Van will bring much-needed mammography to Uganda’s poor

For women in the developed world, mammography is a familiar ritual. The test is a routine way to screen for breast cancer. Once a woman reaches her 40s (or earlier, in women with risk factors for cancer) a mammogram is recommended every one to two years. But for most women in the impoverished East African country of Uganda, getting a mammogram is next to impossible. Little advanced medical care is available there, and many women don’t know about the test and wouldn’t have access to it if they did. As a result, breast cancer in Ugandan women usually goes undetected until it is in advanced stages.

But with a 35-foot van refitted by School of Medicine faculty members with the help of Johnson & Johnson, Fred Okuku, M.D., an internal medicine resident at Makerere University in Uganda’s capital city of Kampala, is bringing breast cancer screening to his home country. Okuku visited Yale this year because “I want to know what is the ideal therapy given here, and how I can modify this to fit [our resources] back home,” he says. At his Ugandan teaching hospital, Mulago Hospital, even necessities like gloves and IV fluids are in short supply. Amidst such poverty small things can make an enormous difference, says Okuku. That’s the idea behind the Uganda, page 6

Quick study, bighearted contributor

United Technologies chief sees a path to better care with new cancer hospital

When Louis Chênevert was named president of United Technologies Corporation (UTC) in 2006, his mentor, Chairman of the Board George David, described him as a quick study with “remarkable skills at learning.” David said, “I think that’s one of the most important challenges in life. People need to rise to new things, new situations, new fact patterns, and to learn from what has gone before. Louis is just awfully good at that.”

As a Director’s Advisory Board member at Yale Cancer Center (YCC) since 2001, Chênevert has been a dedicated student of cancer research and treatment, asking probing questions of faculty members and helping plan the YCC component of the new 14-story Smilow Cancer Hospital that is rising on Park Street, as well as the cancer biology research center envisioned for Yale’s recently acquired West Campus.

“People talk about interdisci- plinary research and the multidisciplinary care of patients. Louis really grasps it,” said YCC Director Richard L. Edelson, M.D., the Aaron B. and Marguerite Lerner Professor of Dermatology. “He understands the importance of having all the services for cancer patients in the same place, rather than dispersed throughout the medical center.”

With his interest has come financial involvement. Chênevert and his wife, Debbie, were tapped as co-chairs of the Campaign for Smilow Cancer Hospital, along with Jonathan and Jody Bush and Marvin and Helaine Lender. In July of this year, several months after Chênevert’s appoint- ment as CEO of UTC, the company announced a $1 million gift to the cancer hospital. The Chêneverts are making a personal gift of $540,000 to complement UTC’s $1 million gift to the new Smilow Cancer Hospital. Hartford, Conn.-based UTC is one of the world’s largest companies serving the aerospace and building industries.

Vessel researcher is appointed as new cardiovascular chief

The medical school has appointed Michael Simons, M.D., as chief of the Department of Internal Medicine’s Section of Cardiovascular Medicine. Simons is a leader in research on the role of angiogenesis, the growth of new blood vessels, in cardiovascular diseases.

He will come to Yale this fall from Dartmouth Medical School in Lebanon, N.H., where he was A.G. Huber Professor of Medicine, professor of pharmacology and toxicology and director of the Cardiovascular Center and the Angiogenesis Research Center at Dartmouth-Hitchcock Medical Center.

“Michael Simons is an outstanding cardiologist, scientist and educa- tor who will lead our program to new heights,” says Jack A. Elias, M.D., chair and Waldemar Von Zedtwitz Professor.

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Petri dishes, power chords

A scientific leader recharges his batteries with rock and roll

Outside on this humid July afternoon, an oppressive heat combines with the noise of road traffic and an Amtrak passenger train rolling through Wallingford, Conn. But inside a nondescript one-story building here, all is dim and cool. Richard A. Flavell, Ph.D., a School of Medicine scientist who heads one of the world’s top programs in immunology research, is in a recording studio laying down backing vocal tracks with his wife, Madlyn.

Clanging guitars and a vocal sound reminiscent of 1960s-era Kinks ballsads fill the mixing booth. On the other side of the glass, Flavell is singing the harmony to a tune decrying the state of the world—one person could have done on his own—"Our strong representation in the New York metro area is at the top of its field."

Richard Flavell says that he and colleagues who founded Yale’s Department of Immunobiology in 1988 set two criteria for recruiting faculty: “We decided we would hire people who were outstanding and who were easy to get along with—no prima donnas.” Twenty years later, the department is at the top of its field.

The list, published in the magazine’s June 16 issue, is based on the and seniors. This year Yale boasts 62 “top docs” (New York Yale Medical Group physicians shine on latest ‘top docs’ list) physicians.

Flavell is singing the harmony to Kinks ballads fill the mixing booth. His switch to biotech and back makes him unusual among academic scientists. “It used to be that you made the jump in one direction; you never came back,” says Carolyn W. Slayment, Ph.D., deputy dean for academic and scientific affairs. “He’s done it, and he’s been extraordinarily successful.”

Immunobiology at Yale is regarded as one of the top programs in the world, ranked No. 6 in the Chronicle of Higher Education’s 2006 Faculty Scholarly Productivity Index, which counts scholarly publications, citations of those papers by other scientists, grant dollars, awards and honors.

Flavell, a Sterling Professor at Yale and a Howard Hughes Medical Institute (HHMI) investigator, runs the department in a way that invites participation and leads to group decisions. “Richard is very good at gathering information, building consensus and then making a decision,” says colleague David G. Schatz, Ph.D., professor of immunobiology. “It’s very inclusive. He’s not afraid to make a decision that will make someone upset, but he’s extremely good at building agreement.”

The department he leads now numbers 13 primary faculty. Flavell’s own lab employs more than 30 people working on a combination of projects funded by HHMI, the National Institutes of Health and the Bill and Melinda Gates Foundation. In 2005, Gates awarded Flavell $7 million to engineer a mouse with a human immune system, a tool that will allow scientists to more readily conceive of and test potential vaccines.

Meanwhile, there is life outside the lab—gardening (Flavell cultivates several hundred species of rhododendron on five acres surrounding his home in Guilford, Conn.) and, of course, music. Science may be a lot harder than three-chord rock and roll, Flavell says, but there are moments in a band that rival those in science, when collaboration and synergy create something that no one person could have done on his own. Plus it’s a good release: “I like rock and roll,” he says. “It’s part of my existence.”

Online: Yale Netcast “Mouse with a human immune system”

New York magazine’s 2008 list of the region’s top doctors once again includes many Yale Medical Group (YMG) physicians.

This year Yale boasts 62 “top docs” in 40 specialties, serving all age ranges from newborns and children to adults and seniors.

The list, published in the magazine’s June 16 issue, is based on the annual Top Doctors New York Metro Area guidebook, published by Castle Connolly Medical Ltd., which invites doctors to nominate peers to be recognized for their medical excellence. According to the company, the annual New York guidebook lists the top 10 percent of the metro area’s physicians. New York magazine’s list is more selective—the top quarter of the top 10 percent, or about 1,400 physicians.

“Our strong representation in the New York metro area highlights the fact that YMG is a regional—and in some cases nation—al player. Patients throughout New York and New England are coming to see YMG as a medical destination of choice,” explains David J. Leffell, M.D., CRO of YMG, deputy dean for clinical affairs and professor of dermatology and surgery.

Richard Flavell—Prof.

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Telephone: (203) 785-6144
Fax: (203) 785-4527
E-mail: medicine@yale.edu
Website: medicine@yale.org
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Genetics researcher is named inaugural Cohen Professor

Matthew W. State, M.D., Ph.D., an authority on the genetics of psychiatric disorders in children, has been named the first Donald J. Cohen Associate Professor of Child Psychiatry. State, also associate professor of genetics, and colleagues have studied rare genetic variations in disorders such as Tourette syndrome, autism and mental retardation. His work on the contribution of the gene SLITRK1 to Tourette syndrome was cited as one of the top 10 breakthroughs of 2005 by the journal Science.

State is co-director of the Yale Program on the Genomics of >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >> >...
Lyme disease has European roots

More than 20,000 cases of Lyme disease, a bacterial infection transmitted by deer ticks, are diagnosed each year in the U.S. Researchers have speculated that Borrelia burgdorferi, the spirochete that causes the clinical symptoms of Lyme disease seen in this country, originated in North America. But a new study published in the June 24 issue of Proceedings of the National Academy of Sciences traces the bacterium’s pedigree to Europe.

Durland Fish, Ph.D., professor of epidemiology at the Yale School of Public Health, worked with an international team that analyzed 64 different samples of bacterial DNA from ticks and infected human patients in both the U.S. and Europe. By looking at mutations in a group of genes essential to basic metabolism, the scientists determined that European strains are more closely related to a common ancestor than are North American strains, indicating a European origin for both diseases.

“Infecting the evolution of pathogens is a key epidemiological tool,” says Fish. “By understanding the evolutionary history of pathogens, we can better predict their evolutionary future.”

Secrets of a stowaway bug

When harmful bacteria enter the body, white blood cells known as macrophages engulf them and sequester them in capsules called phagosomes. These capsules then fuse with lysosomes, spheres packed with enzymes that destroy the bacterium. But some bacteria can survive and continue to cause illness by blocking this process. Scientists have long known that pathogens like Legionella pneumophila, the cause of Legionnaire’s disease, secrete proteins into macrophages. Researchers now know that the condition develops over a long period. Overactive immune T cells mistakenly attack and destroy the insulin-producing beta cells in the pancreas in a battle that can last for years. That realization opened a window of opportunity for therapy, which Kevan Herold, M.D., professor of immunology and medicine, and his colleagues are aiming to exploit.

“We know that when people first present with diabetes, they still make substantial amounts of insulin,” Herold explains. “Over a period of years, they gradually lose that ability. Our idea is to stop the ongoing process of immunologic destruction of insulin-producing cells.”

To do that, Herold and his collaborator Jeffrey A. Bluestone, Ph.D., of the University of California at San Francisco, have developed an antibody that quiets the attacking T cells. In a series of small clinical studies that began in 1999 and 2002, Herold and colleagues demonstrated that patients who received a two-week treatment with the antibody when their diabetes first appeared still had substantial insulin production up to two years later, while untreated control subjects showed the expected continued decline in insulin levels. That antibody is now undergoing testing in larger clinical trials, sponsored by a Maryland biotech company in collaboration with the Juvenile Diabetes Research Foundation International (JDRF), with a target completion date of 2011.

In the meantime, Herold is running his ongoing follow-up experiments with the antibody. His current studies aim to test if booster treatments of the antibody can prolong its effect on insulin production. Also, he wants to know if treatment can still work for people who have had diabetes for a while but continue to make some of their own insulin.

The antibody is not a cure. After treatment, patients still need daily insulin injections, but they need significantly less. Preserving some natural pancreas function helps them to regulate their blood sugar, which is likely to stave off both dangerous swings in blood sugar in the short term, and long-term complications that can include heart disease, high blood pressure, blindness and kidney disease. At the same time, an important plus of the immune treatment is that it does not result in long-term immunosuppression, which carries a risk of infection or cancer. Instead, the antibody appears to produce a state of immune tolerance, where the T cells are retrained and cease to attack vulnerable beta cells. One important question Herold wants to answer is how long that effect can be maintained.

It seems certain that any future cure will feature some form of immune control. Promising approaches include stem cell replacement therapy and beta-cell transplants, but in either case, the new tissues created by these techniques will need protection from the same immune onslaught that destroyed their predecessors. Along those lines, researchers elsewhere are now testing the antibody developed by Herold and Bluestone in conjunction with beta-cell transplants.

But the most exciting prospect for Herold is finding out whether the antibody can actually prevent diabetes in people who are not yet sick, but appear to be headed that way. With support from The National Institutes of Health (N1H), Herold now directs the Trial Net Center at Yale, which promotes studies of the treatment and prevention of type 1 diabetes. A diabetes prevention trial—in which subjects will include relatives of people with type 1 diabetes who still have robust insulin production, but are at risk of developing type 1 diabetes—began in 1999 and 2002. Herold and colleagues demonstrated that patients who received a two-week treatment with the antibody when their diabetes first appeared still had substantial insulin production up to two years later, while untreated control subjects showed the expected continued decline in insulin levels.

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Doctor who stays in touch wins prize for clinical excellence

After so many years of training, one might expect a doctor’s head to be full of nothing but high-level information. But as Lynn D. Wilson, of nothing but high-level information.

Wilson directs patient care in the Department of Therapeutic Radiology and provides radiation therapy for cancer patients.

His clinical and research interests include cutaneous and non-cutaneous lymphoma, and cancers of the lung, head and neck. He serves on the editorial boards of a number of oncology journals and is the principal investigator for a phase I clinical trial using a combination of immunization (an immunotherapy for cancer devised by Richard L. Edelson, M.D., professor of dermatology and director of Yale Cancer Center) and external-beam radiation therapy for the treatment of late-stage non-small cell lung cancer.

Leffell, who endowed the prize to celebrate the 30th anniversary of his graduation from Yale College in 1977, says, “I’m delighted that the inaugural prize is going to Lynn. I’ve known him for many years and believe that his focus on clinical excellence is exactly what this award was designed to recognize. Lynn is a very meticulous, thoughtful and compassionate physician. He’s thoroughly committed to the values of the medical school and to the principles of the practice, which puts excellence in patient care first.”

Presenting the award, Dean Robert J. Alpern, M.D., said that Wilson is “an outstanding educator and clinical researcher” in addition to excelling at patient care.

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Out & about

September 11, 2007: New Haven’s Union League Café was the setting for REMEMBERING AND RECOVERING, a discussion with Steven Marans, Ph.D., M.S.W., Harris Professor of Child Psychiatry at the Child Study Center (CSC), Professor of Psychiatry and Director, National Center for Children Exposed to Violence; and Congresswoman Rosa L. DeLauro (D-CT) to raise awareness and recognize children and families affected by violence and trauma. 1. From left: Marans with Sandy Goodkind and David Goodkind, M.D. 2. From left: DeLauro, Debra P. Hauser, Ph.D., M.S.W., lecturer in the Child Study Center; Janet Levy; and Ana White. The event was sponsored by the CSC’s Child Development-Community Policing program.

June 6, 7: Medical school alumni and their families converged on New Haven for the festivities at REUNION WEEKEND. 1. Dean Robert J. Alpern, M.D., presented Christine A. Walsh, M.D. ’73, professor of clinical pediatrics at Albert Einstein College of Medicine, director of the Pediatric Dysrhythmia Center at the Children’s Hospital of Montefiore and co-director of the Einstein-Montefiore CardioGenetics Center, with the 2008 Distinguished Alumni Award. 2. From left: Harold D. Bornstein Jr., M.D. ’53, and his wife, Maureen Bornstein, in a lively discussion with Donald E. Moore, M.D. ’80, M.P.H. ’81; 3. Lisa Gale Suter, M.D. ’98, with her son, Halvor, at the reunion clambake.

June 16: A reception was held to honor Joan A. Steltz, Ph.D., Sterling Professor of Molecular Biophysics and Biochemistry, winner of the 2008 Albany Medical Center Prize in Medicine and Biomedical Research (see related story, p. 8). 1. Steltz (left) and husband Thomas A. Steltz, Ph.D. (right), Sterling Professor of Molecular Biophysics and Biochemistry and professor of chemistry, celebrate with Andrew D. Hamilton, Ph.D., former provost of Yale University, recently appointed as vice-chancellor of Oxford University. 2. From left: Merle Waxman, M.A., associate dean for academic development, ombudsperson of the School of Medicine and director of the Office of Women in Medicine, with Lawrence S. Cohen, M.D., Ebenezer K.

Hunt Professor Emeritus of Medicine, Sara C. Rockwell, Ph.D., professor of therapeutic radiology and pharmacology. 4. Haifan Lin, Ph.D., professor of cell biology and director of the Yale Stem Cell Center.

www.medicineatyale.org
On-the-spot blood tests make surgery quicker

Patients come to Yale for far and wide for endocrine surgery

Ever take a medical vacation? Stay in a hotel, take in the sights and fit in some surgery? That’s a reality for some of the hundreds of patients each year who come to Yale-New Haven Hospital (YNHH) for parathyroid operations by endocrine surgeon Robert Udelsman, M.D., M.B.A., chair and William H. Carmalt Professor of Surgery. Since his February 2001 arrival at Yale in 2001, the number of such operations has risen steadily from 91 to more than 100 annually. Many of his patients are from out of state, and some fly in from Canada and as far away as Italy and Greece.

By suppressing the Dscam gene in mice that normally cross at the midline of the mouse (see photo) and rat spinal cord during development, the Stein lab, in collaboration with Marc Tessier-Lavigne, Ph.D. of California-based Genentech, found that axons that lack Dscam lose their “sense of direction”; they fail to grow and reach their target. This research is now investigating whether Dscam plays this essential role in wiring up other parts of the nervous system and the nature of its contribution to Down syndrome.

A decline in falls

When taught how to prevent falls, clinicians and their older patients can significantly reduce the likelihood of one occurring. In an article published in The New England Journal of Medicine in July, Yale researchers reported an 11 percent reduction in the rate of older adults visiting an emergency department or being hospitalized because of a fall.

The researchers compared injury rates in a 58-county area in and around Hartford—in which clinicians were encouraged to incorporate evidence-based fall risk assessment and management into their practices—to a control region elsewhere in Connecticut. Their analysis also showed 10 percent fewer fall-related hip fractures and head injuries, some 1,800 fewer emergency department visits or hospitalizations and overall are saving in the study region estimated at $21 million over the two-year study period.

“The research is done,” said senior author Mary E. Tinetti, M.D., the Gladys Phillips Crofoot Professor of Medicine and Epidemiology and Public Health. “The next step is to put it into practice, by making physicians, nurses and physical therapists everywhere more conscious of fall risks among their patients and of what can be done to prevent falls.”

Robert Udelsman (left) consults with a patient. Having lab equipment and a technician in the operating room has allowed Udelsman’s team to assess parathyroidectomy results in just 12 minutes.

Robert Udelsman consults with a patient. Having lab equipment and a technician in the operating room has allowed Udelsman’s team to assess parathyroidectomy results in just 12 minutes.

But it is in the operating room that the uniqueness of Yale’s approach is most evident. For one thing, Udelsman and his colleagues do not routinely place patients under general anesthesia. Instead, the patient receives a series of injections of local anesthetics in the neck to block pain. A small incision is made, the offending adenoma is removed and a blood test is done to check levels of PTH. But rather than having to send the blood sample to another part of the hospital, the lab technician in the operating room tests the patient’s blood immediately, an innovation that greatly speeds up the operation. The surgical team needs to wait only 12 minutes for the blood test results—about a quarter of the time at other institutions, where waiting for results can take longer than the operation itself. If PTH levels have dropped sufficiently, the surgeons can be confident that they have removed the adenoma completely. Then they can sign the patient up.

The entire procedure typically takes half an hour, and the patient goes home—or back to the hotel—a few hours later, returning to the clinic in three days for a follow-up visit. Complication rates are low, cure rates are about 98 percent and the surgery is cost-effective. But most of all, patients are satisfied. According to Udelsman, “Putting the lab technician in the operating room is what made it easy, I think, the premier parathyroid center in the world.” The patients who keep checking into New Haven’s hotels would no doubt agree.

A small incision is made, and a blood test is done to check levels of PTH.

An on-the-spot blood test allows surgery to start within 12 minutes.
occupying the 136-acre complex in West Haven, former home of Bayer Pharmaceuticals’ North American research headquarters.

United Technologies is a global corporation with business units that produce Pratt & Whitney aircraft engines, Sikorsky helicopters, Carrier air conditioning and heating systems, Otis elevators and escalators, Hamilton Sundstrand aerospace and industrial systems, UTC Fire and Security protection services, and UTC Power fuel cells. It had revenue of $45.8 billion in 2007 and employs 235,000 worldwide, including 27,000 in Connecticut, making it the state's largest private employer.

"[Supporting basic research and treatment] is a high priority, because every week some of our employees have to deal with the devastating news of a diagnosis, either for themselves or for someone in their family," Chênevert said. "I lost my Dad to cancer and Debbie lost hers," he added. "Many of the cancers today can be cured because of the great research that has been done, and I think there are a lot of opportunities to find more cures with this new cancer center. Certainly the integrated facility creates a more patient-friendly environment. It's all about science and research, and it feels very good."
Yale lab hones virus that selectively kills brain tumor cells

Specially “trained” virus is a search-and-destroy weapon against cancers

When Senator Edward M. Kennedy of Massachusetts was diagnosed with a malignant brain tumor in May, Ameri- can cancer patients received an ominous reminder: the prognosis faced by many brain tumor patients. According to the National Cancer Institute, of the 20,000 people diagnosed with malignant brain tumors in the United States every year, two-thirds will die in five years or less, only a modest improvement in survival rates from those seen 30 years ago.

Glioblastoma multiforme, the most malignant type of brain tumor, is especially hard to treat because it spreads quickly throughout the brain. Isolated tumor cells invade the surrounding area, migrating deep into normal tissue and making complete tumor removal most impossible with conventional methods such as chemotherapy, radiation and surgery. In addition, there is a risk of the brain being damaged in the treatment process, thus compromising some functional losses.

To avoid these problems, for over a decade scientists have been exploring whether viruses could be made to infect and destroy tumor cells, leaving normal cells intact. While some viruses have a natural affinity for cancer cells, others have to be genetically engineered to increase their tumor-destructing potential. But despite some promising leads, no virus has yet been found that can be used to successfully treat brain tumors in people. Researchers at Yale School of Medicine worked by School of Medicine researchers, however, has unveiled a new virus candidate that might have the potential to completely destroy brain tumors.

The engineered virus, called vsvG30, was first described in 2005 by a team of researchers led by Anthony N. van den Pol, Ph.D., professor of neurosurgery, in the Journal of Virology. The group tested nine viruses against brain tumor cells and found that a virus called vesicular stomatitis virus, or VSV (which causes a mild disease in cattle), worked best. The virus was grown for many generations, allowing the brain cultures of human glioblastoma cells and normal human cells. Viruses that grew on normal cells were discarded until the researchers arrived at a virus population that could completely destroy a tumor with minimal infection of normal cells. “We made the virus do what we wanted it to do by putting evolutionary pressure on it,” says Guido Wollmann, M.D., associate research scientist in the Department of Neurosurgery and lead author of the 2005 study. The resultant virus, with its high selectivity for tumor cells, was named vsvG30.

Wollmann, postdoctoral fellow Koray Ozdemir, M.D., van den Pol and Joseph M. Piepmeier, M.D., the Norwell-German Professor of Neurosurgery, recently tested vsvG30’s efficacy against brain tumors in live animals and published their results in the February issue of the Journal of Neuroscience.

The group injected human brain tumor cells, with an inserted gene from coral that would cause them to glow red under the microscope, into the brains of mice. Solid brain tumors, similar to those seen in humans, soon formed in the mice’s brains. vsvG30, modified with an inserted jellyfish gene that causes green fluorescence, was then injected into the mice’s tail veins. Within 72 hours, the researchers saw that the virus, glowing green, had selectively infected and destroyed the red brain tumor cells while sparing normal cells, even when two or three tumors were present in different parts of the brain.

With vsvG30’s high selectivity for tumor cells the researchers hope they can use the virus to locate and infect cancer cells not only in the main body of the tumor but also cells that have dispersed to other parts of the body.

As a control, normal brain cells were injected into mice and, as predicted, vsvG30 did not infect these cells. One of the greatest difficulties in getting drugs to reach the brain is a protective blood-brain barrier. “We found that the virus managed to cross the blood-brain barrier and infect tumors,” says van den Pol, but it did not cross the blood-brain barrier when there was no tumor. Because the presence of a tumor impairs the barrier, allowing the virus to pass through.

The biggest concern about using viral therapies is the possibility that the viruses might infect normal cells. So far, however, the virus seems to have a preference for tumor cells. Normal cells, when they sense a virus, release interferon that serves as a signal for other cells to up-regulate their antiviral defense. But tumor cells have poor antiviral defense and don’t release interferon when they sense a virus. This, combined with the high sensitivity of vsvG30 to interferon, reduces the affinity of the virus for normal cells, the scientists say.

The group also found that the virus could travel along a nerve fiber and enter the brain. When they injected vsvG30 near the olfactory nerve, the virus entered the brain through the olfactory bulb, a technique that allowed the scientists to avoid placing the virus into the bloodstream. “This is another route we can explore to enhance targeting the problematic part of the brain,” says van den Pol.

In this cross-section of a mouse brain, these tumors (including a small tumor at tower right) have been selectively infected by an engineered virus because of surrounding normal brain tissue is apparent in this image.
Expert on RNA splicing wins Albany Medical Center Prize

In May, Joan A. Steitz, Ph.D., Sterling Professor of Molecular Biophysics and Biochemistry and a pioneer in the study of RNA, was named a winner of the Albany Medical Center Prize in Medicine and Biomedical Research, America’s largest prize in medicine. Steitz shares the $500,000 award with Elizabeth H. Blackburn, Ph.D., one of the first women scientists to win the prize. Steitz, a Howard Hughes Medical Institute investigator, is best known for her discovery and characterization of small nuclear ribonucleoproteins (snRNPs; pronounced “snurps”), intracellular complexes that play a key role in the splicing of pre-messenger RNA, the earliest product of DNA transcription. By excising non-coding regions from RNA and splicing together the resulting segments, snRNPs help to create the messenger RNA (mRNA) templates for making proteins.

Besides illuminating this splicing process, Steitz’s research has served to clarify how splicing expands the coding potential of human chromosomal genes and has provided tools to advance the diagnosis and prognosis of rheumatic diseases.

Blackburn, who was a postdoctoral associate at Yale in the mid-1970s, discovered telomerase, an enzyme that repairs and stabilizes chromosomal telomeres. Telomerase has since been shown to play a crucial role in aging, the development of cancer and the biological effects of chronic stress.

“Many scientists believe that Dr. Steitz’s research may ultimately lead to breakthroughs in treating a variety of autoimmune diseases including lupus,” said James J. Barba, president and CEO of Albany Medical Center, who served as chair of the selection committee for the prize. “Dr. Steitz and Dr. Blackburn are among the greatest scientists of our generation. The potential impact of their research is extraordinary and we all owe them a great debt of gratitude.”

Now in its eighth year, the Albany Medical Center Prize is the second largest medical prize in the world outside of the Nobel Prize. The prize, which was endowed by a gift of $50 million from the Marty and Dorothy Silverman Foundation, is awarded to “a physician or scientist, or group, whose work has led to significant advancement in the fields of health care and scientific research with demonstrated translational benefits applied to improved patient care.”

Steitz entered the Ph.D. program at Harvard University in 1965 in biochemistry and molecular biology, and she was the first female graduate student to work under James D. Watson, Ph.D., who had shared the Nobel Prize the previous year for his discovery of the structure of DNA. After completing postdoctoral work at the Medical Research Council Lab of Molecular Biology in Cambridge, England, she joined the Department of Molecular Biophysics and Biochemistry at Yale in 1970.

Steitz is a fellow of the American Academy of Microbiology and a member of the National Academy of Sciences, the Institute of Medicine, the American Academy of Arts and Sciences and the American Philosophical Society. She is also a fellow of the American Association for the Advancement of Science.

Genome authority is awarded Connecticut Medal of Science

In May, Michael B. Snyder, Ph.D., the Lewis B. Cullman Professor of Molecular, Cellular and Developmental Biology, was awarded the 2007 Connecticut Medal of Science, the state’s highest honor for achievement in science.

The award, given by the Board of Governors for Higher Education of Connecticut, was presented at the annual state award “for scholarship and public service that has contributed to advances in the fields of Arts and Sciences and the American Philosophical Society.”

It was the first in Connecticut to focus on human embryonic stem cells. His team discovered a novel signaling pathway that is essential for embryonic stem cell self-renewal. They then used this information to formulate one of the first media for cell growth that is free of any animal components, a step that is important for the future use of human embryonic stem cells for therapy.

The Connecticut Medal of Science and the Connecticut Medal of Technology were conceived in 1991, when then-Senate majority leader John Larson introduced a bill to initiate an annual state award “for scholarship achievement in science and technology.” The awards process began in 1993.

Professor emeritus of public health is winner of Ivy Award

During his 36-year tenure as professor of epidemiology and microbial diseases at the School of Public Health, Curtis L. Patton, Ph.D., led many research-based efforts aimed at improving public health and served in a number of administrative capacities, including head of the Division of Epidemiology of Microbial Diseases and acting head of the Division of Global Health.

Now an emeritus professor still prominent both on campus and in the broader community, Patton has received one of this year’s Ivy Awards, annual prizes given to Yale faculty, staff and students whose work enhances understanding and cooperation between the city and university.

The awards were given on April 30 by Yale University President Richard C. Levin and City Chief Administrator, representing New Haven Mayor John DeStefano Jr. In the summer of 2004, Patton was asked by Levin to help re-establish and chair the Minority Affairs Committee, which gives advice on the appropriateness of university policies related to minority groups. Patton also serves as chair of the Committee on International Health, which awards Downs Fellowships to Yale students who undertake biomedically, medical, nursing or public health research in developing countries.

Yale’s recognition of Edward A. Bouchet, Ph.D., Yale College’s first African-American graduate and the first African-American to earn a Ph.D. from an American University, is due in part to Patton. Bouchet became a hero of Patton’s while he was an undergraduate student at Fisk University. Since his arrival at Yale, he has worked to ensure that Bouchet is known throughout the campus and community.

Patton has also worked to celebrate the legacy of Cortlandt Van Rensselaer Creed, M.D., the School of Medicine’s first African-American graduate.

In 2007, on the occasion of the 150th anniversary of Creed’s graduation from the School of Medicine, Patton and his colleagues organized a series of events culminating in the dedication of a new permanent memorial to Creed at the Grove Street Cemetery.

Six Elm Awards, which are bestowed on members of the New Haven community (“the Elm City”) and were also given at the April event. The Elm and Ivy Fund, which endows the awards, was established at Yale in 1979 by Fenmore Seton, a 1938 Yale College graduate, and his wife, Phyllis.