibel, M.D., D.SC., Hebert demonstrated in an animal model that diarrhea could be reversed almost immediately by activating the CASR receptor. Such treatment would have a major impact on health problems in developing countries, where diarrheal disease kills some 3 million infants and children each year.

Hebert was awarded numerous professional honors, including the Homer W. Smith Award from the American Society of Nephrology, the A.N. Richards Award from the International Society of Nephrology, and the Carl W. Gottschalk Distinguished Lectureship from the American Society of Physiology. Virginia H. Hulbert, R.N., M.P.H. '50, died on January 31 in Ansonia, Conn. She was 97. After earning her degree in nursing, Hulbert worked for more than 30 years as an assistant professor of health at Southern Connecticut State University, and as head nurse in the school's student health department.

D. Frank Johnson Jr., M.D. '55, died on March 31. He was 78. After completing his internship, Johnson joined the Air Force as a flight surgeon. Following a residency in internal medicine at Minneapolis General Hospital, in 1961 he pursued a career in Billings, Mont. For 25 years he was the continuing medical education director for St. Vincent Hospital, where he founded and directed Montana's first cardiac rehabilitation program. He also helped to develop St. Vincent's ICU, its weight control program and its Lifecare outpatient clinic. He was an associate clinical professor of medicine at the University of Washington School of Medicine in Seattle. Later in his career he focused on weight management, directing clinics in Billings, Helena and Bozeman, Mont., while continuing to serve airline pilots in the state as a senior aeromedical examiner designated by the Federal Aviation Administration. He was a member of the North American Society for the Study of Obesity. Among other honors, Johnson received the American Society of Bariatric Physicians' Bariatrician of the Year award in 2002.

Vincent J. Longo, M.D. '46, died on February 18 in Niantic, Conn. He was 85. During World War II, Longo was a member of the Army Specialized Training Program and received a commission as first lieutenant. Following an internship in surgery, gynecology and obstetrics, and a fellowship in urology, he began a urology practice in New London, Conn., in 1952. He joined the staff of Lawrence and Memorial Hospital in New London and served as chief of urology there from 1976 until his retirement in 1986. Longo was a member of the American Board of Urology, a fellow of the American College of Surgeons, and a certified sex educator and therapist with the American Association of Sex Educators, Counselors and Therapists. After retiring he served with Charles Pfizer Pharmaceuticals as principal clinical investigator in the Viagra program.

Gordon V.K. Reid, M.D., H.S. '69, died on April 15. He was 72. After receiving his medical degree from the University of Rochester and further training at Barnes Hospital in St. Louis, Reid served as U.S. Public Health Service lieutenant commander in the **Epidemic Intelligence Service of** the Centers for Disease Control and was sent to India to do smallpox eradication. In 1968 he came to Yale to finish his training in internal medicine, endocrinology and gerontology. Shortly after joining a New Haven practice in 1970, he co-founded the Community Health Care Plan, where he practiced until 1999. He then co-founded Endocrine Associates of Connecticut. Reid was an associate clinical professor of medicine at Yale, attending in internal medicine and endocrinology, and a preceptor for residents from Yale-New Haven Hospital and the Hospital of Saint Raphael.

Galon S. Rodabaugh, M.D., H.S. '53, died on January 9. He was 95. Rodabaugh completed his medical degree and internship at Ohio State University in 1939; practiced for several years in Basil, Ohio; and served from 1942 to 1945 as a captain with the U.S. Army Medical Corps in England, France, Belgium, Holland, Luxemburg and Germany. He saw combat during in the Battle of the Bulge and received two Bronze Stars. After completing a residency at Yale in 1953, he served as anesthesiologist at the Fairfield Medical Center in Lancaster, Ohio, until his retirement in 1984.

William G. Wysor Jr., M.D., H.S. '52, died on January 3 in Chapel Hill, N.C. He was 81. After receiving his medical degree from the University of Virginia, Wysor received post-graduate training at Yale and the Medical College of Virginia. In 1953 he entered private practice in South Boston, Va. From 1957 to 1969 he served as associate professor of medicine at the University of North Carolina (UNC) School of Medicine. From 1969 until his retirement in 1990, he practiced with **Durham Internal Medical** Associates. His honors included teaching awards from Escola Paulista de Medicina in São Paulo, Brazil, where he was a visiting professor, and from the UNC School of Medicine.

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

## Follow-Up



## After a life in medicine, a career in show business

Brock Lynch, M.D. '47, had been singing and dancing with the Young@Heart Chorus for almost 10 years when it was written up in *Time* magazine in June of 2005, and in *Yale Medicine* [See "Tap Dancing Through Medicine," Autumn 2005]. Since the documentary *Young@Heart* was released in April, Lynch and the other performers in the 27-member Massachusettsbased group of elderly rock singers continue to tour to even greater acclaim.

"Little by little, instead of drooping, it grew," Lynch said of the film, which was released only gradually in the United States. Word of mouth and a free showing at the Sundance Film Festival soon accelerated the film's popularity, and chorus members have subsequently traveled not only to perform but to promote the film. Just prior to its release, Lynch traveled to Washington, D.C., and Boston with two other chorus members to answer questions from an audience of critics.

Children, adolescents, and college-aged audiences, he has long noticed, enjoy the live shows the most, while the older demographic seems less appreciative. "They don't go for that music—that was the music [about which] they told their children, 'Turn it down!' " But now that many audience members have seen the film, Lynch said, the group has "rabid devotees."

Lynch recently sang with Young@Heart in Manhattan at the historic Beacon Theater on Broadway, a mile from Memorial Sloan-Kettering Cancer Center, where he was a surgical teaching fellow in the mid-1950s. The "Alive and Well" concert tour also included stops in Boston and the group's home base of Northampton, Mass. The set list included songs by the Rolling Stones, Nirvana and James Brown.

The group plans next to develop a cabaret act, heavy on the soloists. More tours are also in the works. How do they do it? "With grit, guts and good medication," said Lynch.

—Jenny Blair

## Archives 50 AND 25 YEARS AGO



Report on Alumni Day —Alumni Bulletin May 1958

"In spite of a heavy snowfall the preceding weekend and snow flurries on the morning of Saturday, February 22, many Yale Alumni in Medicine turned out for the annual Alumni Day activities at the school. Almost 200 were present at the afternoon business meeting in Fitkin Amphitheater. Dr. Samuel D. Kushlan ('35) presided. Dean Vernon W. Lippard spoke briefly on recent developments at the medical school. Those attending then heard a lively discussion of coronary heart disease by Dr. Jeremy N. Morris, visiting professor of epidemiology."



The Case of Three Missing Hamsters —Yale Medicine Fall / Winter 1983

"Three infected hamsters reported missing from their cage in the animal containment facility on the ninth floor of the Laboratory of Epidemiology and Public Health became overnight celebrities of a sort. 'Infected Yale Hamsters Escape' was headline news for the wire services, major television and radio networks and newspapers across the nation, including the *New York Times*, which devoted almost half a page to the story.

"The hamsters have not been found, and are presumed dead. Although their disappearance caused considerable stir in the media and concern in the University, the three rodents and others like them in the LEPH-9 facility are of little threat to human health and the likelihood that they escaped from the facility is practically nil. ...

"The hamsters were among several hundred research animals in a major study of Alzheimer's disease ... [they were] infected with Creutzfeld-Jakob virus, a socalled 'slow virus,' which is invariably fatal, and causes symptoms of senility similar to those of Alzheimer's disease. ...

"A series of meetings has since been held to ascertain facts of the escape, and to plan remedial actions."

## PRETTY IN PINK

During the academic year, the stainless steel tables in The Anlyan Center's anatomy labs hold the "donors" who have offered their bodies for the education of future doctors and physician associates. For most medical students this introduction to medicine is a charged and emotional experience. In May the students who completed this first-year course spent two days wrapping pink fabric around the tables where they'd dissected the human body. Their inspirations were the artists Christo and Jeanne-Claude, known for their wrappings of such public spaces as the Pont Neuf in Paris.

"To mark the school year's end, student artists have this time wrapped the lab itself, transforming this familiar space and raising critical questions about our relationship to anatomy," wrote Ryan Blum in the program for the installation, called Recovering the Anatomy Lab. The installation was open to visitors for about two weeks in May and June. "What is hidden in the site of dissection? What damage have we done, and how can we make amends? Can and should the lab be made beautiful? What about ourselves is changed? How can we help future classes of anatomy students with this difficult practice?"

About 50 students gathered to bind the anatomy tables in bolts of fuchsia cloth, said Michael Otremba, who conceived of the idea with classmate Lauren Graber. "It's a sterile, metallic environment," said Otremba, adding that students wanted to comment on what he called "an emotionally significant time." The choice of pink was deliberate. "We wanted to be playful."

"I think it's delightful," said William B. Stewart, PH.D., associate professor of surgery (gross anatomy), who has been guiding Yale medical students through the human body for 30 years. "Art is all about people coming to grips with their feelings."

—John Curtis



Evoking the work of artists Christo and Jeanne-Claude, students wrapped dissection tables in the anatomy lab in pink cloth, an installation that helped them deal with their own reactions to the first-year course.

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