Medicine@Yale

Advancing Biomedical Science, Education and Health Care

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$2 million gift will support training of physician-scientists

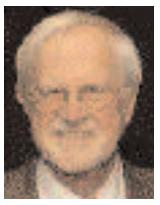
Of all the professions, learning medicine requires the greatest time commitment. After four years of medical school, doctors undertake at least three years of internship and residency before beginning their specialty training. At least two additional years are required to become a surgeon; if the career goal is heart surgery or neurosurgery, add two more years.

But for the one out of 10 students who enroll at the School of Medicine in the Medical Scientist Training Program (MSTP) each year, these numbers tell only half the story. These students aim to earn both the M.D. and PH.D. degrees, embarking on a long academic journey that combines the rigors of medical education with deep research experience in the basic biology of human disease.

The dedication of these students has received special recognition from a donor who wishes to remain anonymous in the form of a $2 million bequest to sustain and expand upon Yale's longstanding commitment to the MSTP, known on campus as the M.D./PH.D. program.

"Yale has an outstanding program with a long tradition and a fantastic success rate in training successful physician-scientists," Dean and Ensign Professor of Medicine Robert J. Alpern, M.D., says. "This very generous gift will allow us to maintain and even improve on the program's excellence."

All told, earning the M.D./PH.D. takes about eight years, after which most students begin a medical residency, a step long since completed by peers in their entering class. "There's a huge amount you have to learn with clinical rotations just for the M.D., and you can't have a half-baked PH.D. in molecular biology and expect to do good research," Program Director James D. Jamieson, M.D., PH.D., says. "There's no shortcut."



James Jamieson

Gift, *page 8*

Preserving options, sustaining hope

Successful new method for freezing human eggs is now available at Yale

Thanks to a transatlantic collaboration forged by Pasquale Patrizio, M.D., professor of obstetrics, gynecology and reproductive sciences and director of the Yale Fertility Center (YFC), patients in the New Haven area, including women newly diagnosed with cancer who wish to preserve fertility during chemotherapy or radiation, can now reap the benefits of a new, uniquely successful form of the egg-freezing technique known as oocyte cryopreservation (OC).

Although OC has been attempted in various forms for about 15 years, it has had a disappointing track record—producing about two babies for every 100 eggs frozen—because of damage done to eggs by freezing.

The new method, which involves bathing eggs in protective solutions, slow-cooling them with liquid nitrogen to minus 321 F and thawing them according to special protocols, doubles the success rate to five or six babies per 100 eggs, an enormous advance over traditional OC, says Patrizio. By comparison, *in vitro* fertilization (IVF) using fresh eggs has a success rate of eight or nine pregnancies per 100 eggs.

Pasquale Patrizio explains oocyte cryopreservation to a patient at the Yale Fertility Center.

Patrizio says that because eggs are not fertilized before freezing, the OC technique has particular appeal for three groups of patients: women diagnosed with cancer at reproductive age, those who oppose embryo-freezing on ethical grounds and those who wish to postpone childbearing for personal or economic reasons but wish to use a future partner's sperm. In December the School of Medicine's Institutional Review Board (IRB) approved the use of the new OC method, and by the end of February, women from all three groups had already frozen eggs at the YFC.

Emre U. Seli, M.D., assistant professor of obstetrics, gynecology and reproductive sciences, says that preserving fertility is especially meaningful for women with cancer. "Anyone who has had someone with cancer in their family knows that quality of life, the way you spend your day after the diagnosis, is dependent on your hope," Seli says. "That this procedure gives you hope is very important."

The OC modifications were devised over the course of two years at Tecnobios Procreazione, a private fertility clinic in Bologna, Italy, in response to a 2004 Italian law that bans the freezing of

Fertility, *page 7*

Boehringer and Yale combine strengths in new research alliance

We live in an age of instant electronic communication, but in some arenas there's no substitute for face-to-face human interaction. That's certainly the case in science, say the principals in a new research alliance between the medical school and Boehringer Ingelheim Pharmaceuticals Inc. (BIPI), the Ridgefield, Conn.-based division of the global German pharmaceutical firm.

Boehringer Ingelheim, a privately held business, is one of the world's top 15 drug companies. BIPI's portfolio of drugs is weighted toward treatments for cardiovascular, inflammatory and autoimmune diseases such as hypertension, asthma and human immunodeficiency virus (HIV), so the expertise of School of Medicine scientists in the Section of Immunobiology and the Interdepartmental Program in Vascular Biology and Transplantation would be reason enough for BIPI's drug discovery team to explore partnerships with Yale.

But Mikael Dolsten, M.D., PH.D., head of worldwide research at Boehringer Ingelheim's headquarters in Ingelheim, Germany, says that the unusually close scientific cooperation afforded by Yale's proximity to Ridgefield sealed the deal.

Alliance, *page 6*

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For Mark Saltzman, the challenge of biomedical engineering is getting "everybody working in sync."

Mending the human machine

Yale's youngest department casts a campus-wide net in search of new therapies

Lifelines
W. Mark Saltzman

With its mirror-like reflection of the grand old houses of Hillhouse Avenue and Trumbull Street, the sweeping glass façade of the Daniel L. Malone Engineering Center is one of the most striking sights in New Haven these days. As the new home for Yale's Department of Biomedical Engineering (BME), the building's placement—between the School of Medicine and Science Hill, a bastion of basic biological research at the northern end of the central campus—could not be more apt.

"Biomedical engineering in the future has to be more intertwined with basic biological science, because we're working deeper in the body, with cells and biological molecules," says department Chair W. Mark Saltzman, PH.D., Goizueta Foundation Professor of Chemical and Biomedical Engineering. "On the other side, biomedical engineers need to be much more involved with translational research, working in unison with clinicians. It's going to take everybody working in sync."

Saltzman has strived to bridge these two realms since his undergraduate days at Iowa State University, where he heard a talk by chemical engineer Richard C. Seagrave, PH.D., that was an epiphany. "He gave a stunning lecture, a tour de force, about how the human body is just a very complex chemical plant," Saltzman recalls. "He explained how the tools you have as a chemical engineer are exactly the right tools for understanding how this system works, and designing approaches for helping when the system fails." Saltzman, an Iowa native, soon melded his long-standing interest in medicine with an affinity for engineering that he attributes to the pragmatic outlook of his grandparents, all Midwestern farmers.

In graduate school at the Massachusetts Institute of Technology (MIT), Saltzman created drug-impregnated implants from plastic-like polymers that slowly and steadily release medicines for long periods. This work is now helping patients in the form of Gliadel, a chemotherapy-infused wafer that neurosurgeons lay on the brain's surface to battle the deadly tumors known as gliomas. While at MIT, Saltzman also worked with Joseph J. "Jay" Vacanti, M.D., of Massachusetts General Hospital, building tubular scaffolds that could be seeded with cells to sculpt new replacement blood vessels for patients with advanced vascular disease.

A fruitful collaboration with Christopher K. Breuer, M.D., assistant professor of surgery, is drawing on both of Saltzman's areas of expertise. Since his MIT days, Saltzman has miniaturized his slow-release polymers into spherical nanoparticles that can be taken up directly by cells. By treating tissue scaffolds with particles that contain molecules to promote proper cell growth, Breuer and Saltzman are engineering better, stronger blood vessels than has previously been possible. In other projects with medical colleagues, Saltzman is testing nanoparticles to deliver vaccines for infectious disease, and drugs for cancer and fertility control.

Though biomedical researchers at Yale have independently adopted engineering approaches for decades, the 2003 founding of BME has given new vigor to interdisciplinary projects that team up top-notch biologists and engineers on Yale's main campus with scientific and clinical experts at the School of Medicine. Saltzman, who oversees 12 faculty members as chair, says that Yale is an ideal venue to carry out the all-encompassing science at the heart of modern biomedical engineering. "Here, success isn't measured by beating the guy in the lab next to you," he says. "Yale's a place that has a history of being collegial—a very congenial, collaborative place."

Medical historian Warner is appointed to Avalon Professorship

John Harley Warner, PH.D., chair of the Section of the History of Medicine at the School of Medicine, was named Avalon Professor of the History of Medicine by the Yale Corporation in December.

John Warner

Warner is an expert on the cultural and social history of medicine in the United States during the 19th and 20th centuries. In his current research, he is analyzing the narrative accounts found in historical patient records to illuminate the evolution of modern medical practice.

After receiving his doctorate in the history of science from Harvard University in 1984, Warner was a postdoctoral fellow at the Wellcome Institute for the History of Medicine in London. He joined the medical school faculty as assistant professor of the history of medicine in 1986 and became chair of the section in 2002.

Under Warner's leadership as founding chair in 2002 of the newly constituted Program in the History of Science and Medicine, Yale College's undergraduate major in the History of Science/History of Medicine, one of Yale's 10 largest majors, attracts about 40 new students per year.

Warner is the author of numerous scholarly articles and two books, *Against the Spirit of System: The French Impulse in Nineteenth-Century American Medicine* and *The Therapeutic Perspective: Medical Practice, Knowledge, and Identity in America, 1820–1885*, which was awarded the William H. Welch Medal from the American Association for the History of Medicine in 1991.

Warner is the third Yale faculty member to be named to the Avalon Professorship, which was established with a grant from the Avalon Foundation, now part of the Mellon Foundation, in the early 1960s.

CT scanning expert is new leader of Yale radiologists

Following a nationwide search, James A. Brink, M.D., a Harvard-trained radiologist, has been named chair of the Department of Diagnostic Radiology at the School of Medicine and chief of diagnostic imaging at Yale-New Haven Hospital.

James Brink

Brink, former vice chair of the department and chief of abdominal imaging, came to Yale in 1997 from the Mallinckrodt Institute at Washington University in St. Louis. He has served as interim chair since 2003.

Brink will lead a department of more than 70 full-time faculty. The department provides diagnostic imaging services for the Yale Medical Group and Yale-New Haven Hospital, conducts research in a variety of disciplines related to clinical radiology and imaging science and offers highly rated postgraduate training programs. In collaboration with the Department of Biomedical Engineering, the radiology faculty also makes important contributions to Yale's undergraduate and graduate programs in imaging science.

Brink is a fellow of the Society for Computed Body Tomography and Magnetic Resonance and of the American College of Radiology; he serves on the board of directors of the Academy of Radiology Research and also on the executive council of the American Roentgen Ray Society. A respected educator, Brink has pioneered technologies for maximizing resolution in CT scanning while minimizing radiation dosage and risk to patients. He has published more than 110 original research articles, reviews and book chapters.

Medicine@Yale

Peter Farley, *Managing Editor*

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Advances

Health and science news from Yale

Bullies are no match for gene knockout

After repeated harassment by larger, more aggressive members of their species, mice withdraw from social contact, exhibiting behavior that is strikingly similar to that seen in humans with depression, social phobia and post-traumatic stress disorder.

Using a video system that creates a map of a mouse's movements, Assistant Professor of Psychiatry Ralph J. DiLeone, PH.D., and colleagues found that a normal mouse (white trail in left panel above) will frequently interact with another mouse placed at one side of its enclosure, but a mouse "defeated" by aggressors (black trail) will shy away.

Pleasurable social experiences activate reward pathways in the brain that are also stimulated by drugs of abuse, so the team wondered whether this socially withdrawn behavior might be governed by those same circuits.

As reported in the February 10 issue of *Science*, when the scientists selectively shut down the gene for a protein known as BDNF in an important brain reward center, mice did not develop social withdrawal in response to aggression, suggesting that BDNF in the reward pathway may be a fruitful target for new psychiatric drugs.

Parasite's accomplice gets genetic mug shot

As many as 500,000 people per year in sub-Saharan Africa contract sleeping sickness, which can cause severe, irreversible damage to the nervous system. The illness is transmitted by blood-sucking tsetse flies, but only when they are themselves infected by the protozoan parasite *Trypanosoma brucei*, which is passed into humans when the tsetse bites.

In addition to *T. brucei*, the tsetse gut is also host to two so-called good bacteria that manufacture nutrients not found in the fly's blood diet but crucial to its survival. In a joint project with colleagues in Japan reported online in the February issue of *Genome Research*, Professor of Epidemiology Serap Aksoy, PH.D., sequenced the complete genome of *Sodalis*, a beneficial bacterium passed on by tsetse mothers to their larvae.

The new sequence will allow scientists to better manipulate the functions of *Sodalis* to gain insights into tsetse biology that could lead to novel ways to fight sleeping sickness, Aksoy says. "If we get rid of these symbiotic bacteria, the flies become sterile. Understanding what they provide to the flies is very important from a vector-control point of view."

Can microRNAs put the brakes on cancer?

The complete sequence of the human genome, with its promise of new insights into disease and a host of novel drug targets, was announced to great fanfare in 2003. But a quieter genetic revolution began a full decade earlier, when Dartmouth College scientists studying the microscopic worm *C. elegans* discovered the first of the powerful genetic switches now known as microRNAs.

It's Biology 101 that genes in DNA are transcribed into long strands of messenger RNA that carry the genes' instructions to the protein-making machinery of the cell. But *lin-4*, the microRNA found at Dartmouth, rewrote the rules. For starters, *lin-4* is only 22 genetic letters long, far shorter than a typical 1,000-letter RNA message—hence the "micro." But more significantly, *lin-4* doesn't help to build proteins. Instead, it sticks to messenger RNA and jams up the works, shutting down the expression of a large assemblage of genes involved in early development and allowing *C. elegans* larvae to progress toward adulthood.

It would be seven years before South African-born Frank Slack, PH.D., showed that *lin-4* was no fluke. In 2000, while a postdoctoral fellow at Harvard Medical School, Slack, now associate professor of molecular, cellular and developmental biology at Yale, identified a second microRNA, *let-7*, that also governs development in *C. elegans*.

Then the floodgates opened. In a series of discoveries that are remarkable even in the dizzyingly fast-paced world of molecular biology, it has been demonstrated over the past five years that hundreds of gene-silencing microRNAs are at work in plants and in numerous animals, including over 200 in humans that may regulate more than a third of our genes. Because half the *C. elegans* genome matches our own, including the gene for *let-7*, Slack's research is having an impact on our understanding of human development, aging and illness, especially cancer.

According to Slack, one of the primary roles of microRNAs is to put a brake on cell proliferation during development. "Initially in the human embryo, you've got cells just dividing, dividing, dividing—to make as many cells as possible," he says. "But at some point you want to make an organ. MicroRNAs come on to tell cells to stop dividing and to start differentiating into organs. And they stay on all through life, to keep the cells from dividing again." Slack believes that the uncontrolled cell division that is a hallmark of cancer might be caused when the check on cell growth imposed by microRNAs is somehow lifted. "In various cancers we've looked at, microRNAs have been shut off," he says. "We think that causes cells to re-enter their cell division program and behave like they're in the embryo."

From petunias to patients: the rapid rise of microRNAs

1990
Researchers insert extra RNA into petunias to make them deeper purple; instead they are pure white, suggesting the existence of a previously unknown gene-silencing mechanism.

1993
Discovery of the *lin-4* microRNA, which guides development of the roundworm *C. elegans*.

1998
RNA interference is discovered in *C. elegans*, solving the petunia puzzle.

2000
A second *C. elegans* microRNA, *let-7*, is identified; the presence of microRNAs in human cells is established.

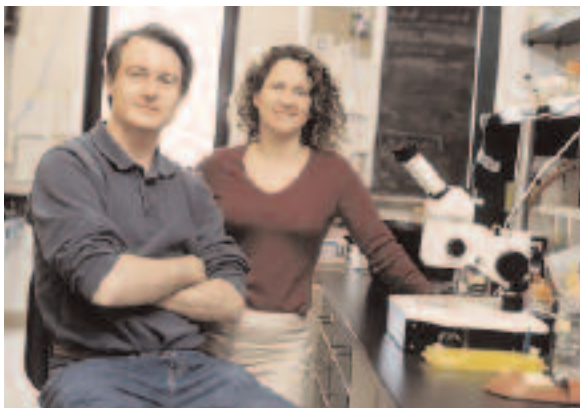
2001
Hundreds of new microRNAs are discovered in animals and plants.

2005
MicroRNA probes far exceed previous techniques at differentiating human tumor types; suppression of *let-7* found in human lung cancer cells.

2006
Preclinical trials of microRNA-based screening and therapy are launched.

1990 · 1995 · 2000 · 2005

In a 2005 paper in the journal *Cell*, Slack showed that *let-7* is tamped down in human tumors, which unleashes *Ras*, a cell-proliferation gene that has long been implicated in cancers of the lung and pancreas. "Frank is doing wonderful science relating gene regulation by microRNAs to control of cell growth," says Philip A. Sharp, PH.D., a Nobel Prize-winning expert on RNA gene silencing at the Massachusetts Institute of Technology. "His finding that the *Ras* gene is regulated by *let-7* was one of the first indications that changes in the levels of small RNAs could be critical in cancer."



Frank Slack and Joanne Weidhaas hope to move microRNAs from the lab to the clinic.

Slack is now collaborating with Assistant Professor of Therapeutic Radiology and Yale Cancer Center researcher Joanne B. Weidhaas, M.D., PH.D., to develop microRNA-based diagnostic tools and treatments. Weidhaas says that genomic analyses of tumors and cancer therapies that target single genes have been disappointing because hundreds of genes are faulty in any given cancer and it has been difficult to discern which mutations are most important. The excitement surrounding microRNAs, she says, stems from their ability to regulate entire suites of genes that underlie biological pathways.

A 2005 study in the journal *Nature* found that measuring the levels of just 217 microRNAs could generate clearer genetic signatures for tumors than 16,000 probes for messenger RNA. Encouraged by these results, Slack and Weidhaas hope within two years to perfect a microRNA-based screening device that could help tailor cancer treatments to patients' tumor types, and they are in the early stages of testing a *let-7* inhalant therapy to rein in uncontrolled cell growth in lung cancer.

In addition, Weidhaas has shown that raising *let-7* levels in *C. elegans* makes the worm's cells more sensitive to radiation, leading her to conclude that a *let-7* treatment could be a powerful adjunct to standard radiotherapy. "Some tumors are simply tougher than normal tissue when we treat them with radiation," Weidhaas says. "If we could make cancer cells more sensitive than normal cells, or even bring them up to the same level, we'd have an enormous advantage."

When he discovered *let-7*, Slack says, he could not have imagined that microRNAs, completely unknown to biologists only 15 years ago, could come so far so fast. "I've been at it from the ground floor," he says, "and it's been a fun ride."

Beverly and Raymond Sackler

Gift honors Nobelist, sponsors visits by top neuroscientists

A lecture series established with a gift from the Raymond and Beverly Sackler Fund for the Arts and Sciences will bring a leading neuroscientist to the School of Medicine each year to speak and to exchange ideas with faculty and students.

The lectureship, named The Raymond and Beverly Sackler Visiting Professor and Lecturer, in Tribute to Julius Axelrod, PH.D., honors a prolific scientist and Nobel laureate whose laboratory at the National Institute of Mental Health (NIMH) was the site of several seminal discoveries in neuroscience. Most notably, Axelrod and his colleagues were the first to describe the synapse-clearing process known as neurotransmitter reuptake, a mechanism that is targeted by many modern psychiatric drugs, including Prozac and Zoloft.

Visiting speakers in the Sackler lecture series will be sponsored by the interdepartmental program in Cellular Neuroscience, Neurodegeneration and Repair (CNNR), a new initiative to bring basic science to bear on neurological disease that was launched by the School of Medicine in January.

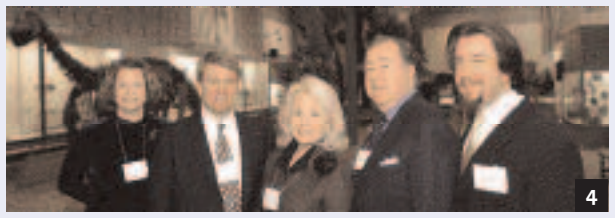
"It has been our experience that visiting professors and lecturers enhance the scientific exchange with faculty and students, stimulating creative research," says Raymond R. Sackler, M.D., co-founder of Purdue Pharma of Stamford, Conn.

"The Sacklers have a long tradition of philanthropy that is really worldwide, extending from the University of Cambridge in England all the way to Tel Aviv University in Israel—not to mention the Metropolitan Museum of Art and the British Museum," says Dean Robert J. Alpern, M.D. "They've also supported a number of programs here at Yale, and we're very appreciative of that."

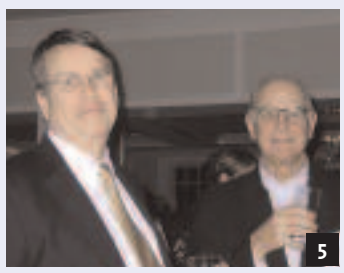
Axelrod, who died in 2004, was a productive scientist for more than 20 years before he returned to graduate school after-hours to receive his PH.D. degree from George Washington University at age 42. He moved to the NIMH at about the same time, and went on to do the work that earned him the Nobel Prize. "F. Scott Fitzgerald once stated that there are no second acts in American lives," Axelrod wrote in a 1988 memoir. "After a mediocre first act, my second act was a smash."

Out & about

November 3: A gathering to celebrate the establishment of the Kenneth and Georgia BARWICK MEMORIAL FUNDS in Pathology and Humanities in Medicine was held at the Union League Cafe in New Haven. **1.** Back row, from left: Dean **Robert J. Alpern**, M.D., **Mark E. Ludwig**, M.D., **Linda Hager**, **G. J. Walker Smith**, M.D., **Richard N. Eisen**, M.D., **Linda Brown**, **Howard M. Spiro**, M.D., **Marian Spiro**, **Thomas P. Duffy**, M.D., **Suzanne P. Lagarde**, M.D., **A. Brian West**, M.D., and **Lynda Tyrrell**. Front row, from left: **Elizabeth Mulvoy**, **Georgia Barwick**, **Sarah Barwick**, and **Lawrence D. True**, M.D. **2.** West with Marian Spiro. **3.** Sarah and Georgia Barwick.



November 14: The Great Hall of Dinosaurs at Yale's Peabody Museum of Natural History was the setting for THINK BIG ABOUT CHILDREN'S HEALTH, hosted by **Margaret K. Hostetter**, M.D., chair and Jean McLean Wallace Professor of Pediatrics, and **R. Lawrence Moss**, M.D., associate professor of surgery and surgeon-in-chief at Yale-New Haven Children's Hospital. **1. Ann Sherred** and **Scott A. Rivkees**, M.D., professor of pediatrics and director of the Yale Child Health Research Center. **2.** Moss with WTNH anchor **Jocelyn Maminta** and **Gary Doyen**. **3. Lauren Tarshis**, **David Dreyfuss**, and **Annick Winokur**. **4.** From left: Hostetter, **Michael Cappello**, M.D., professor of pediatrics and epidemiology and public health, and director of the Yale Program in International Child Health, **Joan R. Halpin**, **Harold J. Halpin Jr.**, and **Harold J. Halpin III**.

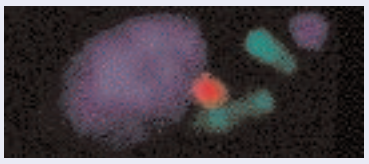


November 11: Supporters of YALE PEDIATRIC SURGERY gathered at the Country Club of New Canaan at the invitation of **Robert and Wendy Dewey**. Associate Professor of Surgery **R. Lawrence Moss**, M.D., surgeon-in-chief at Yale-New Haven Children's Hospital, joined colleagues **Milissa A. McKee**, M.D., M.P.H., assistant professor of surgery, and **Christopher K. Breuer**, M.D., assistant professor of surgery and brother of Wendy Dewey, to present the department's latest research and state-of-the-art surgical techniques for young patients. **1.** Musician **Edie Brickell**. **2. Barbara Breuer**, **Harriet Dewey** and **Jennifer Baxter**. **3. Andrea Ingalls**, **Tim Breuer** and **Eunice Lynch**. **4. Tori Dewey** and **Olivia Tabah**. **5. Robert Breuer** and Robert Dewey. **6. Sarah Grow** and **Kendra Seth**.

November 17: The opening reception for ART PLACE EXHIBIT XI was held at the Yale Physicians Building. Art Place, an exhibit founded and funded by the Yale Medical Group (YMG), enriches the experience of YMG patients and staff with visual art. This year's reception also featured readings from the third edition of *Caduceus*, a journal of poetry published by Art Place. **1.** *Caduceus* editor **Tony Fusco** (back to camera) at the poetry reading. **2.** Exhibiting potter **Sally Tomiko** (left) with friends. **3.** From left: Art Place Director **Lorraine F. Roseman** and Artistic and Technical Advisor **Terry Dagradi** with **Betty Monz**, executive director of the Arts Council of Greater New Haven. **4.** Professor of Medicine and Pathology **Philip W. Askenase**, M.D., with his wife, exhibiting painter **Marjorie Askenase**.

Advances

Health and science news from Yale



Along for the ride when cells divide

When a daughter leaves home, she packs her bags with provisions she'll need to strike out on her own. A daughter cell—the new cell formed when a cell reproduces by dividing—does the same, gathering up copies of its parent cell's organelles before it separates.

One organelle, the Golgi apparatus, sorts and modifies proteins and packages them to be shuttled to proper sites in the cell. In most animal cells the Golgi comprises several hundred stacks stitched together into a ribbon, but in *Trypanosome brucei*, the parasite that causes sleeping sickness, there is just one Golgi stack.

Professor of Cell Biology Graham B. Warren, PH.D., capitalized on this simplicity in a study published in the November 18 issue of *Science* that illuminates how new Golgi are formed in daughter cells. When Warren and his colleagues tagged *T. brucei* organelles with fluorescent labels and watched through microscopes as the parasite divided, they discovered a new, as yet unnamed structure (lower green form in photo) that orchestrates the duplication of Golgi (red) in daughter cells.

Are skin cells guards or go-betweens?

Accounting for 15 percent of our body weight, and with an average surface area of 20 square feet, the skin is the body's largest organ. In addition to providing a rugged protective sheath, the skin is studded with immune system cells. Langerhans cells (LCs) in the epidermis have long been thought to spur the immune system into action when we encounter pathogens, and overactive LCs have been implicated in autoimmune diseases of the skin.

But an unexpected result reported on the cover of the December 15 issue of *Immunity* by Daniel H. Kaplan, M.D., PH.D., assistant professor of dermatology, and Mark J. Shlomchik, M.D., PH.D., professor of laboratory medicine and immunobiology, may force a rethinking of these ideas.

When the researchers engineered mice that lacked LCs at birth, they expected the animals to be resistant to allergic skin reactions. Instead, these mice have skin that is far more sensitive than normal mice.

"We now view these cells not just as sentinels or stimulators of immune reactions, but as peacekeepers with the environment," says Shlomchik. "Failure of this mechanism could result in chronic inflammatory skin conditions like lupus and psoriasis."

Student-run clinic is a haven for uninsured

Yale students across all health professions unite to serve local community

When it comes to health care, New Haven's Fair Haven neighborhood has more than its share of the underserved and uninsured. Thanks to a new free medical clinic launched by students from the School of Medicine, the School of Nursing, Epidemiology and Public Health and the Physician Associate Program, many residents of Fair Haven, including some who have never been to a doctor for chronic, life-threatening illnesses, are getting treatment as well as education to ward off future health problems.

The clinic, known as HAVEN (an acronym for Health Care, Advocacy, Volunteerism, Education and Neighborhood), was the brainchild of Karen Archabald and other students from the medical school's Class of 2007 and Ryan Hebert of the Class of 2008. HAVEN provides an array of medical services to uninsured patients free of charge every Saturday morning, says Mallika Mendu, who is co-director of the clinic with fellow member of the Class of 2008 Margaret Samuels-Kalow.

Each patient at HAVEN is seen by a team of students and an attending clinician who may be a physician or nurse practitioner from the Fair Haven Community Health Center (FHCHC), which houses HAVEN, or a faculty member from the School of Medicine, the School of Nursing or the Physician Associate program.

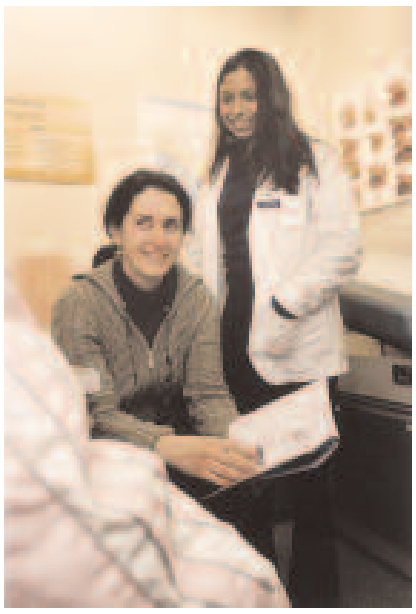
Getting adequate and healthful nutrition is a major issue for the clinic's patients, and most come in with multiple unmanaged chronic diseases, such as diabetes and hypertension, says education coordinator Corinna Levine, a second-year medical student. The students run an educational program to provide general information about diseases and their management that supplements the instructions patients receive from the attending physician. The clinic's personnel offer one-on-one education on these issues during patient visits, and group classes at HAVEN are in the planning stages, Levine says.

Patients also receive a social work consultation from students that informs them about agencies that provide assistance with non-medical issues, such as housing. Cynthia Correll, the clinic's social work coordinator and a second-year medical student, says that most patients are unaware that they may be eligible for public health insurance programs. The applications for such programs are complicated, she says, and they are often not available in Spanish, the language spoken by most of the clinic's patients. Interpreters on the clinic's staff help to overcome the language barrier.

The clinic receives funding from all the Yale health profession programs and is seeking grants from community sources. HAVEN works from a list of generic drugs, but patients still find it difficult to afford prescriptions, and the clinic organizers have built up a stock of commonly prescribed medicines to give to patients at low cost.

Yale-New Haven Hospital is donating laboratory services to HAVEN, and the students who run the clinic have recruited specialists who have agreed to see patients who are referred to them on a pro bono basis. Almost 200 students are involved in the free clinic, about 30 of whom see patients at HAVEN on any given Saturday.

Working around the constraints facing low-income patients is a skill that can only be learned in practice, according to Mary Bartlett, M.S.N., A.P.R.N., a nurse practitioner and 2000 graduate of the School of Nursing who acts as HAVEN's medical director along with Laurie Bridger, M.D., assistant clinical professor of medicine and a medical director of the FHCHC.



Margaret Samuels-Kalow (center) and Mallika Mendu (right) consult with a patient at the new free clinic.

Bartlett says she is impressed that the students who work in the clinic have opted to gain this experience early in their careers and that they are learning to work in interdisciplinary teams. Bartlett was eager to join the project because of the well-researched business plan the students presented and because of their commitment to the clinic, which she says she finds "revitalizing."

For the students, the clinic is a way to make a difference the day they arrive in New Haven. Rachel Solomon, the clinic's phlebotomist and a member of the School of Medicine's Class of 2009, says that although many medical students talk about traveling abroad to do humanitarian work, "there's a real need in our own community."

The power of Botox, a drug with many faces

A "life-changing" treatment that's more than skin deep

For those of us who first learned of Botox from the frothy pages of *People* and *Entertainment Weekly*, it might come as a surprise that a drug that rose to fame in the 1990s as wrinkle-eraser to the stars now makes regular appearances in the venerable *Annals of Neurology*. But Botox is serious medicine, "one of the biggest breakthroughs of the last 50 years," says Yale Medical Group (YMG) physician and Associate Professor of Neurology Jonathan M. Goldstein, M.D., a member of YMG's Botulinum Program.

Botox is a trade name for botulinum toxin type A, the highly potent bacterial substance that causes botulism poisoning. Botulinum makes wrinkles less obvious by relaxing facial muscles, but the drug also eases symptoms in a number of serious medical conditions, including multiple sclerosis, cerebral palsy and chronic muscle spasms. Botulinum is also useful in treating migraines and excessive salivation or sweating.

Bahman Jabbari

Jonathan Goldstein

More than 300 patients with a wide range of symptoms visited YMG's Botulinum Program last year. One, H. Stuart Engar, suffered neck pain from an undiagnosed neurological disorder for 15 years before enrolling in a botulinum study conducted by Professor of Neurology Bahman Jabbari, M.D., who was one of the first researchers to establish the drug's effectiveness in treating pain. Engar says the relief provided by botulinum has been "life-changing." According to Jabbari, Engar's enthusiasm is not unusual, because botulinum can dramatically relieve symptoms in chronic conditions that are otherwise difficult to treat. New uses for the drug continue to evolve at Yale, where Jabbari is testing its effectiveness in pain management and other applications.

Clinical interest in botulinum dates back to the 1960s, when Alan B. Scott, M.D., of the Smith-Kettlewell Eye Institute in San Francisco showed that the toxin could successfully treat disorders of eye muscles. In collaboration with biochemist Edward J. Schantz, PH.D., of the University of Wisconsin, Scott developed a botulinum treatment for humans that was approved by the Food and Drug Administration in 1978.

Ten years later, Allergan purchased the rights to pursue other medical applications of botulinum from Scott, and gave the drug the now-famous Botox brand.

Yale innovation in the art of observation extends its reach

Museum training gets a closer look from medical schools, police

Irwin Braverman and Linda Friedlaender absorb the details in a painting by J.M.W. Turner at the Yale Center for British Art.

You might expect a seen-it-all New Haven police detective to be skeptical about the professional benefits of looking at Victorian paintings. But when Lt. Herman Badger recently tried an exercise that hones observation skills by viewing fine art, he was eager for more. Badger called the experience "fascinating."

Along with Yale University Police Chief James A. Perrotti and several other police supervisors, Badger, chief of detectives for the New Haven police department, carefully examined slides of paintings, including a portrait of two women. He says the group then gave what they believed were exhaustive descriptions of the picture. "The main focus of our job is to be trained observers," Badger explains.

But then they looked again. "Upon looking at it closer," says Badger, a 22-year veteran of the New Haven force, "we would find so many other details that would change our perception of the object we were looking at."

Badger now believes that studying and describing paintings can help him and his colleagues do better police work, so later this month, many of the 40 supervisors at the New Haven department will join 17 from the Yale force at the Yale Center for British Art (YCBA) in a program designed to sharpen their attention to fine visual details.

The phenomenon isn't confined to New Haven: police from New York City to London's Scotland Yard are looking at art to become better cops, thanks to a program developed in 1997 at the School of Medicine when Professor of Dermatology Irwin M. Braverman, M.D., and Linda K. Friedlaender, M.S., the YCBA's curator of education, arrived at the same idea from opposite directions.

Worried that observational skills that are best honed in direct doctor-patient interaction might be waning in an era of laboratory tests, electronic monitors and medical imaging, Braverman wondered if looking closely at art might help young physicians be better observers in the clinic. "Physicians were losing this ability that they all had, and all used, 50 years ago," he says.

At about the same time, Friedlaender had a disappointing experience at the hospital when she saw that a resident examining a friend of hers prior to surgery failed to notice obvious signs that the patient was agitated. Friedlaender told this story to her friend Braverman, and the program, called Enhancing Observational Skills, was born soon after.

The YCBA, the final work of acclaimed architect Louis I. Kahn, houses the largest collection of British art outside the United Kingdom. Each spring, Yale medical students visit the museum for three hours to study and describe paintings, and they then apply their enriched observational vocabulary to images of human skin lesions they are likely to encounter in the clinic.

The program, now required of all first-year students as part of the Preclinical Clerkship course directed by Professor of Medicine Margaret J. Bia, M.D., has proven so successful that two dozen other medical schools have adapted it to fit their own curricula. And educators in professions from law enforcement to business are following suit, putting to work Braverman and Friedlaender's art-based approach to refining powers of observation.

Yale School of Management Dean Joel M. Podolny, PH.D., thought business students also could learn how to size up a situation by looking at art, so as part of their orientation last August newly arrived Yale business students paid a visit to the YCBA.

With Friedlaender's advice, Amy Herman, J.D., M.A., head of education at the Frick Collection in New York, is offering a variation on the program, using her museum's portraits to teach observation skills to about 200 medical students a year drawn from Weill Medical College of Cornell University, Albert Einstein College of Medicine of Yeshiva University, Mount Sinai School of Medicine and New York University School of Medicine.

Two years ago, Herman invited members of the New York City Police Department to take similar training, and 500 city cops attended sessions at the Frick last year. The resulting publicity, including a front page story in *The Wall Street Journal*, brought an invitation to Herman to deliver a presentation on the method at Scotland Yard.

According to Friedlaender, the New Haven police will apply their new descriptive skills to photos of street scenes, not skin lesions.

"This exercise may encourage officers to consider how the museum looking experience might impact their professional duties," Friedlaender says, adding, "I'm sure they could teach me a thing or two."

Alliance *continued from page 1*

"As a global company, we need to be successful in reaching out to networks on an international basis, but innovation is also happening to a very large extent in clusters," Dolsten says. "The cluster is the more 'vertical' innovation where you can go in depth into biological processes. And Yale, with its excellence in immunology and cardiovascular research, offers a real opportunity for mutual benefit."

In recent years there has been a growing realization that cardiovascular diseases, inflammatory processes and immune disorders are tightly linked, and Uwe Schoenbeck, PH.D., vice president for cardiovascular disease research at BIPI, says that research may reveal many other new disease relationships.

"If you drive your drug discovery process in a very limited fashion toward the compound you're looking for, you're lacking on what's left and right of the path," Schoenbeck says. "It's always very important to see what other pathways are affected. That's something we can explore in this collaboration, where we have the expertise on the Yale side about the broad spectrum of pathways involved."

In the alliance, which was formalized last July, BIPI will provide funds of approximately $1 million per year toward research projects at Yale, five of which are already under way.

Like Dolsten, Carolyn W. Slayman, PH.D., the medical school's deputy dean for academic and scientific affairs, believes that both parties stand to gain by the new partnership. "BIPI will draw upon Yale's superb research strengths in immunology, inflammation and cardiovascular biology," Slayman says, "while Yale investigators will have access to expertise and research materials from one of world's most outstanding pharmaceutical companies."

BIPI has been a loyal ally of Yale's Science, Technology and Research Scholars (STARS) program, which provides academic support and research opportunities to minorities, women and physically challenged undergraduates majoring in the natural sciences or engineering. "The most important resource we have is people," Paul Anderson, PH.D., senior vice president for research at BIPI, says of STARS. "It's very important for us to support students in the biological and physical sciences, because they're the lifeblood of our future research."

Dean Robert Alpern with the steering committee that oversees the Yale-BIPI alliance. (Standing, from left) Carolyn Slayman, Mikael Dolsten, Alpern, Paul Anderson, Richard Flavell, Kim Bottomly and William Sessa. (Seated, from left) Jordan Pober and Uwe Schoenbeck.

Dolsten is pleased with the present progress of the alliance. "The interaction with Yale has been very open and trustful and has already had a quick jump-start," he says. "Yale has a very positive spirit on sharing of information and building on partnership, which are the hallmarks of a successful organization. From my experience with many universities, I'm very impressed."

Schoenbeck agrees. "If you don't have the communication, things will thin out over time and disappear," he says. "If you keep your communication going—and that's one of the strengths we have with the people involved in this alliance—you'll have a long run."

Grants and contracts awarded to Yale School of Medicine *September/October 2005*

Federal

Nadia Abdala, NIH, *Identifying HIV-Bridge-Population in STI Clinics in Russia*, 2 years, $148,797 • **Ronald Braithwaite**, NIH, *Defining the Threshold for Alcohol-Induced Nonadherence in HIV+ Patients*, 2 years, $340,221 • **Catalin Buhimschi**, NIH, *Mechanisms of Myometrial Healing and Regeneration*, 2 years, $163,500 **Kathleen Carroll**, NIH, *Clinical Trials Network: New England Node*, 5 years, $6,200,278 • **Gary Cline**, NIH, *Metabolic and Mitochondrial Defects of Islet Beta-Cell of MODY-3*, 4 years, $1,070,622 • **James Comer**, Dept. of Education, *Integrating Instructional Strategies with Systemic Reform*, 3 years, $1,327,331 • **Joseph Craft**, NIH, *CNS Lupus: Mechanistic Dissection*, 2 years, $414,984 • **Francesco D'Errico**, NIH, *Chemotherapy with Injectable Microdroplets*, 1 year, $169,985 • **Sabrina Diano**, NIH, *Learning and Memory in the Melanocortin System*, 4 years, $1,308,000 • **Ronald Duman**, NIH, *Profiling Gene Expression in Major Depression*, 4 years, $1,182,871 • **James Duncan**, NIH, *Image Analysis for Adaptive Prostate Radiotherapy*, 4 years, $1,824,710 • **Jack Elias**, NIH, *AMCase and BRP-39 in Th2 Inflammation and Asthma*, 4 years, $1,635,000 • **Donald Engelman**, NIH, *A High-Capacity Screen for Membrane-Active Compounds*, 1 year, $204,375 **Paul Falzer**, NIH, *Image Theory in Disseminating Evidence-Based Practices*, 3 years, $381,420 **David Fiellin**, NIH, *Counseling for Primary Care Office-Based Buprenorphine*, 5 years, $2,975,029 • **Erol Fikrig**, NIH, *Immune Function and Biodefense in Children, Elderly and Immunocompromised Populations*, 5 years, $11,518,083 • **Brian Forsyth**, NIH, *Promoting Resilience in Young Children of HIV-Infected Mothers in South Africa*, 5 years, $2,804,291 **Shawn Fultz**, NIH, *Markers of Alcohol Toxicity in HIV-Infected Veterans*, 2 years, $341,479 • **Ya Ha**, NIH, *The Structural Basis for APP Cleavability*, 5 years, $1,430,625 • **Theodore Holford**, NIH, *Modeling Interventions for Lung Cancer Mortality*, 5 years, $1,251,389 • **Tamas Horvath**, NIH, *Central Peptidergic Circuits in Metabolism Regulation*, 3 years, $858,375 • **Hetal Kocinsky**, NIH, *The Role of Phosphorylation in the Regulation of NHE3*, 5 years, $718,875 • **Michael Kozal**, NIH, *Hepatitis C Microarrays to Detect Drug Resistance*, 2 years, $358,600 • **Diane Krause**, NIH, *Yale Center of Excellence in Molecular Hematology*, 5 years, $4,985,073 • **Paul Lizardi**, NIH, *Global DNA Methylation Profiles of Head and Neck Cancers*, 1 year, $138,975 **Steven Marans**, *Center for Mental Health Services, SAMHSA Childhood Violent Trauma Center*, 4 years, $600,000 • **Sherry McKee**, NIH, *Investigating Tobacco and Alcohol Use Behaviors Across the Continuum of Use*, 2 years, $145,500 • **Thomas McMahon**, NIH, *Parent Intervention for Drug-Abusing Fathers*, 4 years, $1,371,621 • **David Morris**, NIH, *High Throughput Molecular Screening for Compounds that Alter TGFb1 Signaling*, 1 year, $204,375 • **David Musto**, NIH, *Previous American Drug Experience and Future Perspectives*, 5 years, $715,334 **Nazih Nakhoul**, Tulane University, *Membrane Transport of NH3 and NH4+*, 5 months, $15,280 • **Marina Picciotto**, NIH, *Nicotine Addiction in Mice Lacking the Neuronal nAChR*, 5 years, $1,635,000 • **Marc Potenza**, NIH, *fMRI of CBT and CM for Cocaine Dependence*, 5 years, $1,822,059 • **Carrie Redlich**, NIH, *Program for Patient-Oriented Environment Health Research and Training*, 5 years, $896,295 **Richard Schottenfeld**, NIH, *Improving Efficacy of Drug Abuse Treatment*, 4.5 years, $777,091 **Peter Schwartz**, Health Resources and Services Administration, *Yale Ovarian Cancer and Early Detection Program*, 1 year, $392,826 • **Robert Sherwin**, NIH, *Islet Transplantation and CNS Metabolism in Hypoglycemia*, 3 years, $1,376,105 **Stefan Somlo**, NIH, *Yale Center for the Study of Polycystic Kidney Disease*, 5 years, $5,619,720 **Sandra Springer**, NIH, *Opiate Dependence, HIV and Adherence Interventions*, 1 year, $835,292 • **Tami Sullivan**, NIH, *The Temporal Relationship of Partner Violence and Drug Use*, 5 years, $828,329 • **Ning Tian**, NIH, *NMDA Receptor and Synaptic Plasticity in Retina*, 3 years, $490,500 • **Mary Tinetti**, NIH, *Need for Tailored Clinical Trials: Hypertension and Fall Risk*, 2 years, $367,131 • **Vinzenz Unger**, NIH, *Structure and Function of Copper Transporters*, 4 years, $1,216,957 • **John Wysolmerski**, NIH, *Recovery of Bone Mass After Lactation*, 2 years, $327,000 • **Heping Zhang**, NIH, *Data Management, Statistics and Informatics Core*, 5 years, $10,021,496 • **Tongzhang Zheng**, NIH, *Occupational Exposure and NHL Risk*, 1 year, $9,600

Non-Federal

Serap Aksoy, World Health Organization, Glossina *Developmental-Stage-Specific EST Project*, 1 year, $5,000 • **Luis Anez**, State of CT Dept. of Mental Health and Addiction Services, *Connecticut Co-Occurring State Incentive Grant*, 1 year, $260,000 • **Abdallah Badou**, Boehringer Ingelheim Pharmaceuticals, Inc., *Th1 Cells,* 1 year, $180,000 • **Samuel Ball**, National Alliance for Research on Schizophrenia and Depression, *Psychotic Spectrum Personality Disorders in Homeless Persons*, 2 years, $99,888 **Kevin Behar**, Children's Hospital of Pittsburgh Foundation, *Murine Succinate Semialdehyde Dehydrogenase Deficiency, and Epileptic Disorder with Elevated CNS GABA*, 1 year, $12,435 **Zubin Bhagwagar**, National Alliance for Research on Schizophrenia and Depression, *Serotonin and Vulnerability to Bipolar Disorder*, 1 year, $27,885 • **Walter Boron**, Regents of the University of California, *Bicarbonate Transport in Neurons and Astrocytes in Hypoxia*, 1 year, $243,540 • **Yung-Chi Cheng**, National Foundation for Cancer Research, *National Foundation for Cancer Research Fellowship*, 5 years, $375,000 • **R. Todd Constable**, Pfizer, Inc., *Validation of Next Generation and Analysis Tools for Brain Perfusion*, 1 year, $517,559; Pfizer, Inc., *Test-Retest Variability of fMRI Measures of Working Memory in Healthy Volunteers*, 4 months, $275,249 • **Larry Davidson**, State of CT Dept. of Mental Health and Addiction Services, *Connecticut Mental Health Transformation State Incentive Grant*, 1 year, $863,079 **Michael DiGiovanna**, The Breast Cancer Research Foundation, *Activated HER2 as a Predictor of Therapeutic Response and as a Target in Novel Combination Therapies*, 1 year, $249,343 **Ralph DiLeone**, National Alliance for Research on Schizophrenia and Depression, *The Role of Nucleus Accumbens MCH Signaling in Modulating Mood and Depression*, 1 year, 30,000 **Naomi Driesen**, Pfizer, Inc., *The Effect of Ketamine and Glycine on Working Memory in Healthy Subjects*, 8 months, 257,582 • **Barbara Ehrlich**, Robert Leet and Clara Guthrie Patterson Trust, *A New Role for the Anti-Cancer Drug Taxol on Calcium Signaling and Peripheral Neuropathy*, 1 year, $60,000 • **Jack Elias**, Amrad Corporation Ltd., *Role of IL-11 in Asthma*, 2.5 years, $247,612 • **David Fiellin**, Robert Wood Johnson Foundation, *Evaluating Medicaid and Public Funding for Buprenorphine Treatment of Opioid Dependence*, 3 years, $292,396 • **Tony George**, National Alliance for Research on Schizophrenia and Depression, *Effects of Galanthamine on Neurocognitive Deficits in Smokers and Non-Smokers with Schizophrenia*, 2 years, $99,391 • **Frank Giordano**, Boehringer Ingelheim Pharmaceuticals, Inc., *Pharmacological Manipulation of HIF,* 2 years, $360,000 • **Nora Groce**, UNICEF New York, *UNICEF Violence Against Children Consultation*, 6 months, $9,500 **Steven Hebert**, Boehringer Ingelheim Pharmaceuticals, Inc., *Mouse Kidney Physiology*, 2 years, $180,000 **Richard Hochberg**, Wake Forest University School of Medicine, *Androgen Receptor-Mediated Detection of Cancer Using PET*, 1 year, $49,697 • **Beth Jones**, University of Miami, *Psychosocial Factors, Race, and Cancer Survival*, 6 months, $14,728 • **Susan Kaech**, Cancer Research Institute, *Determining the Role of IL-7 Signaling in Memory CD8 T-cell Development During Acute and Chronic Viral Infection*, 4 years, $200,000 **Daniel Kaplan**, The Lupus Research Institute, *Involvement of Plasmacytoid DCs in the Development of LE (Lupus Erythematosis)*, 3 years, $300,000 • **Michael Kashgarian**, University of California-San Diego, *Hypoxia in Development: Injury in Adaptation Mechanisms*, 5 years, $70,093 • **Steven Kendell**, National Alliance for Research on Schizophrenia and Depression, *Measurement of Riluzole Impact Upon Cortical Amino Acid Neurotransmitter Levels in Treatment-Resistant Major Depressive Disorder*, 2 years, $60,000 • **James Mazer**, Whitehall Foundation, Inc., *The Neural Basis of Natural Vision*, 3 years, $224,000 **Godfrey Pearlson**, Meharry Medical College, *Meharry Alcohol Research Collaborative*, 1 year, $7,711 • **Jordan Pober**, Boehringer Ingelheim Pharmaceuticals, Inc., *Endothelial Cells and Cardiac Myocytes,* 1 year, $90,000 • **Alan Sartorelli**, National Foundation for Cancer Research, *Role of Transcription Factor Scl in Sensitivity of Leukemia Cells to All-trans Retinoic Acid/LiCl Induced Differentiation*, 1 year, $50,000 **Gerald Shadel**, Ohio State University, *Induction of Inflammation by Mitochondrial Proteins*, 1 year, $8,019 • **Gordon Shepherd**, Weill Medical College of Cornell University, *Neuroinformatic-based Neuroscience Information Framework*, 1 year, $125,000 • **Warren Shlomchik**, Medarex, Inc., *Novel Immunotoxins for Depletion of Dendritic Cells*, 1 year, $60,000 **Norman Siegel**, University of California-San Diego, *Renal Tolerance to Anoxia/Ischemia*, 5 years, $240,531 • **Albert Sinusas**, Juvenile Diabetes Research Foundation International, *Targeted Imaging of Angiogenesis and Angiogenic Therapy in Type 1 Diabetes*, 1 year, $110,000 **Stephen Strittmatter**, The Amyotrophic Lateral Sclerosis Association, *Nogo and Nogo Receptor in Transgenic ALS*, 1 year, $97,633 • **Michael Tal**, Pfizer, Inc., *Pancreatic Beta Cell Mass and Function Quantification by Means of Perfusion Imaging*, 2 years, $938,000 • **Nadia Ward**, State of CT Dept. of Higher Education, *Maximizing Adolescent Academic Excellence*, 1 year, $149,500; University of Connecticut, *Maximizing Adolescent Academic Excellence*, 1 year, $70,000 • **Robert Weiss**, Interstital Cystitis Association, *Signaling Pathways in the Urothelium of IC Patients Causing Decreased Urinary Cyclic GMP*, 1 year, $10,450 • **Kimberly Yonkers**, National Alliance for Research on Schizophrenia and Depression, *A Controlled Study of SSRI Exposure in Neonates*, 2 years, $102,756

Fertility *continued from page 1*

human embryos for IVF and allows only three eggs per patient to be fertilized by donor sperm. The law permits OC, because it employs unfertilized eggs that have not developed into embryos.

"Those two years have been very difficult for our patients and for us," explains Tecnobios Director Andrea Borini, M.D. "I have had the honor to lead a team of very strong people expending a great deal of energy to get better and better results after the law was passed."

The modifications to OC pioneered at Tecnobios clearly give superior results to older techniques, but there is much to be learned about why they work so well. Because of Yale's research prowess in human fertility, Borini shared the methods with Patrizio, an Italian native, who will pursue further refinements.

"It's an advantage having this program at Yale, which is a powerhouse of facilities to study subtle changes in success due to small changes in the protocols," says Patrizio, who is joining Dagan Wells, PH.D., assistant professor of obstetrics, gynecology and reproductive sciences, in molecular analyses of frozen oocytes to better understand the basic biology of OC.

Borini says that the collaboration with Yale is "the result of a strong friendship between Dr. Patrizio and me that started almost 15 years ago when we were at the beginning of our careers in infertility. I am very happy that Yale started this program, and I hope that more advances will be achieved."

The American Society for Reproductive Medicine, which classifies OC as an experimental procedure because of its historically low success rate, recommends IRB approval for all OC services, a policy that Patrizio believes is in the best interest of patients. "We are offering a service to the community that was not available, we are doing it with the best people in the world, and we are following the guidelines," he says. "The patient has the benefit of having the latest technology, but in an academic center overseen by an IRB."

Postgraduate Associate Veronica Bianchi perfoms oocyte cryopreservation at the Yale Fertility Center.

Patrizio and his colleagues are busy spreading the word about OC, particularly among local oncologists, who can now offer their patients a new option to preserve fertility.

"We didn't feel comfortable offering this service even a year ago because the results were dismal, fluctuating between a 1 and 2 percent success rate," Patrizio explains. "But once there was improvement, which is remarkable in terms of the numbers, we wanted to jump in and do it right."

Awards & honors

Ronald R. Breaker, PH.D., Henry Ford II Professor of Molecular, Cellular and Developmental Biology, professor of molecular biophysics and biochemistry and Howard Hughes Medical Institute investigator, has received the National Academy of Sciences (NAS) Award in Molecular Biology, one of 15 awards given annually by the NAS to honor pathbreaking research in a range of disciplines. Breaker shares the $25,000 award, which is supported by Pfizer, with Ohio State University's Tina M. Herkin, PH.D., for their work on novel RNA gene-control elements.

Ruslan M. Medzhitov, PH.D., professor of immunobiology, has received the AAI-BD Biosciences Investigator Award from the American Association of Immunologists (AAI) for his outstanding early-career contributions to the field of immunology. Medzhitov's research has advanced our understanding of the immune system, particularly in regard to the family of *toll*-like receptors, which play an essential role in the innate immune response. The award, which has been co-sponsored by BD Biosciences since 1998, will be presented at the AAI's annual meeting in Boston in May.

Manohar M. Panjabi, PH.D., DR.TECH., professor of orthopaedics and rehabilitation and professor of mechanical engineering, received the Wiltse Lifetime Achievement Award from the International Society for the Study of the Lumbar Spine for his "major contribution to the advancement of knowledge in the field of spinal disorders." Panjabi, an expert on spinal trauma, has been at Yale since 1971. He has published over 295 original research articles, two books and 50 book chapters.

Kudos from CASE

We've received many comments and a slew of e-mails and letters of appreciation since launching *Medicine@Yale* last summer for alumni, friends and patients of the School of Medicine and our neighbors across Connecticut.

Now we've begun building our trophy shelf. The judges of one of the premier communications competitions in higher education, sponsored by the Council for Advancement and Support of Education (CASE), awarded the Silver Medal for best newspaper in CASE 's District 1 to *Medicine@Yale*; District 1 comprises the New England states and eastern Canada. The award was given in February at the annual District 1 conference in Montreal. CASE is a professional organization devoted to alumni relations, communications and development at educational institutions throughout the world.

Yale scientist shares $1 million Dan David prize for work on cell signaling and cancer

Though 2006 is not even half over, it's already a year to remember for Joseph Schlessinger, PH.D., chair and William H. Prusoff Professor of Pharmacology. In late January, a new drug based on Schlessinger's research was approved by the U.S. Food and Drug Administration (FDA) for advanced kidney cancer and a rare type of stomach cancer. A month later, Schlessinger learned that he would share a $1 million prize for his scientific discoveries from the Dan David Foundation.

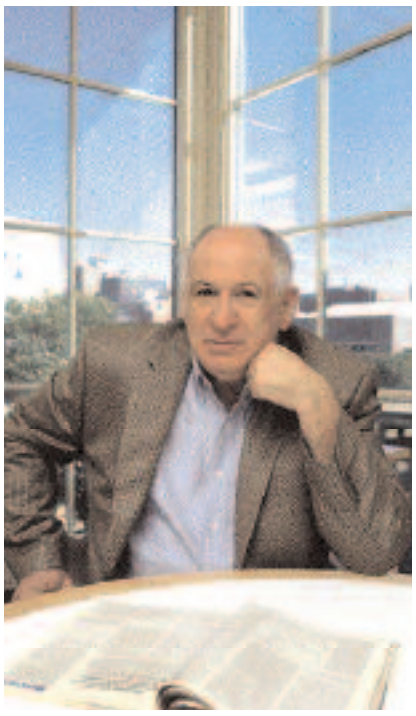
Schlessinger, known to friends as "Yossi," is a leading figure in the field of signal transduction by receptor tyrosine kinases, enzymes that are located on the cell surface and function as receptors for growth factor proteins. When growth factors activate these receptors, their associated tyrosine kinases send out intracellular signals that cause cells to divide and grow. In research spanning more than three decades, Schlessinger and his colleagues have elucidated the mechanism of action of these receptors and demonstrated how dysfunctions in certain kinases can lead to the rampant cell growth seen in cancer.

In 1991, together with Axel Ullrich, PH.D., of the Max Planck Institute of Biochemistry in Germany, Schlessinger formed the pharmaceutical company Sugen—the "S" and "U" in the company's name stand for the two founders' last names—to develop drugs that inhibit faulty tyrosine kinases. The company was acquired by Pfizer in 2003, and in subsequent clinical trials, Pfizer showed the Sugen-developed drug SU11248 to be effective in treating advanced kidney cancer as well as a stomach cancer known as gastrointestinal stromal tumor, or GIST. According to the American Cancer Society, 32,000 Americans are diagnosed with advanced kidney cancer each year, and there are 5,000 new cases of GIST. With January's FDA approval in hand, Pfizer is now marketing the drug under the tradename Sutent.

In 2001, Schlessinger co-founded Berkeley, Calif.-based Plexxikon, a drug-discovery firm focused on the role of kinases and other enzymes in diverse diseases, including cardiovascular disease, diabetes and cancer. He also serves on the scientific advisory boards of several other companies.

The Dan David Foundation, with headquarters at Tel Aviv University in Israel, awards three $1 million prizes annually for cultural, scientific, social or technological impact in three time dimensions—"past," "present" and "future." Dan David, a native of Romania who invented and marketed a variety of photographic technologies including automatic photo booths, inaugurated the prizes in 2001. Schlessinger shares the 2006 award in the Future category with John Mendelsohn, M.D., president of the M.D. Anderson Cancer Center at the University of Texas, who did the science behind the kinase-inhibiting anti-cancer drug Erbitux. Renowed cellist Yo-Yo Ma won in the Past category for preserving cultural heritage through his Silk Road project, and four journalists from around the world shared the Present prize.

Schlessinger says he was "thrilled" when he learned about the prize. "It recognizes the idea that hypothesis-driven research can lead to new understanding of how cells are activated and eventually that such knowledge can lead to new and better drugs," he says. Since coming to Yale from New York University five years ago, Schlessinger has overseen the building of new quarters for the pharmacology department and has recruited six new faculty members. "It takes a long time to build science," he says. "It takes patience."



Prizewinner Joseph Schlessinger's studies of tyrosine kinases have borne fruit in a newly approved drug for cancer.

Schlessinger says that he will attend the Dan David awards ceremony at Tel Aviv University in May, and he adds that he intends to donate a portion of the prize money to further research and education in his department. "This is a recognition of a career," he says of the prize, "one which I hope is not over yet."

Gift *continued from page 1*

A 1964 federal initiative created the MSTP to increase the number of physician-scientists. But despite the explosion of medically relevant knowledge in molecular and cell biology during the past three decades, federal funding for the MSTP, administered by the National Institute of General Medical Sciences (NIGMS), has lagged behind overall funding for the National Institutes of Health (NIH), requiring the 42 NIGMS-approved programs at medical schools across the nation to rely on other sources to support students for the duration of their studies.

Yale's program, now 37 years old, has generally only been able to directly support students for five or six years of their training, says Jamieson, who hopes to use some of the funds generated by the new gift to supplement the NIH training grant that provides the bulk of support to M.D./PH.D. students. Also, because these grants are only available to U.S. citizens, the new gift may give the program the flexibility to consider talented foreign-born applicants.

About a quarter of the 200 alumni of Yale's M.D./PH.D. Program are faculty members in basic science departments across the country, and almost three-quarters are on clinical faculty; the remainder work in private industry.

The alumni roster includes Susan J. Baserga, M.D., PH.D., associate professor of molecular biophysics and biochemistry, genetics and therapeutic radiology, and Michael J. Caplan, M.D., PH.D., professor of cellular and molecular physiology and cell biology, who administer the program under Jamieson's direction along with Professor of Medicine Frederick S. Gorelick, M.D., and Gerald I. Shulman, M.D., PH.D., professor of medicine and Howard Hughes Medical Institute investigator.

Noting that the School of Medicine has required research experience and a thesis of all its students for more than 150 years, Caplan says that Yale provides particularly fertile ground for training future physician-scientists. "Yale is unique as a medical school in its desire to devote a significant portion of its effort toward training future academic leaders," Caplan says, "and I think this program stands at the vanguard of that."

Jena Giltnane

Jena Giltnane, a fifth-year student in the MSTP, says that she interviewed at several institutions, but was ultimately attracted by the Yale program's small scale and open-door culture, which have afforded her close interaction with School of Medicine scientists.

Now studying protein expression profiles in breast cancer in the laboratory of Associate Professor of Pathology David L. Rimm, M.D., PH.D., Giltnane says that her combined experiences in bench science and patient care in the M.D./PH.D. Program will forever inform her perspective as both scientist and physician.

"I feel very gratified when I present my research to someone who's practicing medicine in the field. They understand where I'm coming from, and they can see the impact it will have on their day-to-day work," says Giltnane. "The questions I'm asking will affect the way breast cancer is treated, and that's something I'm really passionate about."