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 open its doors to patients at the end of 2009.

“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...

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.

“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 I. 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

A brother’s gift launches Yale Scholars

Yale alumni 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.E.N.G., 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.

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 1944 and the engineering school in 1949, 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...

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A steady ing influence

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

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 Alan Feinberg, 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 rainforests 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 2005 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.

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 2000 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.
Minimally invasive surgical techniques are on the rise at Yale

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 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 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 new 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 light 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 developed minimally invasive techniques for kidney transplantation. According to Duffy, many surgeons have been eager to adopt the new technology because they think it makes them 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

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 $50,000 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 Hesseltine, 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.P.H., Dean Robert J. Alpenn, 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. 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.

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. 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 Guayanabo.

Cancer continued from page 1


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 merely reading one another’s notes in the chart, is simply the best way to do it.”

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 VCC’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 VCC’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.”

www.medicine.yale.org
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 uncontrollable cell growth seen in cancer. A microvascular network is fundamentally important for tissue engineering,” says Erin Lavik, s.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 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 Gannett 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.”

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

“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 step-wise, 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 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. Broads, the blue reaction product of the enzyme β-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. Broad’s collaborators include Xiansong Chen, Barbara E. Dreyer, Vicki E. Hammond, Julie R. Hens and William M. Philbrick.

Above, left: Crystallized rat bile seen in a brightfield micrograph utilizing Nomarski interference optics by Albert Mennone, research associate in the Yale Liver Center. Right: In this confocal micrograph by Iynn 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 Baros, professor of orthopaedics and cell biology.

Structural images of a portion of tuc, 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. Hodgson, M. Cristina Tettamanzini, and Chenfei Yu.

In the laboratory of Jonathan S. Bogan, assistant professor of medicine, a rat osteoclast has been labeled with fluorescent antibodies that show the cell’s nuclei (blue) and actin filaments (red). The osteoclast is shown at upper left, while particular features are highlighted at upper right. The overall shape of the protein’s backbone is shown at lower left, and the degree of flexibility of various components of the protein is shown at lower right. The electron micrograph was taken in the laboratory of Roland Baros, professor of orthopaedics and cell biology.
Disability is not a 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 Pre-cipitating 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 gained a previously unimagined new perspective on 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 $1.2 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 orthopedic 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 12 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.”

This sustained and regular contact between PEP researchers and participants has yielded a new, more nuanced view of disability 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 been previously 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 7 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 our health care system may be many times 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, has 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, $3,956,397, Goldstein, NIH, Role and effects of posttraumatic stress disorder in rape victims, 3 years, $1,530,501

Non-Federal

Janet Brandma, Go Therapeutics, Inc., Particulate Delivery Vehicle for Ad-Reverse Vaccination Against Cottontail Rabbit Papillomavirus (CRPV) Infection in Rabbits, 10 months, $19,234

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.

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Awards & honors

Alison P. Gabrani, 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 also 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, Hamilton M. Guggenheim. 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 2016 Bristol Myers Squibb Max Hamilton Memorial Prize by the Collegium Internationale Neuro-Psychopharmacology. 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 post-traumatic stress disorder, and has scientifically evaluated therapies for these disorders.

Peter J. Novick, Ph.D., professor of cell biology, has been elected president of the American Academy of Arts and Sciences. Novick, an expert on epidermal growth factor receptor trafficking and cell polarity in yeast, joins over 150 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 scholars, political and legal leaders together “to cultivate every art which may tend to advance literature, 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 annual 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, a native of 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 mechanisms 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, autoimmune disease, atherosclerosis and hormone action,” says John Dirks, M.D., the Gairdner Foundation’s president. Ralph Brinster, 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 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 programmatic, interdisciplinary 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.”

Joan Steitz
Thomas Pollard

Nobel Prize in 1980. The unencumbered time to explore new approaches afforded by the Yale Scholars program is in 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 1818 Yale College graduate. And two of the McCluskey’s three children have Yale degrees, a son from Yale College and a daughter from the law school.

Dean and Ensign Professor of Medicine Robert R. 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 $5,000 is needed to fund a Yale Scholar endowed position, with each dollar matched by the university. These endowments may be restricted 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.

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 be the best recruits,” says Alpern. “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.”

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