Medicine@Yale

Advancing Biomedical Science, Education and Health Care

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City vote clears way for building of cancer treatment center

A unanimous vote by the City of New Haven's Board of Aldermen making changes to the city's zoning regulations and zoning map has cleared the way for the construction of a new clinical cancer facility at Yale-New Haven Hospital (YNHH) fully dedicated to patient care and clinical research. The groundbreaking for the 14-story, $450 million structure will take place this fall, and the facility will open its doors to patients at the end of 2009.

Marna Borgstrom

"Every day nearly 50 people are diagnosed with a new case of cancer in Connecticut. The facility will allow us to meet our mission of providing exceptional care to the most acutely ill patients we serve," says Marna P. Borgstrom, M.P.H., CEO and president of YNHH.

Richard L. Edelson, M.D., Yale Cancer Center (YCC) director and professor of dermatology, agrees. "This is a huge step forward for the Yale Cancer Center's capacity to provide truly state-of-the-art care," Edelson says. "It propels forward our entire enterprise."

The hundreds of physicians, nurses, clinical researchers and laboratory technicians involved in cancer treatment at Yale are now dispersed in several locations at the hospital and medical school. The new "patient-friendly" building will bring all these people under one roof, with immediate benefits for patients, says José Costa, M.D, YCC deputy director and professor of pathology. "Our current facilities are the result of a cancer center that has been in existence for 30 years, and with the passage of time they have grown and have been remodeled to adapt to progress in clinical medicine, but in a less-

Cancer, *page 4*

A brother's gift launches Yale Scholars

Yale alumnus endows medical school initiative to fund young scientists

The Yale Scholars program, a new School of Medicine initiative to support and nurture promising young scientists, has received its first endowment in the form of a major gift from Donald S. McCluskey, M.ENG., an alumnus of Yale College and the Faculty of Engineering. The endowment will be named for McCluskey's brother, Robert T. McCluskey, M.D., the Benjamin Castleman Professor of Pathology, Emeritus, at Harvard Medical School and Massachusetts General Hospital (MGH).

Also an alumnus of Yale College, Robert McCluskey is a prolific physician-scientist who has published more than 200 research articles on the role of the immune system in kidney disease during a career spanning more than 50 years. In an example of McCluskey's extraordinary productivity, he learned recombinant DNA technology just before he "retired" as chief of pathology at MGH at age 70 in 1993 and was awarded a grant by the National Institutes of Health to embark on a new series of studies on the molecular genetics of renal pathology.

"Local boys" Robert and Donald McCluskey show off their sailor uniforms in the Morris Cove section of New Haven around 1933.

During this period he also became an active mentor to residents training in renal pathology, producing a laboratory manual for their daily use. In appreciation, the residents presented him with their Excellence in Teaching award. He officially retired in 2006.

Donald McCluskey, who graduated from Yale College in 1942 and the engineering school in 1959, has made several gifts to his alma mater, but the donation to the Yale Scholars Program in honor of his brother, a member of Yale's class of 1944, is his first to the medical school.

Donald's gift is particularly fitting, Robert says, because the spirit of the Yale Scholars program closely parallels that of an immunopathology research group he joined at New York University School of Medicine in 1955 under the leadership of famed scientist and bestselling author Lewis Thomas, M.D., who went on to become dean of Yale School of Medicine in 1972.

"The setting was exactly right," Robert McCluskey has written of Thomas's experimental pathology unit. "He recruited a group of young investigators who had freedom similar to what the Yale Scholars will enjoy. Members could work on any project they chose, and there were many important accomplishments—not the least of which was the discovery of the genetic control of the immune response, for which Baruj Benacerraf was awarded the

Gift, *page 8*

Medical school names new dean of public health

Paul D. Cleary, PH.D., an expert on how people interact with systems that provide health care, has been named dean of public health and chair of the Department of Epidemiology and Public Health. Cleary has served since 1993 as professor of medical sociology in the Departments of Health Care Policy and Social Medicine at Harvard Medical School.

Paul Cleary

"We are extremely fortunate to have Paul join the School of Medicine and are excited by his vision and commitment," Yale President Richard C. Levin, PH.D., and Dean and Ensign Professor of Medicine Robert J. Alpern, M.D., said in a joint statement announcing Cleary's appointment in March.

Cleary graduated from the University of Wisconsin in 1970 with an undergraduate degree in physics. However, advanced studies in physics seemed too abstract during a time of social ferment inspired by the Vietnam War and the civil rights movement, he says.

After taking time off from school to play in blues and rock bands,

Cleary, *page 8*

Inside this issue

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Geriatrics researcher Mary Tinetti, an expert in falls, believes in treating the whole patient, not single diseases.

A steadying influence

Top geriatrics researcher studies falls in older people, and ways to prevent them

Lifelines
Mary Tinetti

To say that Mary E. Tinetti, M.D., never thought she would find herself in New Haven, hailed as a leading researcher for her breakthrough studies of falling in older people, would be an understatement.

The Flint, Mich., native entered medical school at the University of Michigan fully expecting to practice family medicine on her home state's remote Upper Peninsula. But when she interacted with older patients during her residency in internal medicine at the University of Minnesota, Tinetti was struck by a difference in perspective that sparked her interest in geriatrics, then a relatively new field.

"The patients were concerned with how they were feeling and how they were doing, but we as internists would be concerned with what their blood pressure looked like," recalls Tinetti, now the Gladys Phillips Crofoot Professor of Medicine and professor of epidemiology and public health. "The dichotomy between what physicians and patients were interested in made me think there's got to be a way to bring these together. Geriatrics is the field that does that."

Tinetti began a fellowship at the University of Rochester under renowned geriatrics researcher T. Frank Williams, M.D., but admits she was nonplussed when Williams suggested she study falls.

"I'd just come from a high-powered internal medicine program, and I was almost embarrassed about working on something like falls! It wasn't prestigious, and it wasn't some fancy disease," Tinetti says. "But Frank is a compelling individual, and to placate him I told him I'd work on it for a year or two, thinking I'd either stop doing research altogether or find something more meaningful."

But when Tinetti began to look closely, she found that studying falls provided just the sort of clinical richness that single measures like blood pressure could never achieve. "In the usual scientific method, you isolate a single factor, and you control for all the other differences. But as people grow older, they don't become more the same, they become more different," Tinetti says. "People fall when a lot of things go wrong. It's a combination of their balance, plus their gait, plus their strength, plus their vision, plus confusion, plus blood pressure changes, plus things in the environment."

Tinetti believed that these multiple factors could be measured, and that falls could be predicted and prevented. She came to Yale to test this idea under the tutelage of the late Alvan Feinstein, M.D., whose rigor in studying patients had spawned the field of clinical epidemiology. For 20 years, Tinetti's work on falls at the medical school's Program on Aging has advanced the view that the multiple medical conditions seen in older people directly compete with or mutually reinforce one another. "If you give people antihypertensives, you may decrease the risk of stroke, but the resulting dizziness can increase the risk of hip fracture, and there are many other examples," she says.

In collaborations with nurses and occupational and physical therapists, Tinetti has pioneered treatment strategies that are tailored to individual patients rather than individual diseases. By simultaneously combining several interventions—a reduction in medication, balance exercises, and the removal of environmental hazards, for example—she has shown that falls, and the debilitation and decline that often follow, can indeed be prevented.

"Sometimes little things can make a big difference," Tinetti says. "When you've taken a complex problem and figured out what to do about it, and you can see it make a difference right before your eyes, that's very satisfying."

Yale scientist named "million-dollar professor" for teaching plan

The Howard Hughes Medical Institute (HHMI) has named Scott Strobel, PH.D., newly appointed chair and professor of molecular biophysics and biochemistry at Yale, an HHMI Professor. Strobel, one of 20 new HHMI Professors nationwide, will receive $1 million over four years from HHMI to implement an innovative introductory science course in which undergraduates will take "bio-prospecting" trips to the world's rain forests in search of promising naturally occurring chemicals.

In Strobel's new course, students will spend the spring semester learning evolution, ecology, and molecular and structural analysis. During spring break, they will take a working trek to a rain forest—the Amazon and New Zealand are among the proposed locations—to collect branches and twigs and their associated microbes. Students will spend a rigorous summer session classifying their finds and identifying new bioactive compounds.

Strobel, an expert on RNA splicing and protein synthesis, won Yale's Dylan Hixon Prize for Teaching Excellence in the Natural Sciences in 2004. His father, Gary Strobel, PH.D., professor emeritus of plant pathology at Montana State University, discovered the anti-cancer compound taxol in a fungus that grows on yew trees; the elder Strobel now travels the world in search of other naturally occurring compounds that may lead to the development of useful drugs.

"The scientists whom we have selected are true pioneers, not only in their research but in their creative approaches and dedication to teaching," says Thomas R. Cech, PH.D., HHMI president. "We are hopeful that their educational experiments will energize undergraduate science education throughout the nation."

Pediatric neurologist is new associate dean for YSM admissions

Professor of Pediatrics and Neurology Laura R. Ment, M.D., has been named associate dean for admissions and chair of the admissions committee at the School of Medicine, effective July 1. Ment succeeds Professor of Cell Biology Thomas L. Lentz, M.D., who will step down on June 30 after serving for 38 years in the medical school's Office of Admissions.

Ment, an authority on recovery of function after injury to the developing brain, is the author of more than 150 scholarly articles, including a 2003 report in the *Journal of the American Medical Association* that provided some of the first evidence that cognitive deficits associated with low birth weight diminish in the majority of children by age 8.

Laura Ment

Since arriving at Yale in 1979, Ment has made her mark as a gifted teacher. She has received the Francis Gilman Blake Award, the Leah Lowenstein Award and the Class of 2006 Teaching Award, and in 2003 she was inducted into the Society of Distinguished Teachers.

Ment earned her bachelor's and master's degrees at Brown University, and received her medical degree from Tufts University School of Medicine in 1973. She completed her neurology residency at Massachusetts General Hospital in Boston and a fellowship at Hammersmith Hospital in London, England.

In September 2005, Ment was appointed to the 18-member National Advisory Neurological Disorders and Stroke Council, the major advisory panel of the National Institute of Neurological Disorders and Stroke.

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Advances

Health and science news from Yale

Why 2 percent is a world of difference

Genomically speaking, we are 98 percent chimp, and for decades, biologists have puzzled over how this small genetic modification could create such vastly different creatures.

To explore this question, Kevin P. White, PH.D., associate professor of genetics, and his colleagues developed a gene chip to compare the activity of more than 1,000 genes from humans, chimpanzees, orangutans and rhesus macaques, four species spanning 70 million years of evolution.

As reported in the March 9 issue of *Nature*, the team found that genes that code for regulatory proteins are four times more likely to have increased their expression during human evolution than those that govern housekeeping or metabolic functions.

Monkeying with gene regulators can give rise to dramatically different new traits, like brain size or body shape, because the proteins serve as master switches that influence the activity of many other genes. "For 30 years scientists suspected that gene regulation has played a central role in human evolution," says White. "This helps open the door to a functional dissection of the role of gene regulation during the evolution of modern humans."

This is your brain on an empty stomach

Cutting calories can definitely make you trimmer, and may help you live longer. Now a new Yale study suggests that dieting might also keep you mentally sharper.

Blood levels of a gut hormone called ghrelin (rhymes with "melon") rise when the stomach is empty, flooding the brain's eating control center and stimulating neurons that govern appetite. When Tamas L. Horvath, D.V.M., PH.D., chair and associate professor of comparative medicine, and colleagues injected mice with ghrelin, the hormone rapidly altered circuits in the hippocampus, a brain region that is crucial to learning and memory. Ghrelin-treated mice were significantly better at learning and remembering their way around a maze.

In people, aging and obesity—two factors associated with memory loss in Alzheimer's disease—cause ghrelin levels to fall. Horvath's results, published in the March issue of *Nature Neuroscience*, suggest that shoring up ghrelin levels with weight reduction or drugs that mimic its action could help stave off dementia.

Minimizing pain, accelerating healing

Minimally invasive surgical techniques are on the rise at Yale

Surgery Chair Robert Udelsman (seated) and colleagues (standing, from left) James Wong, Robert Bell and Milissa McKee say savvy patients are seeking out doctors with expertise in endoscopic surgery and other minimally invasive procedures.

After a recent successful intervention at Yale-New Haven Hospital to restore blood flow through a failing hemodialysis graft, a patient shook the hand of Assistant Professor of Surgery and Diagnostic Radiology James Wong, M.D., and declared, "Dr. Wong, you are the best!"

This scene would be unremarkable except for the fact that the man congratulating Wong was still lying on the table where the procedure had been performed. Because Wong had used a balloon angioplasty catheter instead of a surgical incision to open up the graft, the patient remained awake during the procedure and went home immediately afterward.

Balloon angioplasty is just one example of a growing number of procedures that can now be performed with "minimally invasive" techniques, which for patients means little or no pain, extremely small wounds, little scarring, no hospitalization, shorter recovery periods and fewer complications, says Robert Udelsman, M.D., M.B.A., chair of the Department of Surgery and Lampman Memorial Professor of Surgery and Oncology.

Today, Udelsman says, many patients are informed consumers who seek out surgeons trained in minimally invasive surgery. The School of Medicine has retooled its educational programs to train students in these techniques, which generally adds an additional year of training to a resident's preparation for a surgical specialty.

Udelsman is one of the world's foremost practitioners of minimally invasive parathyroidectomy, a procedure to treat cancer or overactivity of the parathyroid glands in which the pea-sized glands are removed from the neck through very small incisions. Udelsman is able to speak to patients during the procedure to ensure that the surgery does no damage to the nearby larynx, and patients can generally return home shortly after the operation.

Vascular surgeons like Wong who typically operate on elderly patients have been eager to adopt minimally invasive methods because these patients are especially vulnerable to pneumonia and other complications following complex vascular surgery. Some of his patients who might have been too frail to undergo traditional surgery have done very well with the newer techniques, Wong says.

But the very young are also benefiting from the new approaches, especially endoscopic surgery, says Milissa A. McKee, M.D., M.P.H., assistant professor of surgery and pediatrics and director of pediatric trauma services at Yale-New Haven Children's Hospital. McKee says that Yale offers more minimally invasive surgical options specifically for children than any other institution in Connecticut. In her practice, McKee often uses endoscopes, devices that can be inserted through tiny incisions and include a camera, a lamp and a channel for surgical instruments. A surgeon operating on an adult might use a 10-millimeter endoscope, McKee says, but she typically works with a 4-millimeter version, about half the diameter of a pencil, to perform major operations, including the repair of defects of the lungs and intestines in newborns.

In some cases, McKee has used endoscopic techniques to treat hereditary conditions in children whose parents had been treated with traditional "open" surgery. She says that children treated with the new techniques are back to school and their normal routines sooner, their parents miss less time at work and hospitalization costs are cut substantially. "The difference is dramatic," McKee says. "This is definitely the future of children's health care."

Studies have shown that kidney donations increased after surgeons developed minimally invasive techniques for harvesting kidneys from live donors. Robert L. Bell, M.D., assistant professor of surgery, has

Surgery, *page 5*

With surgical simulation, practice makes perfect

On a recent day in the School of Medicine's new Surgical Skills and Simulation Center on Cedar Street, a colonoscopy patient groaned in discomfort as residents discussed increasing his sedation. But Assistant Professor of Surgery Andrew Duffy, M.D., said nothing, knowing that young doctors must learn to make decisions independently. Besides, this was no flesh-and-blood patient: the images of the bowel on a video screen, the vital signs readings, even the groans were generated by a computer.

In minimally invasive surgery, surgeons manipulate instruments remotely while watching the results on video screens. The simulation center, made possible by donations from Yale-New Haven Hospital; Norwalk, Conn.-based U.S. Surgical, a manufacturer of surgical devices; and Karl Storz Endoscopy-America, a surgical instrument company, allows future surgeons to log many hours of practice with endoscopic instruments before they operate on their first patient. "It has huge implications for patient safety," Duffy says.

Regulations passed in 2003 prohibit medical residents from working more than 80 hours per week, which gives surgical residents fewer opportunities to participate in operations. Duffy has developed curricula based around the new technology so that faculty can give residents a competency exam before they may assist in the operating room. Since the center's opening in January, attending physicians are reporting that residents and medical students are more skilled when they begin assisting in real surgeries.

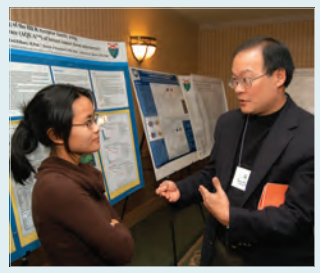
As Duffy looked on, Rachel Friedman, a third-year medical student, was working on one of the center's Storz Box Trainers to develop basic skills and dexterity. Using hand controls to guide an endoscope and long narrow instruments used in minimally invasive surgery, she picked up blocks the size of blueberries, transferred them from her right-hand instrument to her left-hand instrument and threaded them on pegs.

Few medical schools are fortunate enough to have such facilities, according to Duffy. But the technology will soon be considered essential, he says. "This is how we're going to be training surgeons for the rest of the 21st century."

Out & about

November 18: The annual golf tournament to benefit the **T-CELL LYMPHOMA FOUNDATION OF PUERTO RICO** was held at the Dorado del Mar Golf Club in Dorado, Puerto Rico. The tournament raised $50,000 for the Yale Cancer Center's cutaneous T-cell lymphoma program. Under the direction of Francine Foss, M.D., the program strives to draw on findings from the laboratory and clinical trials to develop innovative new treatments for T-cell lymphoma patients. **1.** Sponsors of the tournament included (from left) **Tomy Rodriguez**, **Mario G. Montalvo**, **Nestor Vale**, senior executive vice president of Oriental Financial Group, **Mario J. Montalvo** of Tamaca Realty, **Jorge Ros** of Johnson & Johnson and **Carlos Montalvo**, vice president at V. Suarez & Co. **2.** The tournament was hosted by **Margie and Mario G. Montalvo** of Guaynabo.

December 19: During a **VISIT OF THE UNITED SPINAL ASSOCIATION** to the medical school's Center for Neuroscience and Regeneration Research at the VA Connecticut Healthcare System (VACHS) in West Haven, Conn., the center's members gave a science briefing and United Spinal presented a check for $100,000 to support Yale/VA research on spinal cord repair. Center faculty and staff gathered with leaders of United Spinal on the VACHS campus. (Front row, from left) United Spinal's Executive Director of Research and Education **John Del Colle**, Deputy Executive Director **Paul Tobin**, board member **Edmund Rowan**, President **Clair Russell Hesselton**, Executive Director **Gerard M. Kelly**, board member **Michele A. Leahy**. (Behind Mr. Kelly, from left) Associate Executive Director for Research and Education **Vivian Beyda**, DR.PH., Dean **Robert J. Alpern**, M.D., center Director and Bridget Marie Flaherty Professor of Molecular Neurology **Stephen G. Waxman**, M.D., PH.D.



January 13–15: The **ANNUAL M.D./PH.D. RETREAT** brought students, faculty and administrators from the medical school's Medical Scientist Training Program (MSTP) to Water's Edge Resort and Spa in Westbrook, Conn., for games, panel discussions and informal presentations of research. **1.** Getting together for board games were students (back row, from left) **Mary Whitman**, **Eyal Kimchi**, **Heather McGee**, **Fabienne Meier-Abt**, **Keith Gipson**, **Kumar Narayanan**, (front row, from left) **Sara Crager**, **Ellen Vollmers**, **Rashele Cross**, **Charisse Orme**, **Heather McCrea**, **Katherine Uyhazi**, and **Linda Bi**. **2.** Professor of Medicine **Frederick S. Gorelick**, M.D., delivers the Selma and Karl Folkers Lecture. **3.** Yale MSTP alumni **Jeffrey L. Sklar**, M.D., PH.D., professor of pathology and laboratory medicine, and **Jerry Zeldis**, M.D., PH.D., chief medical officer, Celgene Corp. **4.** MSTP student **Joanna Chin** at the scientific poster presentation with alumnus **Peter T.C. Ho**, M.D., PH.D., vice president of oncology discovery medicine at GlaxoSmithKline, Inc.

Cancer *continued from page 1*

than-ideal fashion," Costa says. "The new building benefits from a clean, forward-looking design."

One of the biggest advantages of the unified facility will be easier access to state-of-the-art care for patients and families facing a challenging illness, Borgstrom says. "This project is all about providing the best care available in the most advanced setting. This building will rival those available anywhere in the world."

According to Edelson a dedicated facility is critically important because it will enhance interaction between patients and the interdisciplinary medical teams at the heart of modern cancer care.

"Cancer care is multidisciplinary, involving important input from several specialties. For example, medical oncologists, surgical oncologists, radiotherapists, diagnostic radiologists, pathologists and other specialists contribute significantly to the management of breast cancer patients," he says. "Having highly coordinated and interactive medical teams will be an enormous advantage. Bringing collaborative physicians together for face-to-face discussions to put their heads together to discuss a challenging case when it is fresh in their minds, rather than simply reading one another's notes in the chart, is simply the best way to do it."

Among the specialists who will advance cancer care in the Yale Cancer Center's new clinical pavilion are (seated, from left) Lyndsay Harris (breast), Gary Friedlaender (sarcoma), Frank Detterbeck (thoracic), Wasif Saif (gastrointestinal), Dennis Cooper (lymphoma/bone marrow transplant), (standing, from left) Mario Sznol (melanoma), Stephan Ariyan (melanoma), Donald Lannin (breast), Francine Foss (lymphoma/bone marrow transplant) and Jack van Hoff (pediatric oncology).

Although it will be more than three years before the first patient is treated in the new facility, Edelson says the project has had a formidable impact even in the planning stages by helping to bring top faculty to Yale.

"We have to have the best doctors that we can possibly have, and we can do a much better job attracting them if we have the very best facilities," Edelson says, adding that plans for the new building were instrumental in the ambitious recruiting efforts of Edward Chu, M.D., the YCC's chief of medical oncology and director of clinical research. In just two years, Chu has brought 11 top clinical investigators to Yale, a "stellar cadre," according to Costa.

The increased capacity of the new building, combined with the expertise of Chu's research team, will allow Yale to direct many more clinical trials of investigational treatments discovered by School of Medicine faculty, Edelson says. "To be able to do more clinical trials and to attract support for those trials, whether it be from the federal government or the pharmaceutical industry, depends on our ability to attract sufficient numbers of patients in sufficiently short time to get important answers."

For Costa, who has been involved in planning of the new pavilion for six years, the building's advancement of both care and research will mark a new era in the YCC's 30-year history. "We want to go beyond where we are now to explore with our patients the novel diagnostic modalities that will enable us to diagnose cancer at the earliest moment, and to use the therapeutics that are the most effective and cancer-specific and the least toxic," says Costa. "We want to be practicing the medicine of tomorrow. Let's not remodel the house; let's build a new house that is ideally suited not just for today, but for where we think we will be in 10 years."

Advances

Health and science news from Yale

Cells fall on sword to stop Legionnaire's

Like a deadly stowaway, *Legionella pneumophila*, the bacterium that causes Legionnaire's disease, (see photo) hides inside cells to evade detection by the immune system. Holed up in sealed vacuoles, the germs multiply, causing fatal pneumonia in up to a quarter of those infected.

But the immune system usually outwits *Legionella*. In the March issue of the journal *Nature Immunology*, Associate Professor of Microbial Pathogenesis Craig R. Roy, PH.D., and colleagues show that immune cells detect *Legionella* and destroy it by inducing cells to commit suicide.

Roy's team found that a protein called Birc1e detects any bits of bacteria that escape vacuoles and activates the caspase-1 protease, a master regulator of cell death. Caspase-1 degrades proteins in infected cells, starting a cascade of events that end with the cell's demise—and the elimination of *Legionella*.

"Identification of Birc1e and the caspase cascade gives us information about the process of how the body fights off infection by a potentially lethal microbe, as well as possible targets for treatments," says Roy.

Maki de Sade: wasabi really hurts!

For pain researchers, the recent discovery of a neuronal receptor that relays the zip of wasabi holds more than gastronomic interest: the sinus-clearing kick of the Japanese condiment registers not on the taste buds, but in pain-sensing nerve cells in the nose.

According to Assistant Professor of Pharmacology Sven-Eric Jordt, PH.D., and collaborators, the newly identified receptor is also key to garlic's bite, and to the toxic and inflammatory effects of many environmental irritants.

As reported in the March 24 issue of *Cell*, mice lacking the TRPA1 receptor experience little pain or irritation when mustard oil, the pungent ingredient in wasabi and mustard, is applied to their paws. Neurons in these mice also failed to respond to the main irritant found in tear gas, wood smoke and car exhaust, and the animals were less sensitive to some types of inflammatory pain.

Jordt says that finding ways to shut down the TRPA1 receptor in people could yield much-needed new pain therapies for injuries and diseases from arthritis to cancer, and that manipulating the receptor might also help pollution-related diseases like asthma and chronic cough.

Meeting the demand for blood supply: Yale makes strides in vessel engineering

Although blood vessels may seem like mere plumbing compared to organs like the brain or eye, they are complex and dynamic components of the body, and building vessels from scratch has been a challenge for scientists in the field of tissue engineering. Having the ability to create vessels from patients' own cells would be a boon for cardiovascular bypass surgery, for restoring circulation to blood-starved limbs or as replacements for failing vascular grafts used in kidney dialysis.

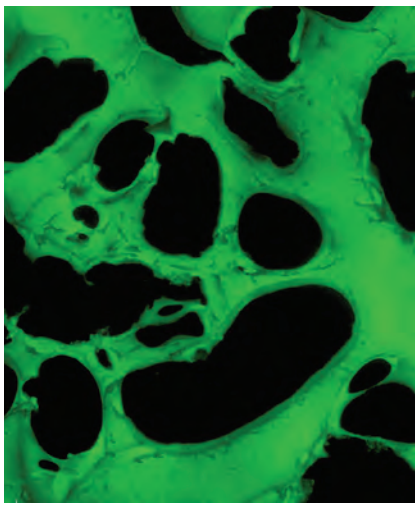
Two recent Yale studies, both published in the February 21 issue of the *Proceedings of the National Academy of Sciences*, have moved vessel engineering closer to clinical application. In one, researchers created a tiny, water-rich scaffold that can nurture and shape microvascular networks to provide tissues with a new blood supply; in the other, scientists demonstrated that they could tweak a molecule to prolong the life of blood vessel cells from elderly donors without causing those cells to spiral toward the uncontrolled cell growth seen in cancer.

"A microvascular network is fundamentally important for tissue engineering," says Erin Lavik, SC.D., assistant professor of biomedical engineering and co-author of one of the studies, but "stability of microvascular networks has been a challenge."

To create new blood vessels, tissue engineers generally build scaffolds from polymers and seed them with human blood vessel cells. Like trellises that train rosebushes, vessel scaffolds guide cell growth to create a tubular structure that blood can flow through.

Because Lavik's team wanted to build networks of the tiniest vessels, they devised a "micro-scaffold" from a hydrogel, a gelatin-like material that

Yale tissue engineers (clockwise from left) Erin Lavik, Joseph Madri and Laura Niklason are breaking new ground in building new blood vessels.



Pores through a hydrogel scaffold created by Yale scientists provide pathways for growing blood vessels.

can be chemically treated to form numerous pores (see photo below). As their name implies, hydrogels are mostly water, which makes them highly compatible with the body's tissues.

In collaboration with Joseph A. Madri, M.D., PH.D., professor of pathology and of molecular, cellular and developmental biology, Lavik and colleagues seeded the gels with blood vessel cells and implanted them under the skin of mice. After six weeks, using a technique known as intravital fluorescence microscopy, the team observed red blood cells flowing through functional and stable vessel networks that had formed in the pores of the hydrogel implant.

Using more conventional scaffolds, scientists have been able to build larger human blood vessels outside the body from a donor's own cells, but cells taken from older people—those most in need of new vessels—are less viable than cells from younger people, which results in weaker vessels.

Last year, researchers led by Laura E. Niklason, M.D., PH.D., associate professor of anesthesiology and biomedical engineering, used gene therapy techniques to deliver telomerase, an enzyme that extends cells' normal lifespan, to blood vessel cells from older donors.

The technique extended the life of the cells, even those taken from patients as old as 85. In addition, Niklason showed that it was possible to culture new arteries for these older patients *in vitro* after the cell lifespan was extended.

However, it is well known that telomerase is highly active in cancer cells, which gave Niklason pause about moving the technique toward the clinic. "One of the outstanding questions is, 'How safe is this?'" she says. "One of the main reasons tumors can grow forever is because they can activate telomerase."

In the February study, which involved nine mostly elderly patients, Niklason's team took cells obtained during a coronary bypass procedure and added telomerase. The group was reassured to discover that, in so doing, they had not produced cancerous cells. "Just turning on telomerase by itself is not enough to create cancer," Niklason says. "It's necessary, but not sufficient."

Niklason says much more work is needed, but that techniques like hers may one day enable the making of replacement tissue the way replacement parts are now made for automobiles.

Yale advances in blood vessel engineering don't end there. Christopher K. Breuer, M.D., assistant professor of surgery and pediatrics, has received a $625,000 grant from the National Heart, Lung and Blood Institute to develop new vessels for patients with serious cardiovascular disease.

In a technique Breuer is pioneering with W. Mark Saltzman, PH.D., chair and Goizueta Foundation Professor of Chemical and Biomedical Engineering, Breuer is creating more stable and reliable grafts for cardiovascular operations by treating vessel scaffolds with a cocktail of proteins that stimulate cell growth and promote vessel formation.

Surgery *continued from page 3*

observed a similar phenomenon since the advent of laparoscopic gastric bypass procedure to treat extreme obesity (a laparoscope is a thin endoscope specially designed to be inserted through the abdominal wall).

Bell, one of three surgeons at Yale meeting the growing demand for the gastric bypass procedure, now does almost all of these operations laparoscopically, and he says there are numerous advantages to minimally invasive techniques.

Patients now opt for the surgery much sooner (heading off many of the health problems that accompany prolonged obesity), recovery time is measured in days rather than weeks and complications are minimized, says Bell.

When patients come in for check-ups two weeks after surgery, Bell says that he can tell them, "Go to the gym today and lift as much as you want."

Diving deep into a data wave to help make surgery safer

Monitoring expert devises clever new way to manage blood loss

When patients undergo surgery, it's inevitable that they will lose some blood, so surgical teams strive to replenish patients' fluids over the course of an operation. But the most common technique to track blood volume—catheters inserted through the heart that provide a readout on a monitor—are invasive and not particularly accurate.

According to Kirk H. Shelley, M.D., PH.D., associate professor of anesthesiology, the flaws of catheter-based monitoring often engage operating room personnel in a delicate clinical balancing act with very high stakes. "Too little fluid can put a tremendous amount of stress on the kidneys, the cardiovascular system and the central nervous system. Organs need a certain amount of blood, and you're risking a patient going into shock," Shelley says. "But if you give too much fluid for the heart to pump, it backs up, causing bloating and pulmonary edema. Every day in the operating room, we try to find the right balance between these two extremes."

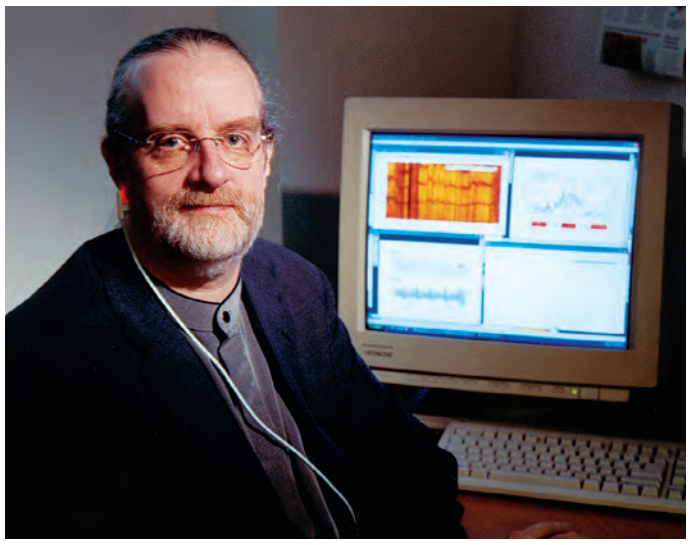
Now Shelley, who as chief of ambulatory surgery takes part in about 8,000 surgeries a year at Yale-New Haven Hospital, has found a possible solution to this daily surgical dilemma that's already very close at hand—or more precisely, clipped to patients' fingers—in hospitals around the world. By combining a clinical insight from the 1870s with data provided by the modern pulse oximeter, a clothespin-like clip placed on a fingertip, ear or toe to measure the oxygen level in the blood, Shelley has discovered a noninvasive, precisely quantified method to monitor blood loss and guide difficult decisions in the operating room.

The pulse oximeter has become a common sight in hospitals since it was first introduced in the 1980s. The clips contain light-emitting diodes that shine both visible red and infrared light through the skin. Because deoxygenated hemoglobin allows infrared light to pass but absorbs red light, while oxygenated hemoglobin allows red light to pass and absorbs infrared, the oximeter can detect changes in the blood's oxygen saturation by calculating the relative absorption of red and infrared light.

Shelley, who changed specialties from internal medicine to anesthesiology in the late 1980s, began a residency in his new field just as pulse oximeters appeared on the scene. In those early days, Shelley discovered that oximetry clips generated exceedingly complex waveforms that were "cleaned up" by oximeter manufacturers in favor of clear, simple signals. But Shelley's curiosity about the wealth of information produced by early oximeters—"One man's artifact is another man's signal," he says—prompted him to devise software to sift through the raw oximetry signal for potentially valuable clinical information.

In 1873 an observant German physician, Adolf Kussmaul, coined the term "pulsus paradoxus" for a phenomenon in which blood flow drops slightly after a deep breath, a dip caused when blood remains in the lungs and doesn't reach the heart. Shelley discovered that pulsus paradoxus produced by the mechanical ventilation that accompanies general anesthesia could be detected in the raw oximetry waveform, and that this information could be combined with other data in the waveform to precisely manage fluid replacement in surgical patients.

L. Alan Carr, PH.D., a senior licensing associate in Yale's Office of Cooperative Research who shepherded the discovery through a patent application, says that Shelley found treasure where others saw trash.



Kirk Shelley says that pulse oximeters like the one clipped to his ear provide a wealth of untapped clinical information.

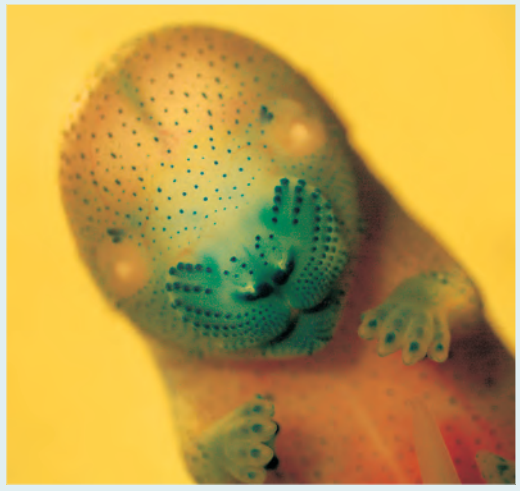
"There's all sorts of wild, raw data that comes off the pulse oximeter that companies have worked hard to eliminate, because it has been seen as just noise," Carr says. "What's ironic is that the background data actually had useful information in it."

As a member of an active research group headed by Professor of Anesthesiology David G. Silverman, M.D., which is devoted to noninvasive monitoring, Shelley is now adapting his method for use in non ventilated patients suffering from blood loss, such as trauma patients arriving at emergency departments. He plans to mine the pulse oximeter signal for more clinical riches, explaining that his affinity for noninvasive medical gadgetry stems from watching *Star Trek*'s Dr. McCoy in action.

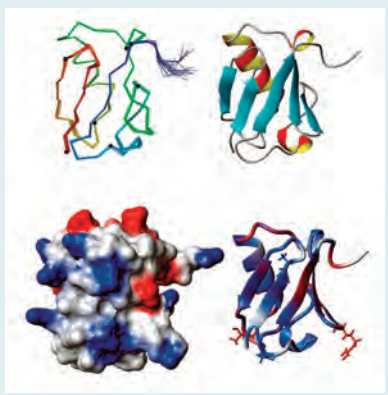
"McCoy would pass his devices over the patient and would know exactly what to do with the patient," Shelley says. "I really think the newer generations of the pulse oximeter and the new information we're going to get out of them are going to be like that. We're going to continue stepwise, evolving this."

An eye for science

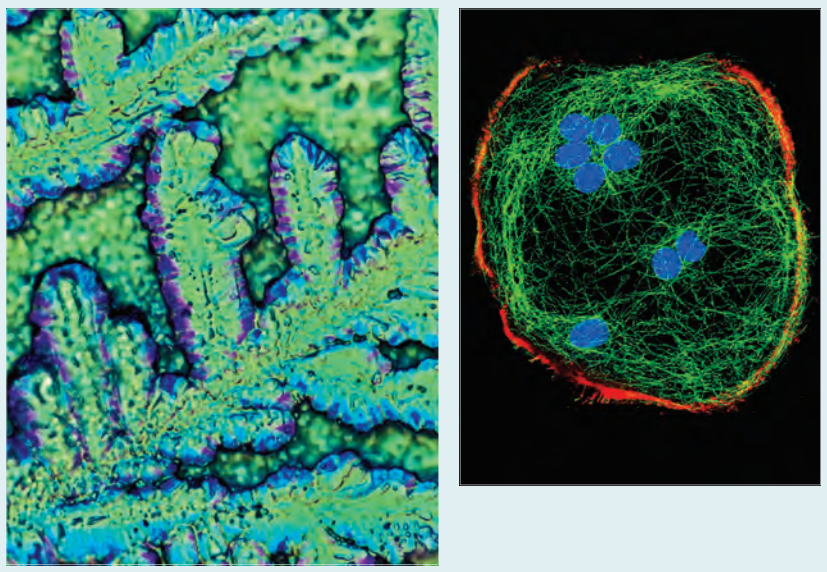
Because we learn so much about our world through vision, images have become a crucial part of modern science. Pictures lend an immediacy and a deeper understanding of complex phenomena, from cells to stars, that cannot be captured by numbers alone. But in addition to providing compelling data, scientific images can also be valuable for their sheer beauty. A selection of dazzling images from the life sciences now adorns the TAC Gallery, a permanent exhibit adjoining The Anlyan Center, a hub of biomedical research at the School of Medicine. We will feature more images from the TAC Gallery in this space in future issues.



In a micrograph from the laboratory of Ensign Professor of Medicine Arthur E. Broadus, the blue reaction product of the enzyme ß-galactosidase identifies sites of expression of a protein related to parathyroid hormone in a 15-day-old embryonic mouse. Prominent among these sites are whisker and hair follicles, nailbeds, the epithelia of the nostrils and mouth and cartilage in the mouse's growing skeleton. Broadus's collaborators include Xuesong Chen, Barbara E. Dreyer, Vicki E. Hammond, Julie R. Hens and William M. Philbrick.



Structural images of a portion of TUG, a protein involved in glucose metabolism, from the laboratory of Jonathan S. Bogan, assistant professor of medicine. The overall shape of the protein's backbone is shown at upper left, while particular features are highlighted at upper right. The electrostatic charge present at the protein's surface is shown at lower left, and the degree of flexibility of various components of the protein is shown at lower right. Bogan was joined in this work by Michael E. Hodsdon, M. Cristina Tettamanzi, and Chenfei Yu.



Above, left: Crystallized rat bile seen in a brightfield micrograph utilizing Nomarksi interference optics by Albert Mennone, research associate in the Yale Liver Center. Right: In this confocal micrograph by Lynn Neff, an osteoclast, a type of cell that degrades and resorbs bone, has been labeled with fluorescent antibodies that show the cell's multiple nuclei (blue), microtubules (green), and actin filaments (red). Neff's work was carried out in the laboratory of Roland Baron, professor of orthopaedics and cell biology.

Disability is no dead-end for elders, Yale research finds

$3.2 million grant will sustain fruitful study of disabling events

Between the daunting complexities of Medicare's new prescription drug plans, the uncertainties surrounding the solvency of Social Security and the rising rates of Alzheimer's disease and other ailments of the elderly, it would seem that bad news about America's older persons decidedly outweighs the good. But over the past nine years, geriatrics researcher and Associate Professor of Medicine Thomas M. Gill, M.D., has pieced together some surprising and uplifting news about disability among our aging population using a simple but powerful tool: the telephone.

In 1997, Gill enrolled over 750 elderly New Haven-area residents in an ambitious study known as the Precipitating Events Project (PEP). Since then, over the course of 55,000 telephone interviews and 3,200 at-home visits with the study participants, Gill and his team have overturned previous views about chronic disability among the elderly and revealed that older Americans surmount most physical setbacks with remarkable resiliency.

In November, the National Institute on Aging recognized Gill's accomplishments with a $3.2 million MERIT award—a designation reserved for the "most outstanding" grant proposals "from superior researchers"—that will allow him to continue to follow his original study group for several more years.

When Gill arrived at Yale as a Robert Wood Johnson Clinical Scholar in 1993, national survey data indicated that the rate of chronic disability—defined as disability lasting at least three months—among older persons had fallen markedly over the previous 20 years, probably due to a decline in smoking and advances in cardiovascular and orthopaedic medicine such as coronary bypass surgery, anti-hypertensive drugs and prosthetic knee and hip replacements. But the same surveys showed that this trend had been offset by the overall aging of the population, so the conventional wisdom in geriatrics held that, despite improvements in medical care, the total number of chronically disabled older Americans had remained about the same.

However, the surveys in question were conducted two to five years apart and required many participants to rely on their memories of past disabling events—and sometimes even asked respondents to predict future disability. Gill launched PEP to explore whether a finer-grained and less subjective analysis might yield a more reliable picture of chronic disability. Over the course of the study, the PEP research team has conducted phone interviews with each study participant every month and has paid them personal visits every 18 months. And participants' commitment to the project has been extraordinary, according to Gill.

"PEP was originally envisioned as lasting only two or three years, but it's exceeded our wildest expectations," Gill says. "Our completion rate for these telephone interviews is 99 percent. We have very little missing data, and very few participants—about 4 percent—have dropped out over the course of the study. We follow individuals in and out of hospitals, in and out of nursing homes, and when they make a transition between living in the community to assisted living."

Thomas Gill (right) and Denise Shepherd (left) have made regular phone calls and home visits to New Haven residents like Grace Cook (center), a long-time participant in Gill's PEP study, to create a detailed picture of the impact of disability on older persons.

This sustained and regular contact between PEP researchers and participants has yielded a new, more nuanced view of the challenges presented by disability in old age. "When you look every month, the rates of disability over time are much higher than those shown in the single snapshots of surveys," Gill says. "The difference was dramatic, and the only way that could happen is if people were recovering at much higher rates than had previously been reported. Prior reports said that about a third of older people will recover after a disabling event, but we found that when you look carefully, every month, these recovery rates are up to 80 percent."

The bottom line, Gill says, is that for most older persons disability is not irreversible, but a recurrent event from which they recover. Therefore, there are probably about 5 million chronically disabled older Americans at any given time, 2 million fewer than estimated by previous research. This means that the total impact of disability on the health care system may be much smaller than predicted by older studies.

Gill says that the medical school's long-standing tradition in geriatrics research, exemplified by the Yale Program on Aging and the Claude D. Pepper Older Americans Independence Center, have played no small part in PEP's success. "A project like this would be difficult to pull off without the Pepper Center and the Program on Aging because they provide a stable cadre of superb researchers who've been moving from project to project over the past 20 years with established links to the community," Gill says. "That cannot be replicated."

Grants and contracts awarded to Yale School of Medicine

November/December 2005

Federal

Robert Alpern, NIH, *General Clinical Research Center* (Robert Sherwin, M.D., Director), 5 years, $23,993,166 • **Daniel Goldstein**, NIH, *Role of Innate Immunity in Transplantation Tolerance*, 4 years, $1,308,000 • **Karl Insogna**, Dept. of Agriculture (US), *Dietary Protein Affects Intestinal Calcium Absorption: Consequences and Mechanism*, 3 years, $475,000 **Michael Koelle**, NIH, *G Protein Signaling in the* C. elegans *Nervous System*, 5 years, $1,823,147 **David McCormick**, NIH, *Calcium Signaling & Prefrontal Deficits in Schizophrenia*, 3 years, $6,187,258 • **Sherry McKee**, NIH, *Do Pharmacological Treatments for Smoking Cessation Reduce Alcohol Drinking?*, 4 years, $1,178,552 • **Hongyu Zhao**, NIH, *Statistical Methods to Map Genes for Complex Traits*, 4 years, $1,238,739

Non-Federal

Janet Brandsma, Go Therapeutics, Inc., *Particulate Delivery Vehicle for Ad-Based Vaccination Against Cottontail Rabbit Papillomavirus (CRPV) Infection in Rabbits*, 10 months, $19,234 **David Cheng**, Pfizer, Inc., *Y-003-04 Study-Increasing* FDG-PET *Specificity with Krebs Cycle Flux Using Spectroscopy*, 2 years, $588,301 **Jin-Young Choi**, Arthritis Foundation, Toll-*like Receptor Stimulation in CNS Lupus*, 2 years, $150,000 • **Lauren Cohn**, Millennium Pharmaceuticals Inc., *Direct Measurement of AHR in CRTH2-Deficient Mice*, 1 year, $16,350 • **Cynthia Epperson**, National Alliance for Research on Schizophrenia and Depression, *Serotonin, Neurosteroids and GABA Contributions to SSRI Treatment Response in PMDD: A 1H-MRS Study*, 2 years, $100,000 • **Durland Fish**, New York Medical College, *Genotypic Variation and* B. burgdorferi *Pathogenesis*, 11 months, $42,189 • **Judith Ford**, University of California–Irvine, *Function BIRN (Bioinformatics Research Network)*, 1 year, $235,000 • **Liana Fraenkel**, Arthritis Foundation, *Improving Informed Choice for Patients Considering TJA*, 1 year, $100,000 • **Joel Gelernter**, University of Connecticut Health Center, *Genetic Versus Phenotype Markers of Relapse Risk*, 5 years, $46,649 **Cary Gross**, Common Sense Media, *Media Evidence Assessment Project*, 1 year, $10,000 **Handan Gunduz-Bruce**, National Alliance for Research on Schizophrenia and Depression, *GABA-Glutamate Interactions and Psychosis*, 2 years, $60,000 • **Keith Hawkins**, Alzheimer's Association, *Neuropsychological Norms for Older African-Americans*, 3 years, $239,992 • **Steven Hebert and John Geibel**, Amgen, Inc., *CaSR Modulations*, 2 years, amount confidential **Yingqun Huang**, Fannie E. Rippel Foundation, *Use of a Novel siRNA Delivery System to Restore Chemosensitivity to Epithelial Ovarian Cancer Cells*, 2 years, $150,000 • **Judith Lichtman**, Fannie E. Rippel Foundation, *Determinant of Disparities in the Care and Outcomes for Young Women with Acute Myocardial Infarction*, 1 year, $150,000 • **Xiaomei Ma**, Myeloproliferative Disorders Foundation, *Epidemiology of Chronic Myeloproliferative Disorders*, 1 year, $128,500 **John Macmicking**, Searle Scholar Program, *p47 GTPases: Decoding the Language of Immune Recognition for Phagosomal Pathogens*, 3 years, $240,000 • **Robert Malison**, Hartford Hospital, *Cocaine-Induced Place Preference Using Virtual Reality*, 2 years, $74,589 • **Graeme Mason**, Dana Foundation, *Quantitative MR Imaging and Spectroscopy in Alcoholism: GABA and Glutamate Impact of Genetic Vulnerability to Alcoholism*, 3 years, $100,000 • **Sarah Paterson**, National Alliance for Autism Research, *Brain Morphometry in Newborns at Risk for Autism: An MRI Study*, 2 years, $118,360 • **Jill Reiter**, Breast Cancer Alliance, Inc., *Quantitative Analysis of EGFR Variants in Breast Cancer*, 2 years, $125,000 • **Jennifer Ruger**, Open Society Institute, *Health Governance Project*, 6 months, $49,611 • **Albert Sinusas**, Bristol-Myers Squibb Company, *Noninvasive Imaging of Matrix Metalloproteinase in Chronic Rat Models of Myocardial Ischemic Injury: Implications of Early Prediction of LV Remodeling*, 1 year, $108,788 • **Jane Taylor**, Tourette Syndrome Association, Inc., *Instrumental Habit Behavior as an Animal Model of Tourette's Syndrome: Investigation of the Role of Striatal and Frontal Cortical Signaling Pathways*, 1 year, $60,825 • **Edward Uchio**, American Geriatrics Society, *Aging Effects on the VHL Tumor Suppressor Pathway in the Development of Renal Carcinoma*, 2 years, $75,000 • **Agnes Vignery**, Boehringer Ingelheim Pharmaceuticals, Inc., *Identification and Functional Characterization of New Molecular Targets to Treat Osteoporosis and Rheumatoid Arthritis*, 2 years, $180,000 • **Joanne Weidhaas**, Breast Cancer Alliance, Inc., *Defining the Best Treatment Options in BRCA1-mediated Breast Cancer Using a* C. elegans *Model of Radiosensitivity*, 2 years, $125,000 **Kevin White**, University of California–San Diego, *Molecular Basis of Cell Tolerance to O_2 Deprivation*, 7 months, $10,014 • **Scott Woods**, Research Foundation for Mental Hygiene, *D-Serine Treatment of Schizophrenia*, 1 year, $193,150 • **Kimberly Yonkers**, State of CT Dept. of Public Health, *Provider Education for Perinatal Depression*, 6 months, $125,000

Awards & honors

Alison P. Galvani, PH.D., assistant professor of epidemiology, has received a Guggenheim Foundation Fellowship for her research on the public perception of influenza vaccination policies. Guggenheim Fellows are appointed not only on the basis of past achievements, but on the promise for exceptional future achievements. The John Simon Guggenheim Memorial Foundation was established in 1925 by former United States Senator Simon Guggenheim and his wife in memory of their son. The Foundation supports individuals in the fields of natural sciences, social sciences, humanities and creative arts.

Alexander Neumeister, M.D., associate professor of psychiatry, was awarded the 2006 Bristol Myers Squibb Max Hamilton Memorial Prize by the Collegium Internationale Neuro-Psychopharmocologium. The prize, which carries a cash award of $10,000, recognizes a young scientist for outstanding contributions to psychopharmacology. Neumeister studies the molecular and genetic bases of anxiety and mood disorders, especially depression and post-traumatic stress disorder, and has scientifically evaluated therapies for these disorders.

Peter J. Novick, PH.D., professor of cell biology, has been elected to the American Academy of Arts and Sciences. Novick, an expert on vesicle trafficking and cell polarity in yeast, joins over 130 other Yale faculty as a fellow of the Cambridge, Mass.-based Academy. The Academy was founded in 1780 by John Adams, James Bowdoin, John Hancock and other Revolutionary leaders to bring scholarly, political and business leaders together "to cultivate every art and science which may tend to advance the interest, honour, dignity, and happiness of a free, independent, and virtuous people."

Jody L. Sindelar, PH.D., professor of public health, has been named president of the newly formed American Society of Health Economists (ASHE). Sindelar, who studies the economics of smoking, alcohol and illicit drugs, is a founding member of ASHE, a professional organization dedicated to promoting excellence in health economics research in the United States. She was program chair for ASHE's inaugural conference, to be held in Madison, Wis., in June 2006. The biennial meeting will provide a forum for emerging ideas and empirical results in health economics research through over 400 paper and poster presentations, as well as multiple plenary sessions.

Two Yale biologists receive Gairdner Awards

Joan A. Steitz, PH.D., Sterling Professor of Molecular Biophysics and Biochemistry and a Howard Hughes Medical Institute investigator, and Thomas D. Pollard, M.D., chair and Sterling Professor of Molecular, Cellular and Developmental Biology, are winners of the 2006 Gairdner International Awards, which are among the most prestigious in science.

Steitz was named by the Toronto, Canada-based Gairdner Foundation, which sponsors the awards, for her discovery of snRNPs (pronounced "snurps"), complexes of protein and RNA that edit and splice other RNA strands to form messenger RNA, the genetic recipe used by the cell's protein-making machinery. Other RNAs and proteins studied by Steitz are believed to play roles in fertility, development, viral infection, autoimmune disease and cancer.

Pollard was cited along with Alan Hall, PH.D., of the Memorial Sloan-Kettering Cancer Center in New York, for discovering the molecular basis of cellular motility and the mechanism of its regulation, fundamental knowledge required to understand embryonic development, defense against infections and the spread of malignant tumors in the body.

The awards, which will be presented in October in Toronto, "honor outstanding achievements in our understanding of our cells with major ramifications for cancer, nutrition, auto-immune disease, atherosclerosis and hormone action," says John Dirks, M.D., the Gairdner Foundation's president. Ralph Brinster, V.M.D., PH.D., of the University of Pennsylvania's School of Veterinary Medicine, and Ronald M. Evans, PH.D., of the Salk Institute for Biological Sciences, will also receive Gairdner International Awards from the foundation.

The Gairdner Foundation was established in 1957 by Toronto stockbroker and industrialist James A. Gairdner, whose lifelong interest in medical research led to his conviction that the achievements of medical scientists should be acknowledged in a tangible way.

Since 1959, the Gairdner International Awards have honored outstanding contributions by medical scientists worldwide whose work will significantly improve the quality of life. Of the 279 Gairdner winners, 65 have gone on to win the Nobel Prize.

Joan Steitz

Thomas Pollard

Awardees are chosen in a two-stage process, through two medical advisory committees of leading Canadian and international medical scientists. Each prize carries a cash award of $30,000 (Canadian). As part of the Gairdner Foundation's mandate to communicate the work of medical researchers, Gairdner winners visit universities across Canada to present academic lectures on their area of expertise.

In 2004, another member of the medical school faculty, Arthur L. Horwich, M.D., the Eugene Higgins Professor of Genetics and Pediatrics and a Howard Hughes Medical Institute investigator, won a Gairdner International Award for his influential research on protein folding mechanisms in the cell.

Cleary *continued from page 1*

Cleary chose to study medical sociology, also at Wisconsin.

In 1982 Cleary joined the faculty at Harvard as professor of health care policy. His work has sought better ways to find out how patients view their care and has studied what determines variations in the quality of health care. He has traveled the world to study behavioral aspects of HIV/AIDS, smoking, alcohol abuse and mental illness. "The things I have focused on are health behavior, analytic methods, social epidemiology, statistical modeling, health policy and behavioral science," Cleary says.

Cleary begins his work at the School of Medicine in July, succeeding Michael H. Merson, M.D., the Anna M.R. Lauder Professor of Public Health, who stepped down as dean in 2005 after 10 years in the post, and Interim Dean Brian P. Leaderer, M.P.H., PH.D., the Susan Dwight Bliss Professor of Epidemiology.

Cleary believes that faculty members have their own vision guiding their research. "My philosophy of organization," he says, "is that I should make it easier for the faculty to do their job better. What can I do as a leader of the organization to enable them to realize that vision?"

Nonetheless, Cleary, a member of the National Academy of Science's Institute of Medicine, strongly favors collaborative research. "Let's say you have two people, three people, four people who want to focus on cancer research. They may reinforce each other. You may be able to get more support for certain programs. You may be more likely to have an impact. Young assistant professors who want to work in that area will have mentors," Cleary says. "I feel very strongly about developing research programmatically, fostering multidisciplinary collaborations and developing excellence in focused areas."

In announcing the appointment, Levin praised Cleary's background in quantitative methodology and analysis. "I know that many of you, as I do, look forward to working with him in the years ahead," Levin told a gathering of public health faculty in the Winslow Auditorium. "You will find that he can be a sympathetic listener, someone who can pay attention to people and at the same time be capable of independent thinking and leadership."

Gift *continued from page 1*

Nobel Prize in 1980. The unencumbered time to explore new approaches afforded by the Yale Scholars program is the ideal way to uncover new pathogenic mechanisms, which may lead to effective forms of treatment."

Like their father, the McCluskey brothers grew up in the Morris Cove section of New Haven. "In those days," Donald says, "Yale was either preppies or local boys." Donald's wife, Dorothy, also has an advanced Yale degree, from the School of Forestry and Environmental Studies. She graduated in 1973, then went into politics, serving as a state representative from North Branford in the Connecticut legislature. Her Yale connections reach back to a great-uncle, Josiah Hazen, an 1898 Yale College graduate. And two of the McCluskeys' three children have Yale degrees, a son from Yale College and a daughter from the law school.

Dean and Ensign Professor of Medicine Robert J. Alpern, M.D., who launched the Yale Scholars Program in order to attract the best young scientists to the medical school faculty, hopes to be able to name five Yale Scholars each year. A gift of at least $2.5 million is needed to fund a Yale Scholars endowment, with each dollar matched by the university. These endowments may be restricted according to a donor's wishes, and donors will receive an annual report on the work of the scientists they have supported. Each Yale Scholar will receive $1 million in startup funding, distributed over four years. "The Yale Scholars program funds an investigator at an early stage in his or her career and passes every four years to a different one," Alpern says.

Robert and Donald McCluskey at Robert's home in 2005.

McCluskey's gift provides the endowment for the first Yale Scholar, who will be chosen from new faculty recruits arriving this summer and fall. "Being named a Yale Scholar will be an honor for young scientists, and it is only going to go to the best recruits," says Alpern. "We at the School of Medicine are deeply grateful to Donald McCluskey for initiating this program, and it is a privilege to name the first Yale Scholar endowment after such a distinguished physician-scientist."