Medicine@Yale

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Advancing Biomedical Science, Education, and Health Care

Alumna supports doctors who join her on a road less traveled

Medicine offers satisfying careers in both science and patient care, and at the School of Medicine, students and faculty are encouraged to creatively combine these two vocations as physician–scientists. But Marie-Louise T. Johnson, M.D., PH.D., has forged a career path that is "utterly unique in our field, and an exceptionally lofty model," says Richard L. Edelson, M.D., chair of the Department of Dermatology, who calls Johnson "a physician, scientist, humanist."

At age 83, Johnson maintains a busy dermatology practice in Kingston, N.Y., a city of 23,000 on the Hudson River about 100 miles north of New York City, which draws patients from a wide swath of the surrounding Hudson Valley and Catskills region. But she also boasts a curriculum vitae that bristles with honors, including the Master Dermatologist Award from the American Academy of Dermatology and membership in the National Academy of Sciences' Institute of Medicine. What makes Johnson special, says Edelson, Aaron B. and Marguerite Lerner Professor of Dermatology, is that she blends clinical care with biomedical insight and inspirational teaching. "She sees every medical problem as a mystery inviting a solution, a teaching opportunity, and a very personal challenge."

The rarity of the particular constellation of qualities possessed by Johnson is a testament to the challenges faced by physicians who are as dedicated to advancing medicine as they are to the well-being of their patients. To help others attain this uncommon balance, Johnson has recently made a gift of $1 million to the School of Medicine, creating an endowment to support "clinical scholars" at Yale.

Marie-Louise Johnson

"As a role model, she presents a very high bar," Edelson says of Johnson, who on many Wednesday mornings drives over 90 miles from her home to attend Dermatology Grand Rounds at Yale, often transporting a patient with an unusual or difficult illness. "Though she will be quite hard for anyone to emulate, this gift will help future generations of potential Marie-Louise Johnsons reach for that bar."

Johnson graduated from the medical school in 1956, having already earned her PH.D. in microbiology at Yale in 1954. Since her medical school training preceded the arrival of Yale's first chair of dermatology, she became troubled during her internship at Grace-New Haven Community Hospital (now Yale-New Haven Hospital) by her lack of comprehension of the many skin lesions and rashes she saw in patients admitted // Gift *(page 7)*

Yale's picks to beat cancer: a pair of aces

An illustrious new chief of medical oncology, a leader for the Yale Cancer Biology Institute boost efforts to develop better drugs for cancer

It has been an eventful December for the advancement of basic and translational cancer research at Yale. On the 13th, Yale University announced that Joseph Schlessinger, PH.D., a world-renowned scientist with an unparalleled track record of identifying molecular targets for novel anticancer drugs, was named the first director of the University's new Cancer Biology Institute (CBI), one of five major interdisciplinary research initiatives located on Yale's West Campus.

Just a week before, Thomas J. Lynch Jr., M.D., director of Yale Cancer Center (YCC), broke the news that YCC has appointed Roy S. Herbst, M.D., PH.D., who has also had a distinguished career in the development of new cancer therapies, as chief of medical oncology at Smilow Cancer Hospital and associate director for translational research.

Schlessinger, whose appointment is effective immediately, will retain his positions as chair and William H. Prusoff Professor of Pharmacology at the School of Medicine, dividing his time between the medical campus and West Campus. Herbst comes to Yale in March 2011 from MD Anderson Cancer Center at the University of Texas in Houston, where he is professor of medicine, chief of the section of thoracic medical oncology, and Barnhart Family Distinguished Professor in Targeted Therapies. His appointment marks Herbst's return to Yale, where he received his undergraduate and master's degrees.

TERRY DAGRADI

Joseph Schlessinger (above) will direct the Yale Cancer Biology Institute, a major research initiative that will bring as many as 11 new principal investigators and 150 research scientists to West Campus over the next few years. Roy Herbst (left) has led several clinical trials of the latest anticancer compounds at the MD Anderson Cancer Center in Houston, Texas.

"Dr. Schlessinger has significantly expanded the footprint and faculty roster of the Department of Pharmacology, which was ranked in the top three departments this year by the National Research Council," says Robert J. Alpern, M.D., dean of the School of Medicine. "His taste for excellence has resulted in outstanding faculty recruitments, and we look forward to the application of his talents in building an outstanding Cancer Biology Institute." // Cancer *(page 7)*

Built from scratch, lungs are a big leap in bioengineering

Laura Niklason

Laura Niklason, M.D., PH.D., has spent the past 15 years in the lab developing ways to build new arteries using tissue engineering techniques, but as an anesthesiologist who works in the intensive care unit, she always had another idea rolling around in the back of her head.

Niklason, professor of anesthesiology and biomedical engineering, was troubled that a large number of her patients suffered damage to the lungs, organs that simply don't fix themselves very well after injury or serious illness. Hundreds of thousands of Americans die from lung disease each year, and the only effective treatment for severe cases is transplantation. Unfortunately, this expensive procedure is associated with high mortality and is also limited by an // Lungs *(page 7)*

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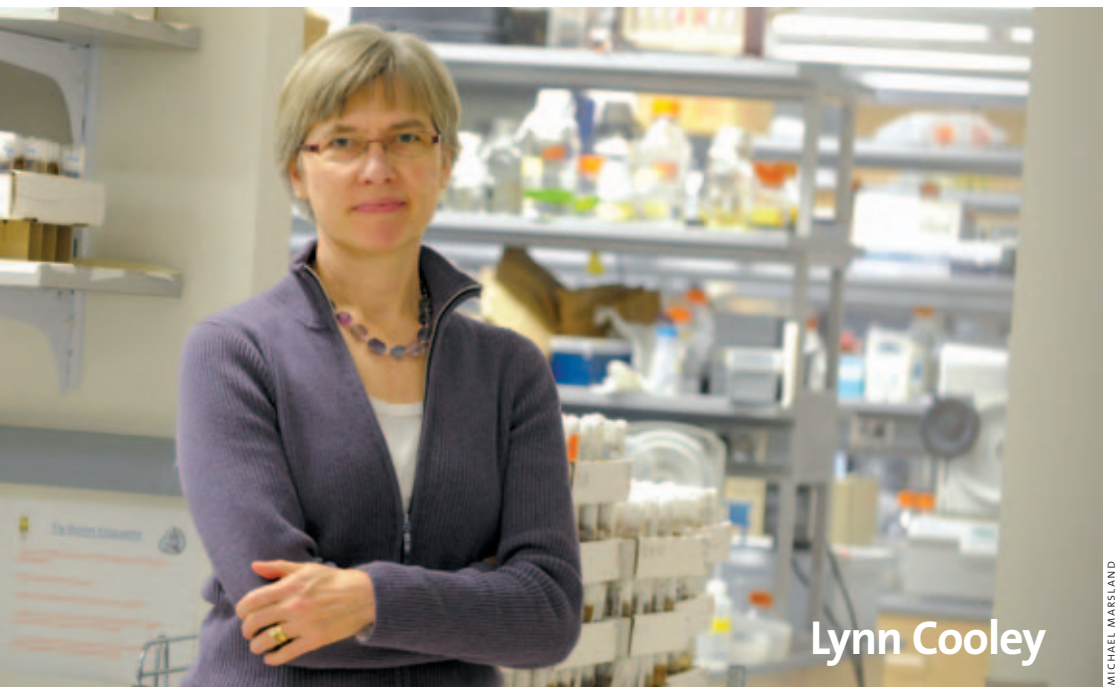

MICHAEL MARSLAND

In an age of increasing emphasis on research explicitly directed toward treatments for human diseases, Lynn Cooley is a passionate advocate of basic, "curiosity-driven" research, which often provides insights that later prove useful in the clinic. Recent studies of ovarian muscle in the fruit fly *Drosophila melanogaster* in Cooley's lab have shown that the fly could provide an important new model of human diseases such as muscular dystrophy.

Putting eggs in a new basket

Science for its own sake can also hatch payoffs, says a Yale geneticist

The laboratory of Lynn Cooley, PH.D., is abuzz, not only with thousands of vials of live fruit flies, but with the excitement scientists experience when their research may cross a new threshold.

Cooley, an authority on oogenesis (egg development) in the fruit fly *Drosophila melanogaster*, says that until recently she would have characterized her work as "one hundred percent basic science." But Cooley believes that recent findings in her lab have great potential for important new insights into human diseases such as muscular dystrophy.

Fruit flies are an all-too-common nuisance in kitchens around the world. But the ubiquity of these tiny flies belies their tremendous importance to biology. More than a century of work on *Drosophila*—a species that is unusually amenable to genetic manipulation and that reproduces and matures rapidly—has helped to unravel the molecular basis of core biological functions; over 60 percent of *Drosophila* genes have counterparts in the human genome.

As a graduate student at the University of Texas–Austin, Cooley, now professor of genetics, cell biology, and of molecular, cellular, and developmental biology, studied proteins in the cytoskeleton, the "scaffolding" of cells. After earning her master's degree, she left graduate school for a time and worked in the Yale lab of Dieter G. Söll, PH.D., Sterling Professor of Molecular Biophysics and Biochemistry and professor of chemistry, "probably the most important influence in my career," she says.

Though Cooley eventually received her doctorate from Texas, she conducted her dissertation research in Söll's lab, studying the formation of histidine transfer RNA, a molecule involved in protein synthesis, in both yeast and *Drosophila*. During a postdoctoral fellowship with Allan C. Spradling, PH.D., at the Carnegie Institution for Science in Baltimore, Md., Cooley began her explorations of oogenesis, working exclusively with *Drosophila*, and settled on the research niche and the model species that have defined her work ever since.

Cooley and those in her lab study not only the formation of eggs but the chambers in which eggs form, the flow of information and nutrients from so-called nurse cells to oocytes (developing eggs), changes in the cytoskeleton during egg development, and the role of muscle tissue in the progression of developing egg chambers through the *Drosophila* ovary.

In a 2008 study reported in *Developmental Biology,* Cooley and colleagues used a technique known as protein trapping to selectively tag specific components of ovarian muscle in *Drosophila* with fluorescent molecules, revealing surprising details of these structures that had previously received little attention from scientists.

"Then a student started trying to use the ovarian muscles as a model for studying mutations in proteins that cause muscular dystrophies," says Cooley. "So now I feel at least I have a toe in the door for developing what we love about *Drosophila* oogenesis as a more translationally oriented model."

But Cooley, who also directs the cross-campus PH.D. program known as the Combined Program for Biological and Biomedical Sciences, emphasizes that the potential of *Drosophila* ovarian muscle as a model for human disease was revealed by basic research, which is in danger of being "downgraded" by society's increased demand for translational work. It's essential, Cooley believes, "for curiosity-driven science to continue, since you never know where efforts to figure out how biology works will lead."

Associate dean wins top honor in medical education

Rosemarie Fisher

Rosemarie L. Fisher, M.D., professor of medicine and pediatrics and associate dean for graduate medical education, has received the Dema Daley Founders Award, the highest honor bestowed on medical educators by the Association of Program Directors of Internal Medicine. The award honors a member of the internal medicine community recognized internationally as an educator, innovator, and leader.

Fisher has spent 35 years on the School of Medicine faculty, including 12 as director of graduate medical education at Yale-New Haven Hospital (YNHH), a role in which she oversees all residency programs, and seven as associate dean. She is the former program director for the Department of Internal Medicine's residency program. As a member of the YNHH Nutrition Support Team, Fisher's research has focused on the role of nutritional support such as intravenous feeding in gastrointestinal diseases.

She received her medical degree from Tufts University School of Medicine in 1971 and completed a residency in internal medicine at Montefiore Hospital and Medical Center in New York City. She completed fellowships in gastroenterology at both the Royal Free Hospital in London and at Yale. Fisher is board-certified in gastroenterology and internal medicine.

In 2006, Fisher was one of two people to win the first Parker J. Palmer Courage to Lead Award from the Accreditation Council for Graduate Medical Education, which honors excellence in overseeing residency programs.

Annual auction nets more than $25,000 for New Haven charities

The annual student-run Hunger and Homelessness Auction, held on November 18, garnered more than $25,000 for New Haven charities.

The event started with a silent auction featuring California wines, fencing lessons, movie tickets, and an incomparable evening of watching sports or action movies on TV (plus dinner of corn dogs and turkey burgers).

Some off-beat services were offered by students to bidders: "I will be your running buddy for any distance and any speed"; "I will make a breakup phone call for you and explain to your significant other why the relationship is over."

At an evening live auction, first-year students Alex Kula and Conor Brady served as auctioneers and led the bidding on items that included a faculty vs. medical student softball game; a dinner and wine tasting at the home of Dean Robert J. Alpern, M.D., Ensign Professor of Medicine; tickets to a Red Sox baseball game; and a four-hour cruise on the sailboat of James D. Jamieson, M.D., PH.D., professor of cell biology.

This year's proceeds will benefit Loaves and Fishes, Columbus House, New Haven Home Recovery, Downtown Evening Soup Kitchen, Community Health Care Van, and the Community Soup Kitchen.

JOHN CURTIS

First-year medical students Alexandra Adler (left) and Eileen Harder (right) make bids at the student-run Hunger and Homelessness Auction.

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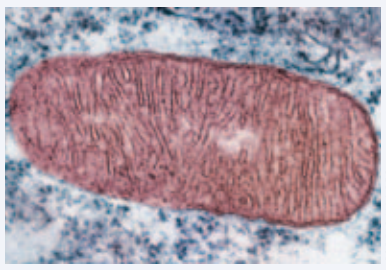
It all adds up: diabetes and oxidative stress



CORBIS IMAGES

We need oxygen, but it comes with a catch. Aerobic metabolism produces reactive oxygen species (ROS), which are toxic to mitochondria (one is pictured above), the "power plants" of cells.

Gerald I. Shulman, M.D., PH.D., the George R. Cowgill Professor of Physiological Chemistry, has proposed that type 2 diabetes mostly affects older people because cumulative ROS-induced damage reduces mitochondrial activity, which predisposes older individuals to intracellular fat accumulation and insulin resistance—the major factor in the development of the disorder.

Shulman and colleagues engineered mice to express high levels of the antioxidant enzyme catalase in mitochondria to tamp down ROS. As reported in the December issue of *Cell Metabolism*, the mice were protected from age-related declines in energy metabolism, intracellular fat accumulation, and insulin resistance.

"It is estimated that 40 percent of the U.S. population over 65 has impaired glucose tolerance or type 2 diabetes. Targeting ROS in mitochondria may prevent and treat diabetes in these individuals," Shulman says.

How the brain may find a way around autism

Research at the medical school's Child Study Center (CSC) has shown that autism spectrum disorder (ASD) can disrupt children's ability to recognize "biological motion," the distinctive repertoire of movements made by living things, including other people.

In a study reported in the December 7 issue of *Proceedings of the National Academy of Sciences*, Kevin Pelphrey, PH.D., Harris Associate Professor in the CSC, first author Martha D. Kaiser, PH.D., and colleagues used functional magnetic resonance imaging (fMRI) to scan the brains of children with autism, their unaffected siblings, and typically developing children as the children watched animations of biological movement. The team identified three distinct "neural signatures": trait markers—reduced regions of activity in both children with ASD and their unaffected siblings; state markers—reduced activity seen only in children with ASD; and compensatory activity—enhanced activity seen only in unaffected siblings of ASD patients.

This enhanced compensatory brain activity is of particular interest, say the researchers, because it may reflect a developmental process by which unaffected children overcome a genetic predisposition to develop ASD.

Medical school's mentors 'pay it forward'

Seasoned pros are vital in preparing students to succeed on their own

HAROLD SHAPIRO

Pediatric surgeon and scientist Christopher Breuer (left) is "a very easy person to talk to," says Daniel "Pete" Duncan (right), a student spending an additional year of medical school doing research in Breuer's lab. Breuer and colleague Toshiharu Shinoka are pioneers in the use of tissue engineering techniques to build new blood vessels for children with heart disease.

Though few of the hundreds of busy people who pass through the doors of Sterling Hall of Medicine each day notice the Greek inscription on a plaque overhead, the language there says much about life at the School of Medicine. In translation it reads, "Those having torches will pass them on to one another."

Some torches are passed straightforwardly. During their training, medical students, doctoral students, and even postdoctoral associates learn facts, many thousands of them. But as in all fields, from the law to violin-making, to ultimately succeed in medicine or science there is no substitute for learning the ropes from a seasoned mentor. Throughout its 200-year history, mentorship has been integral to the mission of Yale School of Medicine, where it plays a part today in nearly every sphere.

A hand up in medicine

Until recently, Associate Dean for Student Affairs Nancy R. Angoff, M.P.H., M.D., served as advisor to every member of every medical class at Yale, providing counseling in every realm from the academic to the personal. In 2009 the advising duties were split among four faculty, each of whom guides one quarter of each class. While they are not mentors in the strictest sense of the word, the new advisors—John S. Francis, M.D., PH.D., assistant professor of medicine; Karen J. Jubanyik-Barber, M.D., assistant professor of emergency medicine; Michael K. O'Brien, M.D., PH.D., assistant professor of surgery; and Patrick G. O'Connor, M.D., M.P.H., professor of medicine—meet with students individually during students' first year, and in groups thereafter. Angoff still stands by to lend a hand with personal or social challenges, but the new advisors concentrate on "any kind of academic problems, struggles, issues," Angoff says.

The School of Medicine requires that medical students complete a thesis based on original research. Students are encouraged to independently seek out and contact researchers they'd like to work with, but many begin their research after their first year, before they are familiar with the many research options available to them. One role of the advising team is to help pair up students with mentors who can best guide medical students through the projects that will ultimately form the basis for their theses.

Medical student Daniel "Pete" Duncan, who is spending an extra year at Yale devoted to research, chose to work with Christopher K. Breuer, M.D., assistant professor of surgery and pediatrics, who uses tissue engineering techniques to build new blood vessels for children with congenital heart disease. With colleague Toshiharu Shinoka, M.D., PH.D., associate professor of surgery, Breuer has pioneered the use of tissue-engineered vascular grafts (TEVGs). Created by seeding a biodegradable scaffold with a patient's bone marrow cells, TEVGs are living vessels that live and grow with the patient and are not prone to the immunological problems that affect transplanted tissue.

Despite Breuer's busy schedule, which also includes clinical work as a pediatric surgeon, "somehow he is always keeping track of what we're doing," Duncan says. "When he's in his office, he is always available. I'm interested in pediatrics, and he is very excited about that, very supportive, and willing to help in any way. He's a very easy person to talk to."

For his part, Breuer stresses that mentoring students is a two-way street, with great benefits for his lab. "It's a wonderful give-and-take relationship," he says. "I've got incredibly enthusiastic and accomplished people that come and help me with my project. I'm a huge beneficiary of working with these bright, hard-working people."

Faculty and graduate students

In addition to future doctors, future scientists also train in many departments at the School of Medicine, ultimately earning the PH.D. Graduate students study at the medical school via the Medical Scientist Training Program (MSTP; known more commonly on campus as the M.D./PH.D. Program), which is devoted to educating physician–scientists, and the Combined Program in Biomedical and Biological Sciences (BBS), which gives PH.D. students experience in several labs at both the university and the medical school before they settle into a BBS-affiliated department, many of which are at the School of Medicine.

Daniel Okin, a member of the medical school's Class of 2014 in the M.D./PH.D. Program, and Noah Palm, a doctoral candidate in the BBS program, both work in the laboratory of Ruslan Medzhitov, PH.D., the David W. Wallace Professor of Immunobiology and a Howard Hughes Medical Institute investigator. Medzhitov is world-renowned for his work on the innate immune system, the body's first line of defense against infection.

"When I heard about him and read some of his papers, I was immediately drawn to working with him," Okin says of Medzhitov. "Ruslan is probably one of the most creative thinkers that I've ever encountered."

After doing a rotation in Medzhitov's lab, Okin decided to join the research team during his second year of medical school. Okin, who is conducting research on the innate immune system's response to nonpathogenic stressors such as obesity, describes Medzhitov's approach to mentorship as "very collaborative. It's very much that you work with him, together, to define an area that you're both interested in, and to define a project that would be interesting both intellectually and scientifically." Having spent more than

// Mentors *(page 6)*

To honor your own mentor . . .

Ask any successful person about their road to achievement and you're likely to hear the story of a valued mentor or advisor who played a key role. Your gift can help faculty members at the School of Medicine to provide guidance and inspiration to the next generation of physicians and scientists.

- **Support student research:** Every medical student at Yale completes a thesis based on original research; access to research funds gives students the opportunity for meaningful participation in the laboratories of top faculty researchers.
- **Endow an advisor:** The Yale System of medical education encourages students to explore their individual interests and to advance at their own pace within the curriculum. In this individualized program, each student needs an advisor to get all they want and need from their education.

Who helped you along the road to success? Honor them today with a gift to help others "pay it forward." For more information, contact Jancy Houck, assistant vice president for development and director of medical development, at (203) 436-8560.

MEDICINE » tomorrow

OUT & ABOUT

September 30 Faculty and staff of the School of Medicine and Yale Cancer Center joined employees of Tucker Mechanical, of Meriden, Conn. (an EMCOR Company) to form a **Human Pink Ribbon** in support of Breast Cancer Awareness Month. More than 160 people participated in the event.

TERRY DAGRADI

October 16 At **Community Day**, part of a series of events celebrating the School of Medicine's Bicentennial, faculty and staff provided tours, demonstrations, and lectures for members of the New Haven community. **1.** New Haven Mayor **John DeStefano Jr.** made remarks on the steps of Sterling Hall of Medicine. **2. Linda Pellico**, PH.D., A.P.R.N., assistant professor at Yale School of Nursing (right), led an educational session for children. **3. John Gallagher**, M.L.S., deputy director of public services at the Cushing/Whitney Medical Library, led a tour of the new Cushing Center, which houses brain specimens, photographs, drawings, and memorabilia collected by famed neurosurgeon and Yale College alumnus Harvey W. Cushing, M.D.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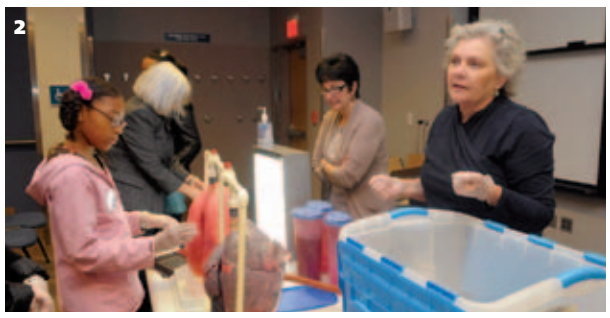
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MICHAEL MARSLAND (3)

October 16 At the **Discovery to Cure Gala**, held at the Stamford Marriott Hotel & Spa in Stamford, Conn., over $200,000 was raised for cancer screening for women at high risk, the training of high school students for careers in biomedical research, and the translation of basic research in gynecological oncology into practical treatments. **1.** News analyst and political commentator **Cokie Roberts** delivered the evening's keynote speech. **2.** (Seated, from left) Discovery to Cure committee members **Michelle Mills**, **Gladys O'Neil**, **Stephanie Ercegovic**, **Arlene Schwartz**, and **Judi Egbert**. Top: **Gil Mor**, M.D., PH.D., professor of obstetrics, gynecology, and reproductive sciences and creator of the Discovery to Cure program; **Peter E. Schwartz**, M.D., the John Slade Ely Professor of Obstetrics, Gynecology, and Reproductive Sciences; **Thomas J. Rutherford**, PH.D., M.D., associate professor of obstetrics, gynecology, and reproductive sciences; **Jacques Dickinson**, and **Charles J. Lockwood**, M.D., the Anita O'Keeffe Young Professor of Women's Health and chair of the Department of Obstetrics, Gynecology, and Reproductive Sciences. **3.** (From left) **Melissa Sheehan**, **William B. Sheehan**, Discovery to Cure committee member **Wendy Long**, and **James Long**.


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HAROLD SHAPIRO (3)

October 28 The Branford, Conn.-based **Jack of All Hearts Foundation** (JOAH) made a gift of $3,000 to support pediatric cardiology programs at Yale-New Haven Children's Hospital and a fellowship in pediatric cardiology at the School of Medicine. **Laura and Mark Hanson**, whose son, Jack, was born with a rare congenital heart defect, cofounded the organization. In September, the first JOAH Walkathon netted $10,500. (From left) **Clifford W. Bogue**, M.D., associate professor of pediatrics; Mark Hanson; Laura Hanson; **Alan H. Friedman**, M.D., professor of pediatrics; and JOAH board member **Melissa Thibeault**.

COURTESY OF JOY CARRIGAN

TERRY DAGRADI

November 4 A reception was held in the Medical Historical Library honoring **John A. Persing**, M.D., professor of surgery and neurosurgery, recently named the inaugural **Irving and Silik Polayes Professor in Plastic Surgery**. The new professorship was established with a $2.5 million gift from the late Maurice B. "Moe" Polayes, and is named in honor of his brother, Irving M. Polayes, M.D., and his late great-uncle, Silik H. Polayes, PH.D. Irving is a retired New Haven surgeon and dentist who was a voluntary faculty member in the Department of Surgery's Section of Plastic Surgery from 1965 to 1997. Silik earned his graduate degree from Yale in 1921 and worked as a pathologist in New York. From left: Persing with Maurice Polayes's children, **Amy Polayes Margolis** and **Roy Polayes**.

Stomach acid zapped by a single dose of zinc


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Gastroesophageal reflux disease (GERD, or "heartburn") and related diseases caused by excess stomach acid affect more than a quarter of Americans, but existing therapies often don't work. About 60 percent of patients still experience symptoms while taking commonly prescribed proton-pump inhibitors (PPIs) such as omeprazole (e.g., Prilosec).

These drugs have been linked to the depletion of zinc, an essential nutrient that protects the stomach lining and heals ulcers. In a new study led by John P. Geibel, M.D., D.Sc., professor of surgery and of cellular and molecular physiology, a team of Yale and Swiss researchers found that zinc itself is significantly better than omeprazole at combating stomach acid. As reported online August 24 in the *American Journal of Gastroenterology*, adding zinc to sections of stomach tissue immediately abolished acid secretion triggered by the compound histamine, and oral zinc treatment in rats prevented acid secretion.

The researchers also found that zinc treatment in healthy humans is faster and more effective at lowering gastric acid levels than omeprazole: a single dose works within seconds and lasts for about three hours. "This opens a promising new avenue of treatment for suffering patients," says Geibel, "especially the many who continue to have symptoms of acid-related illness even after a standard dose of PPIs."

Connections that stick: SynCAM 1 and synapses

Synapses, the junctions where signals pass between nerve cells, are crucial to thought and behavior. Plasticity, synaptic reorganization throughout life, underlies learning and memory. School of Medicine scientists have discovered that SynCAM 1, an "adhesion molecule" that spans synapses, is essential for synapse formation during development and maintenance in adulthood.

In the December 9 issue of *Neuron,* Thomas Biederer, PH.D., associate professor of molecular biophysics and biochemistry, and colleagues describe mice in which the SynCAM 1 gene could be switched on and off at will. More synapses formed during development when SynCAM 1 was overexpressed, and the molecule was required to maintain synapses in adults. But mice lacking SynCAM 1 showed enhanced plasticity, performing better on spatial learning tests than mice overexpressing it.

"Some SynCAM 1 is needed to promote contact," Biederer says, "but too much glues down the synapse and inhibits its function. These findings provide new molecular insight into synaptic aberrations underlying developmental brain disorders such as autism."

Tiny scope is a big advance for GI cancers

New confocal laser endomicroscopes offer doctors an unprecedented view to diagnose early malignancies


ROBERT A. LISAK

(From left) Yale Medical Group's Harry Aslanian, Priya Jamidar, and Uzma Siddiqui are using powerful new high-resolution microscopes to peer deep into the digestive tract, making it possible to detect cancers at early stages when they can be successfully treated.

Last year, when Harry Aslanian, M.D., associate professor of medicine, first looked at images produced by a new diagnostic device known as a confocal laser endomicroscope, he saw what no one had seen before: stunning, high-resolution images of cells, individual red blood cells within vessels, and scar tissue within a pancreatic tumor, all magnified 1,000 times.

For the first time, a miniaturized prototype microscope was passed into a pancreatic mass via a small needle that traveled through the stomach wall, obtaining amazing real-time pictures of an organ that is notoriously difficult to reach, and tricky to evaluate even by CT scans or MRI.

"The quality was very good," recalls Aslanian, associate director of endoscopy for Yale Medical Group (YMG), who was taking part in the world's first visualization of the interior of a pancreatic mass using confocal laser endomicroscopy (CLE).

Aslanian and Uzma Siddiqui, M.D., specialize in combining ultrasound and endoscopy to evaluate and perform biopsies in pancreas disorders. Previously, endosonographic views of the pancreas showed only its overall texture, and needle biopsies were required to examine and stain individual cells outside of the body. Aslanian and Siddiqui are participating in an international trial using CLE to diagnose precancerous pancreatic cysts, which can be surgically removed. "Now we're in the process of fine-tuning this, making a road map to identify precancerous change," Aslanian says.

High-resolution confocal microscopes are a mainstay in biomedical research, but they have evolved from what Aslanian calls "tabletop versions" to scopes that measure only 2.5 millimeters in diameter. Yale Cancer Center and Smilow Cancer Hospital at Yale-New Haven are among only a handful of institutions in the world and the only centers in Connecticut using the technology. The microscopes fit through the biopsy channels of many endoscopes, the lighted optical instruments gastroenterologists use, to look deep inside the body to spot cancer and precancerous tissue at their earliest stages of development, when many conditions are curable with surgery.

Doctors at YMG are also using CLE to gain new views of the colon, bile duct, and esophagus. Siddiqui, YMG's director of endoscopic ultrasound, has used the technique to examine patients with Barrett's esophagus, a disorder associated with long-term esophageal reflux disease that can be a precursor to esophageal cancer. Siddiqui says the microscopic probe helps her target the most suspicious regions of dysplasia, or precancerous tissue changes. Meanwhile, gastroenterologist Priya Jamidar, M.D., director of endoscopy at YMG, is using CLE to diagnose bile duct tumors, where current tissue sampling techniques are only reliable about half the time.

"It's an impressive technology that is much less invasive for our patients, providing on-the-spot information that can guide the endoscopic evaluation, and, in some cases, treatment," says Aslanian. In cases of early esophageal and colon cancer, he says, the earliest tumors can be removed through the scope during the same procedure with the specialized techniques of endoscopic mucosal resection. "The potential for the microscope is that we can look at the cells in real time and identify the ones that are likely to progress to cancer."

Yale cell biologist is honored with two awards

James E. Rothman, PH.D., the Fergus F. Wallace Professor of Biomedical Sciences and chair of the Department of Cell Biology, has been awarded both the E.B. Wilson Medal and the Massry Prize for his seminal contributions to the field of cell biology.

The Wilson Medal, the highest honor for science presented by the American Society for Cell Biology (ASCB), is awarded "for far-reaching contributions to cell biology over a lifetime in science." The Massry Prize, established in 1996 and awarded by the Meira and Shaul G. Massry Foundation, honors individuals who have made "outstanding contributions to the biomedical sciences and to the advancement of health."

Rothman is widely recognized as a pioneering researcher in membrane trafficking, the means by which proteins and other materials are transported within and between cells.

Rothman has made particularly important contributions to our understanding of exocytosis, a form of trafficking in which spherical sacs called vesicles fuse with cell membranes to deliver their contents outside the cell. Exocytosis plays a crucial role in the nervous and endocrine systems. In neurons, vesicles carrying neurotransmitters pass on chemical messages that govern movement, perception, cognition, memory, and mood. In hormone-producing endocrine cells, substances such as insulin enter the extracellular space or the bloodstream via exocytosis.


James Rothman

For three decades, Rothman has performed elegant, focused experiments that have revealed the molecular machinery of membrane trafficking in fine detail. Much of this work was done using an innovative "cell-free" approach, in which Rothman sidestepped the complexities of working with complete cells by isolating the intracellular components crucial to membrane trafficking. This strategy allowed him to propose that complexes of membrane-associated proteins which he named SNAREs are required for vesicles to fuse with membranes.

Rothman, who has spearheaded the creation of a new Center for High-Throughput Cell Biology at Yale's West Campus, came to Yale from Columbia University in 2008. A 1971 Yale College graduate, he is the recipient of some of the top honors for biomedical research, including the Louisa Gross Horwitz Prize and the Albert Lasker Basic Medical Research Award. In June of this year, Rothman shared the Kavli Prize in Neuroscience with Thomas Sudhöf, PH.D., of Stanford School of Medicine, and Richard H. Scheller, PH.D., executive vice president of Genentech, for his work on exocytosis.

The ASCB, founded in 1960, aims to promote and develop the field of cell biology, and to ensure the future of basic scientific research by providing opportunities for scientists and keeping Congress and the American public informed about the importance of biological research.

The Massry Foundation was created by Shaul Massry, M.D., professor emeritus of medicine, physiology, and biophysics at the University of Southern California's Keck School of Medicine. The non-profit organization is dedicated to the promotion of education and research in nephrology, physiology, and related fields.

Grants and contracts awarded to Yale School of Medicine

March/April, 2010

Federal

Steven L. Bernstein, NIH, *Treating Low-Income Smokers in the Hospital Emergency Department,* 5 years, $3,343,594 • **Linda K. Bockenstedt,** NIH, *Real-Time Imaging Analysis of Vector-Borne Lyme Borreliosis Pathogenesis and Persistence,* 5 years, $2,068,750 • **Sonia Caprio,** NIH, *Neural Functioning of Feeding Centers in Obese Youth,* 5 years, $2,726,025 • **Jessica A. Cardin,** NIH, *Impact of Local Network Dynamics on Visual Cortex Function,* 3 years, $607,988 • **Katarzyna Chawarska,** NIH, *Development of Face Processing in Infants with Autism Spectrum Disorders,* 5 years, $2,068,750 • **Jersey Chen,** Agency for Healthcare Research and Quality/DHHS, *Geographic Variation in Use of Imaging with Cardiac Stress Testing,* 5 years, $723,060 • **Nihal C. deLanerolle,** Office of Naval Research, *Understanding the Biomechanical, Biochemical, Physiological and Functional Consequences of Explosive Blast Injury to the Human Brain—PREVENT Phase II,* 2 years, $1,409,700 • **Gary V. Desir,** NIH, *Renalase Deficiency and Cardiovascular Complications of Chronic Kidney Disease,* 1 year, $500,000 • **Sabrina Diano,** NIH, *A Carboxypeptidase in the Regulation of Hypothalamic Circuitry,* 4 years, $1,443,989 • **Robert Dubrow,** NIH, *Patterns of Care and Outcomes for Glioblastoma Patients,* 2 years, $165,500 **Veraragavan P. Eswarakumar,** NIH, *Mechanisms of FGFR2 Signaling in Craniofacial Development,* 5 years, $2,079,310 • **Adrienne S. Ettinger,** NIH, *Genetic and Epigenetic Modifiers of Maternal–Fetal Transfer of Toxicants & Outcomes,* 20 months, $256,017 • **Carlos A.V. Fragoso ,** NIH, *Defining Chronic Obstructive Pulmonary Disease in Older Persons,* 2 years, $135,710 • **Patrick G. Gallagher,** NIH, *Molecular Biology of Human Erythrocyte Alpha Spectrin,* 4 years, $1,655,000 **Peter M. Glazer,** NIH, *Epigenetic Regulation in Hypoxic Cancer Cells,* 5 years, $1,682,723 **Michelle Hampson,** NIH, *Biofeedback of Real-Time fMRI to Control Activity in the Orbitofrontal Cortex,* 2 years, $496,500 • **Kazue Hashimoto-Torii,** NIH, *Mechanisms Leading to Cortical Dysplasia in Fetal Alcohol Spectrum Diseases,* 2 years, $176,874 • **William H. Konigsberg,** NIH, *Molecular Biology and Structure of DNA Replicase,* 4 years, $1,456,400 • **Gary Kupfer,** NIH, *HTLV-I Tax1 Protein Chemosensitization of p53 Mutant Tumors,* 2 years, $395,959 • **Janghoo Lim,** NIH, *The Role of Nemo-Like Kinase in Neurodegeneration,* 3 years, $249,000 • **Steven Marans,** Substance Abuse and Mental Health Services Administration, *Childhood Violent Trauma Center,* 3 years, $1,799,997 **James C. McPartland,** NIH, *The Developmental Neuroscience of Social Perception in Infants At Risk for Autism,* 4 years, $728,429 • **Peter T. Morgan,** NIH, *Modafinil, Sleep Architecture, and Cocaine Relapse,* 5 years, $2,558,685 • **Walther H. Mothes,** NIH, *A Novel TRIM Protein Involved in Innate Immunity,* 2 years, $496,500 • **Michael H. Nathanson,** NIH, *A Confocal Endomicroscope for Clinical Research,* 1 year, $159,900 • **Kitt Falk Petersen,** NIH, *Mechanisms of Insulin Resistance in the Aged,* 5 years, $1,696,375 • **Marc I. Rosen,** NIH, *Benefits Management for People with Psychiatric Disabilities,* 3 years, $480,324 **Joseph Santos-Sacchi,** NIH, *Membrane Properties of Cells Comprising the OHC System,* 5 years, $2,294,887 • **William C. Sessa,** NIH, *MicroRNA Regulation of Endothelial Functions,* 4 years, $1,904,610 • **Gerald I. Shulman,** NIH, *Cellular Mechanisms of Insulin Resistance in Humans,* 5 years, $764,317 • **Stefan Somlo,** NIH, *A Forward Genetic Screen for PKD Pathways in Mice Using the PiggyBac Transposon,* 1 year, $500,000 **Bing Su,** Department of the Army, *The Role of MTOR Signaling in the Regulation of RAG Expression and Genomic Stability during B Lymphocyte Development,* 3 years, $1,198,036 • **Tami P. Sullivan,** Department of Justice, *Achieving Successful Researcher–Practitioner Partnerships that Strengthen Practice and Policy: Lessons Learned from the Field,* 2 years, $343,565 • **Yulia Surovtseva,** NIH, *Analysis of Mammalian Mitochondrial Transcription Machinery,* 2 years, $99,316 **Benjamin A. Toll,** NIH, *Advancing Tobacco and Cancer Control: Reducing Alcohol Use to Promote Smoking Cessation,* 2 years, $798,162 **Benjamin E. Turk,** NIH, *Global Peptide Microarray Profiling of Tyrosine Kinase Deregulated in Cancer,* 2 years, $359,962 • **Anthony N. Van den Pol,** NIH, *Arcuate Nucleus Glutamatergic Neurons Modulate Energy Homeostasis,* 4 years, $1,455,158 • **Andrea H. Weinberger,** NIH, *Gender Differences in the Association of Depression to Transitions in Smoking,* 2 years, $70,750 • **John J. Wysolmerski,** Department of Defense, *Effects of Nuclear Parathyroid Hormone-Related Protein Signaling in Breast Cancer,* 2 years, $620,626 **Andrew Xiao,** NIH, *A Novel Enzymatic Activity of WSTF and its Role in Tumorigenesis,* 3 months, $72,040 • **Jiansong Xu,** NIH, *fMRI and DTI Study on Neural Predictor of Treatment Outcome in Cocaine Dependence,* 5 years, $801,726 **Hongyu Zhao,** NIH, *Statistical Methods to Map Genes for Complex Traits,* 4 years, $1,406,752

Non-Federal

Marcus W. Bosenberg, Pennsylvania State University, *Targeted Chemoprevention for Melanoma,* 5 years, $311,414 • **Igor E. Brodsky,** Harvard Medical School, *Inflammasome Activation by* Yersinia *Virulence Factors,* 2 years, $291,085 • **R. Todd Constable,** The John B. Pierce Laboratory Inc., *The role of the amygdala in weight gain susceptibility,* 5 years, $67,057 **Lynn Cooley,** Howard Hughes Medical Institute, *Yale Medical Research Scholars Program,* 4 years, $700,000 • **Michael P. DiGiovanna,** Connecticut Breast Health Initiative Inc., *Combination Targeting of IGF-1 Receptor and HER2 in Breast Cancer,* 1 year, 50,000 • **Marie E. Egan,** Cystic Fibrosis Foundation, *A Model of Chronic Airway Inflammation in CFTR$^{-/-}$ mice,* 1 year, $43,200 **Brian W. Forsyth,** American Medical Association Foundation, *An SMS-Based Peer Support Group: A Pilot Project Using Mobile Technology to Increase Social Support for HIV-Positive Women,* 1 year, $2,010 • **Gerald Friedland,** Albert Einstein College of Medicine, *Molecular Epidemiology of HIV-Associated Extensively Drug Resistant Tuberculosis in Rural South Africa,* 1 year, $43,813 • **David C. Glahn,** Southwest Foundation for Biomedical Research, *Identification of Novel MicroRNAs Associated with Brain Structure and Function,* 6 years, $19,264 **Jeffrey R. Gruen,** University of California–San Diego, *Creating a Pediatric Imaging–Genomics Data Resource,* 6 months, $221,639 • **Yiyun H. Huang,** University of Montana, *Positron Emission Tomography Imaging for ALS Therapy,* 10 months, $72,000 • **Leonard K. Kaczmarek,** FRAXA Research Foundation, *Development of Pharmacological Activators for FMRP-Regulated Potassium Channels,* 1 year, 45,000 • **Jason W. Mastaitis,** Juvenile Diabetes Research Foundation International, *Investigation of the Role of Hypothalamic MAP Kinase in Counterregulation,* 2 years, $47,704 • **Linda C. Mayes,** Baylor College of Medicine, *Maternal Brain and Behavioral Responses to Infant Cues in Cocaine-Exposed Mothers,* 5 years, $377,281 • **Michael J. Paidas,** CerviLenz Inc., *Establishing the Utility of Cervilenz as a Predictor of Short Cervical Length and Preterm Delivery in the Mid–Second Trimester of Pregnancy (CL-1003),* 20 months, $200,005 • **Lubna Pal,** Virginia Commonwealth University, *Pharmacogenetics of Metformin Action in PCOS,* 1 year, $34,126 • **Robert S. Sherwin,** The John B. Pierce Laboratory Inc., *The Role of the Amygdala in Weight-Gain Susceptibility,* 5 years, $62,844 • **Rajita Sinha,** The John B. Pierce Laboratory Inc., *The Role of the Amygdala in Weight-Gain Susceptibility,* 5 years, $776,061 • **Barbara Szepietowska,** Juvenile Diabetes Research Foundation International, *Role of EphA5 in Hypoglycemia,* 2 years, $51,004 **Hugh S. Taylor,** Brigham and Women's Hospital, *The Kronos Early Estrogen Prevention Study (KEEPS) Mammographic Density and Breast Health Ancillary Study,* 10 months, $8,250 **Wang-Jing Xiao,** Alfred P. Sloan Foundation, *Sloan–Swartz Annual Meeting 2010 on Computational Neuroscience,* 7 months, $25,047

// Mentors *(from page 3)* six years in Medzhitov's lab, Palm has learned and grown, he says, and has himself become a sort of mentor to new lab members. "There is a real feeling of responsibility in the lab of helping out the new students and postdoctoral fellows to become used to the lab, to feel welcomed, but also to get up to speed," Palm, who plans to begin a postdoctoral fellowship at Yale next year, says. "When I came in, the people who are now long gone helped me, so it's kind of a 'pay-it-forward' scheme," he says.

Last April, Medzhitov became one of the youngest members ever to join the elite National Academy of Sciences. But despite his accomplishments, Medzhitov is extraordinarily dedicated to those under his wing. "He has an amazing track record of producing really top-notch scientists," says Palm. "As far as I know, there's no better lab in the world to have been in during the past five to 10 years, in terms of going on to really great positions at great universities and continuing to publish really great papers."

Medzhitov sees developing a student's individual interest as vital to the role of an advisor. "The challenge is to nurture that interest and to develop a certain set of skills that are necessary to do research, which are beyond just technical skills." Among these skills, he says, are "the ability to see the big picture, to see why the problem is important and interesting, to be able to define important and interesting questions, and to see where that line of investigation will go and how it fits into the broader picture," Medzhitov explains.

A continuing cycle

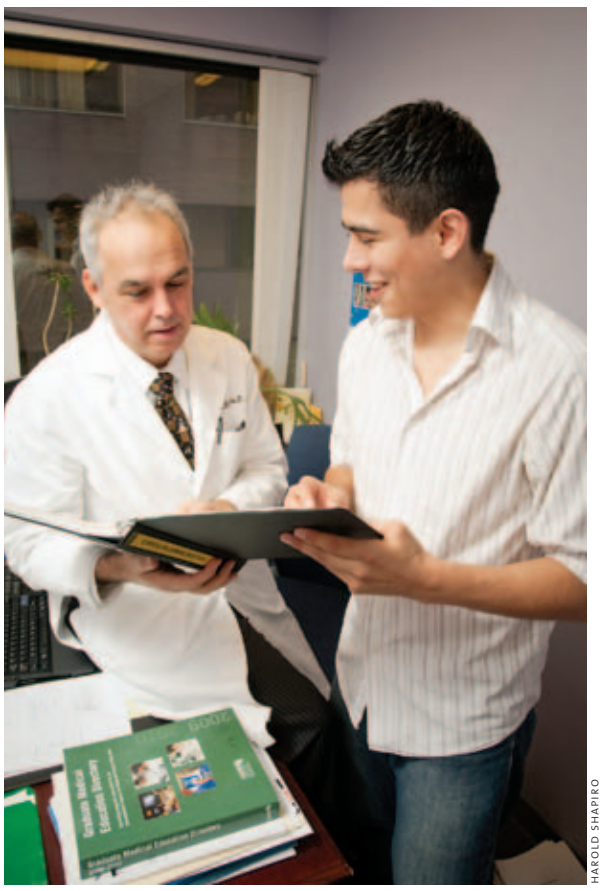
Mentorship continues to play an important role even after a person finishes medical or graduate school. Scientists holding a doctorate still need the guidance of mentors before they strike out on their own.

Michael J. Caplan, M.D., PH.D., knows this well. As a graduate student at Yale School of Medicine, Caplan, now chair and C.N.H. Long Professor of Cellular and Molecular Physiology and professor of cell biology, gained vital experience working jointly with Professor of Cell Biology James D. Jamieson, M.D., PH.D. (now director of the M.D./PH.D. Program) and George E. Palade, M.D., the late Romanian-American cell biologist and Nobel laureate.

Last April, Caplan received the first annual Yale University Postdoctoral Fellows Mentoring Award. The fellows who nominated Caplan described three ways in which he is an exceptional mentor: he checks in with his lab members daily to talk about experimental data and to challenge them to think creatively about interpreting their results; he helps postdoctoral scholars advance their own careers by helping them to think strategically about their futures, providing extensive feedback on their grant proposals and participating in mock job interviews as they prepare for real interviews; and, not least, he strives to maintain a "family-friendly" climate in his lab that acknowledges and accommodates the challenges of balancing a scientific career with family life.

Mentorship is cyclical: mentees become mentors, and knowledge is continually passed on. As with parents and children, one generation of scientists raises the next, "just like we hear our parents' voices in our heads when we're talking to our children," Caplan says. In the laboratory, as in parenting, maturity and confidence come with time—and when they do, the rewards are unparalleled, he says.

Caplan likens scientific training to an apprenticeship in carpentry: "There are people who come in knowing how to use all the tools and having a tremendous intuition for the wood, and there are people who don't." And with the latter, "the great pleasure comes from watching as, either suddenly or gradually, they acquire that intuition."



HAROLD SHAPIRO

Michael O'Brien (left), one of a new team of four advisors to medical students, works with Jorge Ramallo (right) of the Class of 2013.

// Gift *(from page 1)* through the emergency room. And she was struck by the myriad cutaneous ways in which a disease could manifest itself in different patients. Skin problems, she says, "looked different, even when they were the 'same diagnosis.' "

At that time, the medical school offered electives in microbiology and electrocardiology to interns. Having already earned a doctorate in the former, "I could find my way around a microbiology lab," Johnson says, and the cardiology elective held little interest. She petitioned the medical school to allow her to pursue her budding interest in dermatology as an elective, and got a green light.

As it happens, Aaron B. Lerner, M.D., PH.D., had joined the Yale faculty in 1955 to head the Department of Internal Medicine's Section of Dermatology. Lerner, who would go on to make medical history as discoverer of the hormones α-MSH and melatonin, was an ideal mentor to immerse Johnson in the scientific life; she still recalls him tinkering with the chemical models he kept on the ledge of his office blackboard, deciphering the structure of α-MSH "click-by-click."

Before long, Johnson was directing the Section of Dermatology's inpatient and outpatient services. She held that post until 1964, when she and her husband, cardiologist Kenneth G. Johnson, M.D., were dispatched to Hiroshima, Japan, where Marie-Louise served as chief of dermatology on the Atomic Bomb Casualty Commission (ABCC), which was conducting rigorous long-term studies of the medical effects of radiation released by the atomic bombs dropped on Japan at the close of World War II. Her experiences there led Johnson to become an active member of International Physicians for the Prevention of Nuclear War.

She vividly remembers the polio epidemic and "life before penicillin," when people routinely died of what would now be considered minor infections, and she believes that physicians, and dermatologists in particular, have a vital role to play in ensuring the continuation of the advances in medicine she has witnessed since her youth.

"The skin is the body's largest organ, and it gives protection to the body in its interactions with everything that's outside," Johnson says. "It's pretty important!" Nonetheless, she adds, medical dermatology is being absorbed into other specialties, as in the case of lupus, which is generally treated by rheumatologists despite the disease's significant effects on the skin. "This is a disservice to dermatology," Johnson says, "because there is something to knowing the skin and to knowing what these serious diagnoses do in the skin."

Her gift, she says, is "to encourage the young, able, innovative dermatologist to pursue new avenues opened by his or her inquisitive mind and give funding so he or she not be compelled to work in the clinic at the expense of time to think. You have to have support to do that."

Edelson says he can think of no better person than Johnson to inspire young physicians in the field. "She is precisely the physician any of us would want for ourselves, and she is precisely the teacher any of us would want to have—or to be."

// Lungs *(from page 1)* extreme shortage of donor organs. An alternative solution is to create synthetic lungs, but past attempts to do so have failed because the lungs, with networks of branching airways and vasculature, are so spatially complex, says Niklason.

She and her research team took a leap forward recently, when they engineered the first lungs that are capable of exchanging oxygen and carbon dioxide, an achievement that was reported in the journal *Science* this past July.

The key to the Niklason group's success was finding a suitable scaffold for supporting lung tissue, and they did so by adapting a tissue engineering technique that has been applied to the heart, liver, and kidney. By using detergent solutions to wash cells out of lung tissue from rats, the researchers removed all cellular components that could cause an immune reaction after transplantation.

What remained was a hollowed-out matrix with the right three-dimensional shape, mechanical properties, and vasculature. Unexpectedly, molecular cues that could guide cells to appropriate regions had been preserved in the matrix as well; when the scientists placed various neonatal lung cells inside the scaffold, the cells positioned themselves in the correct locations.

"I was surprised by how much information is in the matrix," Niklason says. "I expected the different cell types to go helter-skelter, but by and large, the cells landed in their correct anatomic locations. This tells me that the matrix has 'zip codes,' or information about who should go where."

The next challenge was to develop a bioreactor—a system to mimic the environment in which lungs develop in the fetus, such as the flow of liquid through the growing vasculature. To provide ventilation, the researchers used a syringe pump to withdraw air, which caused the lungs to inhale liquid from the windpipe.

In the reverse process, the pump returned air to the bioreactor, causing the lungs to exhale liquid. Inside the bioreactor, the lungs even produced proteins that allowed the organs to inflate normally.

By imitating natural conditions, the researchers improved the clearance of secretions in the airway, enhanced cell survival, and fostered the growth of the major cell types found in the lung. After culturing the tissue inside the bioreactor for about a week, the researchers implanted it into rats and observed that the lungs exchanged gas for a few hours—a major accomplishment.

The team saw similar results with human cells, suggesting that the same approach, perhaps using stem cells, could help to treat diseases in humans.

Niklason cautions that "it will take us another 10 or 20 years of work to develop reliable and robust means of differentiating primitive stem cells into the lung cell types we're looking for and keeping them stable over time."

But the wait will be worthwhile, Niklason says. "The potential advantage in the long run is that we could take a biopsy from a patient who needs a lung replacement, generate stem cells from that biopsy, and from those cells regenerate a whole lung that we could implant without it being rejected," she says. "It could really be a new era for organ transplantation."

// Cancer *(from page 1)* Under Schlessinger's direction, the CBI plans to hire 150 research scientists, including 11 principal investigators, over the next three to four years, with the primary goal of pinpointing root molecular causes of cancer, identifying new molecular targets, and developing new drug treatments.

These researchers will work in concert with scientists at the neighboring Yale Center for Genome Analysis, using state-of-the-art genomic sequencing techniques to better understand and exploit the molecular profiles of various tumor types.

The institute will significantly increase the extent of basic research on cancer at Yale, especially in the areas of computational biology, cancer genomics, cancer immunology, and drug discovery, and it will complement Yale's translational and clinical research programs, including a major expansion of clinical trials planned by YCC.

Schlessinger, known to colleagues and friends as "Yossi," is a pioneer in the field of signal transduction, the means by which receptors in the cell membrane, when bound to certain molecules, pass signals to the interior of the cell that guide basic processes such as cell division and cell growth.

In particular, over several decades, his group has done fundamental research on signaling by receptor tyrosine kinases (RTKs), a set of related cell-surface proteins that affect cell proliferation, differentiation, and survival. Certain mutations in RTKs can result in faulty signaling, which in turn can cause aberrant cell proliferation that may ultimately lead to cancer.

Blocking RTK activation has become a major strategy in anticancer drug design. Schlessinger and colleagues have formed three companies—Sugen Inc. in 1991, Plexxikon in 2001, and Kolltan in 2008—and drugs based on insights gained in his laboratory are having a major impact in the lives of patients with liver, kidney, stomach, and skin cancers.

Sugen's drug Sutent, approved by the FDA in 2006 for kidney and stomach cancers, was one of the first in a new generation of targeted cancer drugs. An experimental compound, PLX4032, which was discovered by Plexxikon and is currently in clinical development in partnership with Roche, has attracted wide media coverage for its unprecedented success in early-stage clinical trials for the treatment of melanoma. The drug is now in Phase III trials for melanoma, and is also in Phase I trials for the treatment of colorectal cancer.

Schlessinger, who was recruited to Yale in 2001, was born in Croatia and educated at Hebrew University and the Weizmann Institute of Science in Israel. He was a member of the Weizmann Institute from 1978 to 1991, and moved to New York University School of Medicine in 1990.

He is a member of the National Academy of Sciences and the Institute of Medicine and serves on the editorial boards of numerous journals, including *Cell* and *Molecular Cell*. He received the Taylor Prize in 2000, the Dan David Prize in 2006, and the Pezcoller Prize from the American Association for Cancer Research (AACR) in 2010.

Drugs that target RTKs have also been of great interest to Herbst, who has spearheaded clinical studies of many such drugs over the last several years. His work using erlotinib (Tarceva) in combination with bevacizumab (Avastin) was among the first to combine multiple targeted agents for non-small cell lung cancer (NSCLC).

Herbst is co-principal investigator of the Biomarker-Based Approaches of Targeted Therapy for Lung Cancer Elimination Program (BATTLE) Trial, which has significantly advanced "personalized" therapy of NSCLC by using molecular analysis of tissue biopsies to determine the best available targeted treatment for each patient. He recently developed a BATTLE-2 trial to explore novel combinations of agents to target genetically mutated pathways in lung cancer and to overcome drug resistance. Herbst plans to open this study at Yale and to bring this approach to other forms of cancer.

In his new position, Herbst hopes to bring novel and more personalized therapies to cancer treatment to improve efficacy and reduce toxicities. He will work to help integrate Yale's strengths in basic science and translational medicine to have a more direct impact on clinical care.

"Dr. Herbst is nationally recognized for his leadership and expertise in lung cancer treatment and research," says YCC Director Lynch, also physician-in-chief of Smilow Cancer Hospital at Yale-New Haven. "He is a natural leader and will have a critical role in building our cancer program while mentoring the next generation of cancer doctors at Yale."

Herbst is a member of the AACR, for which he is senior editor of *Clinical Cancer Research*, as well as the American Society of Clinical Oncology and the Institute of Medicine's National Cancer Policy Forum. He is a fellow of the American College of Physicians. He has authored more than 200 peer-reviewed papers and has current grant funding for his work from numerous sources, including the National Cancer Institute, the AACR, and multiple charitable foundations.

Herbst received his medical degree from Cornell University Medical College and earned a PH.D. in molecular cell biology from the Rockefeller University. He completed his medical oncology fellowship at Dana-Farber Cancer Institute and a medical hematology fellowship at Brigham and Women's Hospital in Boston, where he additionally received a master's degree from Harvard University's clinical investigator training program.

Neurologist is named first Zimmerman and Spinelli Professor

David M. Greer, M.D., M.A., a specialist in the areas of coma, neurocritical care, stroke, and neuroimaging, has been named the inaugural Dr. Harry M. Zimmerman and Dr. Nicholas and Viola Spinelli Associate Professor of Neurology.

Greer's research focuses on vascular neurology and on improving the ability of doctors to give an accurate prognosis for patients in coma, particularly after suffering a cardiac arrest. He is also interested in the use of hypothermia to improve neurological outcomes for various brain injuries.

After earning his M.D. and a master's degree in English Literature from the University of Florida, Greer trained in neurology at Massachusetts General Hospital (MGH), where he underwent specialized fellowship training in stroke and neurocritical care. He was an associate neurologist and attending physician in neurology at Brigham and Women's Hospital in Boston, and an attending physician and director of Neurology Consultive Services and the Inpatient Stroke Service at MGH, where he was also the program director of the Partners Neurology Residency Program.

Greer was an associate professor at Harvard Medical School before coming to Yale earlier this year as clinical vice chair and associate professor of neurology. At Yale, he also serves as program director of the Neurology Residency Program and director of the Outpatient Neurology Clinic.

Greer has also served as a specialty consultant to the New England Patriots, the Boston Bruins, and the Boston Red Sox. His numerous honors include a 2010 Teacher of the Year Award from the Partner Neurology Residency at Massachusetts General Hospital, where he also received several Partners in Excellence Awards, among other distinctions.

The new professorship was established through the bequest of Nicholas "Nick" Spinelli, M.D., a beloved alumnus of Yale College and the School of Medicine who died in 2007, and his sister, Viola Spinelli, M.P.H., a 1964 graduate of the Yale School of Public Health. It honors Harry M. Zimmerman, M.D., a notable neuropathologist during Nicholas Spinelli's student days at the medical school who became the founding director of the Albert Einstein College of Medicine in Bronx, New York. In addition to the professorship, the Spinellis' $4.5 million bequest supports a scholarship fund for medical students.

TERRY DAGRADI

David Greer, the inaugural Dr. Harry M. Zimmerman and Dr. Nicholas and Viola Spinelli Associate Professor of Neurology, spoke at a celebratory reception in the Cushing/Whitney Medical Historical Library with a portrait of the late Nicholas Spinelli standing nearby. Spinelli established the chair with his sister, Viola, in honor of Zimmerman, a neuropathologist on the School of Medicine faculty during Nicholas Spinelli's student years who later became founding director of Albert Einstein College of Medicine.

Nicholas Spinelli, a native of Stratford, Conn., entered Yale College in 1937 at 16 years old. After graduating in 1941, he entered the School of Medicine, and, like the rest of his classmates, was inducted into the Army as part of Yale's Company C, combining his medical studies with military drills on the New Haven Green. After graduating, Spinelli served as an Army physician in Germany. Spinelli practiced medicine in Stratford until 1968, when a heart condition forced him to give up his practice. He was able to continue working, however, and served thereafter as director of medical education at Bridgeport Hospital. He was a familiar face on campus, serving from 1985 to 1990 as alumni director for Yale School of Medicine.

Expert on genetics of psychiatric disorders is appointed Foundations' Fund Professor

Joel Gelernter, M.D., the newly named Foundations' Fund Professor of Psychiatry, focuses his research on the genetics of psychiatric illness.

Joel Gelernter

The director of the Division of Human Genetics in the Department of Psychiatry, Gelernter seeks to identify genes that predispose individuals to substance-dependence traits—primarily cocaine, opioid, nicotine, and alcohol dependence, as well as to other psychiatric traits, especially anxiety disorders. In addition, he explores the genetics of other phenotypes, such as neuroimaging measures and basic issues in population genetics. His laboratory is engaged in ongoing research collaborations on the genetics of substance dependence with colleagues at the Chulalongkorn Faculty of Medicine in Bangkok, Thailand, and he helps to train Thai investigators in substance-dependence genetics at Yale. He has also conducted research in China and Israel.

Gelernter is a 1979 graduate of Yale College. He received his M.D. at SUNY Downstate Medical Center in 1983, and fellowship training at the National Institute of Mental Health. He has been a full professor at the School of Medicine since 2002, and is currently professor of psychiatry, genetics, and neurobiology.

He also is affiliated with the Molecular Cell Biology, Genetics, and Development track of the Combined Program in the Biological and Biomedical Sciences.

An associate editor of *Neuropsychopharmacology*, Gelernter is on the editorial boards of *Biological Psychiatry*, *The American Journal of Medical Genetics Part B*, *Psychiatric Genetics,* and *Asian Biomedicine*.

The professorship was established with contributions from The Foundations' Fund for Research in Psychiatry, established by philanthropist Charles B.G. Murphy, a member of the Yale College Class of 1928.

Neuropsychiatrist, stem cell researcher is new Harris Professor of Child Psychiatry

Flora M. Vaccarino, M.D., who studies the pathophysiology of neuropsychiatric disorders and has elucidated how neural stem cells self-renew, survive, and differentiate, has been named Harris Professor of Child Psychiatry.

Flora Vaccarino

Members of Vaccarino's laboratory study the proliferation and differentiation of neural stem cells during prenatal and postnatal development and after injury, as well as the diversity and function of astroglial cells in neuropsychiatric disorders. A member of the faculty at the Yale Child Study Center and in the Department of Neurobiology, Vaccarino was the principal investigator of a 2003 study which found that patients with Tourette's syndrome have fewer GABA interneurons in their brains than those without the syndrome. She is known in the neuroscience community for discovering the role of fibroblast growth factors in the growth of the cerebral cortex during mammalian development.

She recently helped found the Program in Neurodevelopment and Regeneration, an interdepartmental initiative that will use induced pluripotent stem cells as a research tool to understand neuronal development in individuals with specific neuropsychiatric disorders.

Vaccarino earned her medical degree at Padua Medical University in Italy and studied neuropharmacology and cell biology at the National Institutes of Health as a research fellow before starting her residency in psychiatry at Yale School of Medicine. After her residency, Vaccarino studied developmental biology and genetics, and joined the Yale faculty in 1994. Also affiliated with the Yale Stem Cell Center, Vaccarino became a full professor in 2009.

Her honors include a National Alliance for Research in Schizophrenia and Depression (NARSAD) Young Investigator Award, a Lustman Award from Yale, two Tourette's Syndrome Association Awards, a Women in Research and Education Award from the National Science Foundation, and a NARSAD Independent Investigator Award.

Development and function of the retina are research interests of Marvin Sears Professor

Z. Jimmy Zhou, MS.C., PH.D., newly designated as the Marvin L. Sears Professor of Visual Science, studies the physiology and development of the mammalian retina under normal and pathological conditions, as well as the organization and function of retinal synapses and circuits.

Research in his laboratory is focused on the cellular and network mechanisms underlying the generation of spontaneous rhythmic activities (retinal waves) in the developing retina and the functional role of such activities in the development of neuronal circuits in the visual system.

Z. Jimmy Zhou

His team also explores the mechanisms of visual signal processing in the mature retina, particularly the physiology of the neuronal circuits responsible for detecting image movement and movement direction.

Zhou earned his B.S. at Fudan University in China and his master's and doctoral degrees at the University of Houston. After postdoctoral studies at the University of California–Los Angeles, Zhou joined the faculty at the University of Arkansas. He came to Yale in 2008. He is vice chair and director of research in the Department of Ophthalmology and Visual Science and is affiliated with the Combined Program in the Biological and Biomedical Sciences and the Graduate Program in Cellular and Molecular Physiology.