

centerpoint

Yale Cancer Center's community newsletter winter 2010

Yale **CANCER CENTER**
A Comprehensive Cancer Center Designated
by the National Cancer Institute



Judy sought inspiration from her own patients during her cancer treatment.

Nurse Draws Hope from Patients

Judy Reardon, a registered nurse at Yale-New Haven Hospital, wasn't entirely shocked when she was diagnosed with papillary thyroid cancer in late October. Having worked at Yale since 1982 and as a nurse since 1976, she has cared for hundreds of cancer patients over the years; she understands first hand that cancer can happen to anyone.

While at her desk on a phone call, Judy was resting her hand across her neck when she felt a lump. After talking with a nurse practitioner in the office, she made an appointment with her doctor for the next day to have it checked. They performed an ultrasound and completed a biopsy that day. No other symptoms alerted Judy to the fact that there may be something wrong. A week later she received the results that it was in fact thyroid cancer.

The biopsy indicated that the tumor had not spread to her lymph nodes and she immediately made an appointment with Dr. Robert Udelsman, Chairman of the Department of Surgery at Yale School of Medicine.

She also made an appointment with Dr. Elizabeth Holt, Assistant Professor of Internal Medicine in Endocrinology. "From what I had researched I knew that papillary thyroid cancer was one of the more easily treated types. It was slow-growing, and I am lucky that it was caught early, before it had time to spread," Judy said.

Dr. Udelsman commented that thyroid nodules are common, and are detected in 15% of women in the United States. However, most of them turn out to be benign. The important thing is to discriminate between the benign nodules that are simply watched and followed, and the malignant ones that are proven to be cancerous.

"We have a true multidisciplinary approach to the treatment of thyroid cancer, and that's exactly what Yale Cancer Center does so well. There are an array of individuals and procedures to offer patients with cases that range from straightforward, to the world's most complex case," Dr. Udelsman explained. "The surgical nursing staff also plays a huge role in this

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Virus Studies, a Shot in the Arm for Cancer Research

When a vaccine was developed for human papillomavirus (HPV), cervical cancer, which is caused by HPV, became preventable through a simple inoculation. Scientists at Yale Cancer Center are determined that this won't be the last time defeating a virus means defeating a cancer. Viruses, according to Daniel DiMaio, MD, PhD, Director of Yale's Molecular Virology Research Program and Scientific Director of Yale Cancer Center, cause about 15 percent of all human cancers. Studying those viruses will lead to more effective treatments for the cancers they cause and even to vaccines that can prevent those cancers entirely.

Yale Cancer Center was recently awarded an \$8 million National Cancer Institute grant to continue work in tumor virology. This program of research, which has been ongoing at Yale for 37 years and is now headed by DiMaio, delves into the biology by which viruses induce the cellular transformation that leads to cancer. In addition to the three senior scientists working on this Program, about 40 laboratories throughout Yale are involved in other virology research.

HPV is not the only virus that causes cancer. For example, Epstein-Barr virus causes some lymphomas and forms of Hodgkin's disease, as well as other cancers. Hepatitis B virus and hepatitis C virus cause liver cancer. In addition to cervical cancer, HPV itself

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Gifts that Change Lives

Everyone is touched by cancer in some way and there are many opportunities at Yale Cancer Center to help patients and families who will face a diagnosis of cancer. Each gift touches a life by funding innovative research, new treatments, and important patient services. Donors may never know the people that benefit from their philanthropy, but their generosity has a profound impact on the lives of so many. Without the support provided by people wishing to make a difference, cancer research and care would not be nearly as advanced as it is today. Your gift enables us to continue to make critical advances tomorrow.

Many donors choose to make a gift each year to Yale Cancer Center to honor friends and loved ones who have faced cancer. We encourage you to consider this as part of your philanthropy, possibly at a birthday, anniversary, or other important time.

Please use the enclosed envelope to make a gift to Yale Cancer Center. Remember, no gift is too small and each gift makes a difference.

If you have any questions, please call
(203) 436-8527.

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Yale Cancer Center's quarterly newsletter is written to inform the public and the Center's friends, volunteers, donors, and staff on current items of interest at Yale Cancer Center. All inquiries should be addressed to Renee Gaudette, Director of Public Affairs and Marketing, 157 Church Street, New Haven, CT 06510-2100. Yale Cancer Center complies with the Health Insurance Portability and Accountability Act (HIPAA) of 1996.

New Option May Improve Outcomes in Allogeneic Stem Cell Transplantation

Stem cell transplantation is often the treatment of choice for patients with cancers of the blood, including leukemia and lymphoma. The process is a potent weapon against these diseases but it is often a difficult procedure for patients that includes a lengthy recovery time and the development of Graft-versus-host Disease (GVHD) in 40-80% of patients. Research from Yale Cancer Center has led to a clinical trial seeking to decrease the incidence of GVHD following allogeneic stem cell transplantation, while improving immune reconstitution.

GVHD is a common and serious complication where the immune cells in the transplanted blood mount an attack on the recipient's tissues. All patients receive some type of immunosuppression prior to a stem cell transplant, which reduces GVHD but it also makes patients more susceptible to infections.

Dr. Warren Shlomchik, and his brother Mark, members of Yale Cancer Center and the Department of Immunobiology, have discovered that memory T cells have a reduced capacity to induce GVHD, but can still transfer functional T cell memory. This result suggests that GVHD could be reduced and immune reconstitution improved by removing naïve T cells and only transferring memory T cells during a transplantation.

"Our laboratory research showed that it was safer to use memory T cells during a transplant process. The next step is to test our hypothesis in patients by determining whether GVHD is reduced by depleting naïve T cells from donor stem cell grafts and whether the memory T cells transferred improve immune reconstitution," explained Dr. Shlomchik, Associate Professor of Medicine and Immunobiology at Yale Cancer Center.

Dr. Shlomchik is the principal investigator on a Phase II clinical study at Yale Cancer Center testing the selective transplantation process in patients with acute leukemia. The Yale Stem Cell Processing Shared Resource will process the blood products from the transplant donor to remove the naïve T cells and ensure only memory T cells are transplanted to the patient.

The trial will evaluate the efficacy and safety of this new approach to stem cell transplantation and will employ progressively less immunosuppression as the study progresses, provided GVHD is reduced in incidence and severity. The ultimate goal will be to vaccinate donors against antigens expressed by the patient's cancer cells, thereby creating memory T cells reactive against them. Then the transfer of memory T cells could improve both immune reconstitution and the anti-cancer immunotherapy. ☺

The clinical trial is currently available to patients at Yale Cancer Center and the Fred Hutchinson Cancer Research Center in Seattle, Washington.

For more information, call (203) 785-5702.

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process, and is essential to optimizing patient care."

In Judy's role as an RN in the Department of Diagnostic Radiology at Yale, she cares for many patients, including those with cancer. She provides care while monitoring patient safety, and minimizing pain during interventional radiology procedures. Judy had an understanding before her own experience with cancer of what patients go through and how difficult a diagnosis of cancer can be. Having this knowledge did not cause her fear, however, but instead gave her hope and inspiration.

"I have seen patients with thyroid cancer over the years do well, and that gave me hope that I would do well too. The way in which I have seen some patients handle what they are going through is inspirational to me. Many patients deal with diagnoses more complex than what I am dealing with, and they are still able to take it in stride and have a positive attitude," Judy said. "I am not sure where their strength comes from, but it gave me encouragement for my own battle."

Surgery was Judy's primary method of treatment. Her thyroid gland was removed, along with associated

lymph nodes. There are side effects that can occur after a surgical procedure such as Judy's but she was very comfortable having Dr. Udelsman be the one to perform her surgery.

"The more experienced and skillful your surgeon is, the less chance there is for adverse effects. It was important to me to have a skilled surgeon like Dr. Udelsman performing my surgery," Judy said. "Patricia Donovan, his clinical coordinator, was extremely helpful too. She was always accessible and it was great to have her to communicate with whenever I had questions."

Dr. Udelsman explained that Judy presented in a very typical way for papillary thyroid cancer, and her excellent prognosis is typical as well. Judy will receive a dose of radioactive iodine treatment as follow-up to her surgery, and will continue to be monitored by Dr. Holt.

"It's hard to know how you will react when you are faced with a situation like this, but I wanted to set a good example for my kids and tried to deal with everything as it came," Judy said. "It was important that I not let myself fall apart, but follow the example of the patients I see bravely continuing their fight every day." ☺

►► **Virus Studies** continued from page 1

is implicated in many head-and-neck cancers. The list could grow. But it is important when talking about tumor virology to restate the obvious: Cancer is not contagious. Catching a cancer-associated virus does not equal catching cancer. Most people infected with these common viruses will never develop cancer. Finding out why that is may hold clues to better treatments.

“We need basic research to make the next breakthrough. Our findings can seed many labs across the country and across the world.”

Daniel DiMaio, MD, PhD
Director of Yale’s Molecular Virology
Research Program and Scientific
Director of Yale Cancer Center

DiMaio discovered that, even when HPV is present, specific viral genes must be expressed if cancer cells are to proliferate. He has been able to suppress those genes in laboratory samples and stop cancer cells from multiplying. John F. Enders Professor of Pediatric Infectious Diseases, George Miller, MD, a co-investigator in the Program, has identified the viral genes that switch two other cancer viruses from a latent to an active stage.

Other viruses may cause cancer in a “hit and run” attack, explains co-investigator Joan Steitz, PhD, Sterling Professor of Biophysics and Biochemistry. The virus may start the process that leads to uncontrolled cell division but is no longer present when the cancer is diagnosed. Such virus/cancer connections easily go uncovered because the virus has left the scene of the crime. Steitz concentrates on viral non-coding RNAs. Most RNAs are coding; they carry the genetic code from the DNA to the ribosomes that make proteins. Steitz discovered certain non-coding RNAs present in high numbers when viruses multiply. It took her 23 years of research to uncover the function of one of the non-coding RNAs on her radar.

Many advances in tumor virology are made by researchers who are as interested in pure science as they are in medical progress. Viruses make great biology teachers. “They basically have co-evolved with cells, so they know everything the cell knows,” explained Miller. Watching viruses work within host cells gives researchers insight into basic cellular functions. Because the structure of viruses is far less complex than the structure of a cell, they are easily manipulated, a simplicity that makes them valuable tools of discovery. “We need basic research to make the next breakthrough,” said DiMaio, who is also the Waldemar Von Zedtwitz Professor of Genetics and Professor of Therapeutic Radiology and Molecular Biophysics and Biochemistry. “Our findings can seed many labs across the country and across the world.”

In addition to her research, Steitz considers herself a teacher first. Her office is filled with champagne bottles, autographed in silver paint by students who wrote their dissertations while assisting in her lab, where they



Daniel DiMaio, MD, PhD, Scientific Director of Yale Cancer Center

learned about the determination science requires. “You have to have a real curiosity about how things work,” she said. “You have to love puzzles. And you have to be really turned on by being the first person to know something.”

Miller knows that feeling. He was the first to demonstrate that a human virus could cause cancer in a laboratory animal. “I didn’t believe it, at first,” he recalled. Miller has also created cell lines that are used by researchers and clinicians. A former post-doctoral associate, Cliona Rooney, PhD, used one of those cell lines to develop an immunotherapy for patients with Epstein-Barr-associated cancers. As the technology to study viruses evolves, there are more discoveries to be made. “This is not going to stop,” he said. ☺

event calendar

March 10, 2010

Understanding Cancer Lecture Series

Treatment Options for Colorectal Cancer

Dr. Edward Chu, Deputy Director
and Chief of Medical Oncology, Yale
Cancer Center

6:00 PM; YNHH East Pavilion Cafeteria

For reservations, call (888) 700-6543

March 24, 2010

Colorectal Cancer Town Hall

Dr. Thomas Lynch, Dr. Edward Chu, and
Ellen Matloff, MS

8:00 PM; Connecticut Public Broadcasting

Network, Hartford, CT

For more information, call (860) 278-5310

March 25, 2010

Esophageal Cancer CME Dinner

A Panel of Presenters from Yale
Cancer Center

6:00 PM; Morton's The Steakhouse,

Hartford, CT

For more information, call (203) 785-4578

March 26, 2010

4th Annual John Murren Oncology CME Symposium

Melanoma Research and Treatment

The Red Rock Conference Center, Las

Vegas, NV

For more information, call (203) 785-4578

March 27, 2010

Lung Cancer Symposium

The Changing Face of Lung Cancer

A Panel of Presenters from Yale
Cancer Center

8:00 AM; Park Street Auditorium

For reservations, call (888) 700-6543

April 14, 2010

Understanding Cancer Lecture Series

New Technological Discoveries in Cancer Care

Dr. Thomas Lynch, Jr., Director, Yale
Cancer Center and Physician-in-Chief,

Smilow Cancer Hospital at Yale-New Haven

6:00 PM; YNHH East Pavilion Cafeteria

For reservations, call (888) 700-6543



American Red Cross
Connecticut Blood Services Region

Providing for patients at Yale Cancer Center.
Please consider yourself asked and donate blood.
1-800-GIVE LIFE

Smilow Cancer Hospital - Now Open!

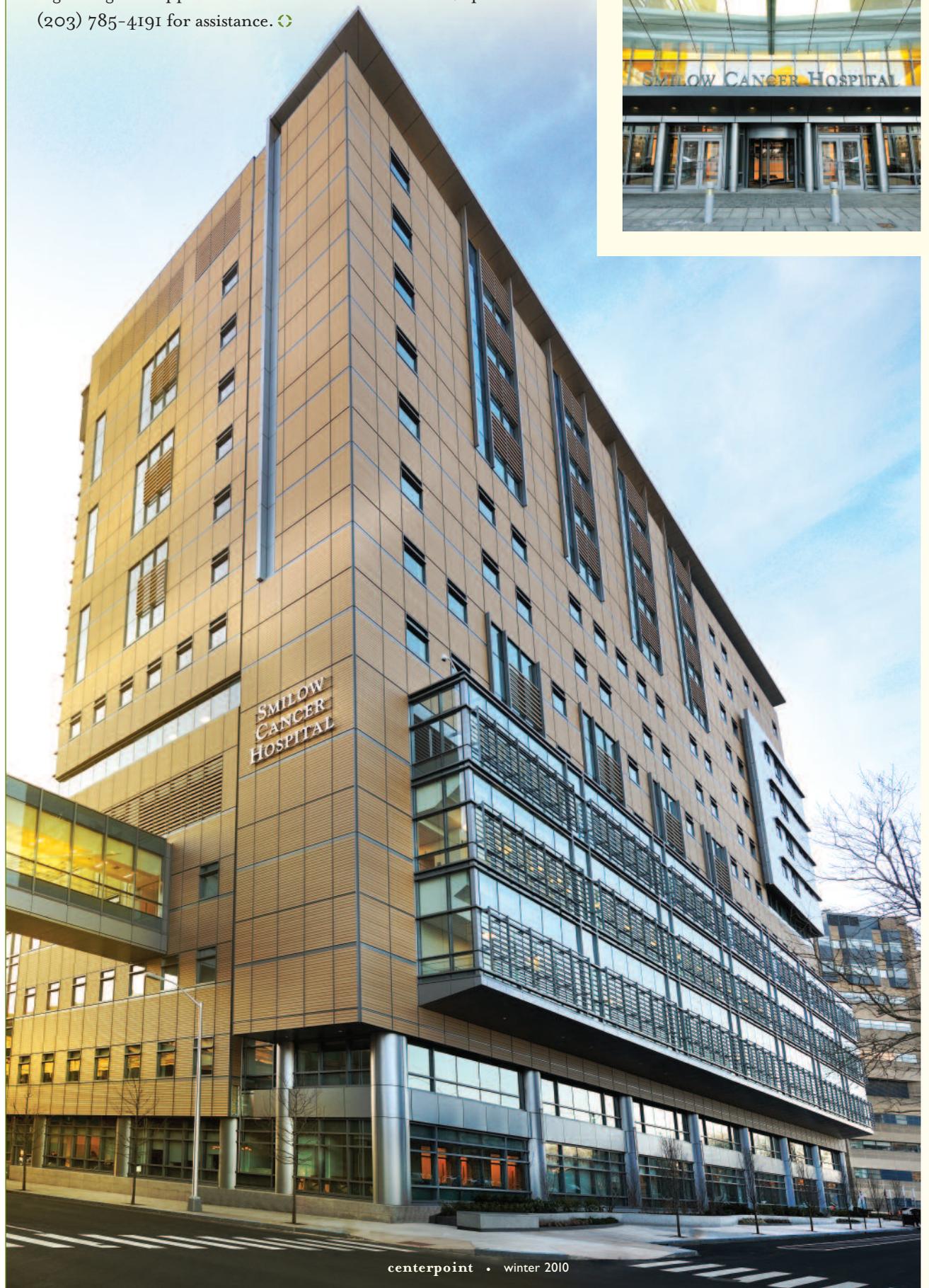
After years of careful planning, Yale-New Haven Hospital, Yale Cancer Center, and the physicians of Yale Medical Group are excited to announce the opening of Smilow Cancer Hospital at Yale-New Haven. When fully open in April, the facility will house all inpatient and outpatient cancer services for our patients, making it the most comprehensive, single destination for cancer care in the Northeast.

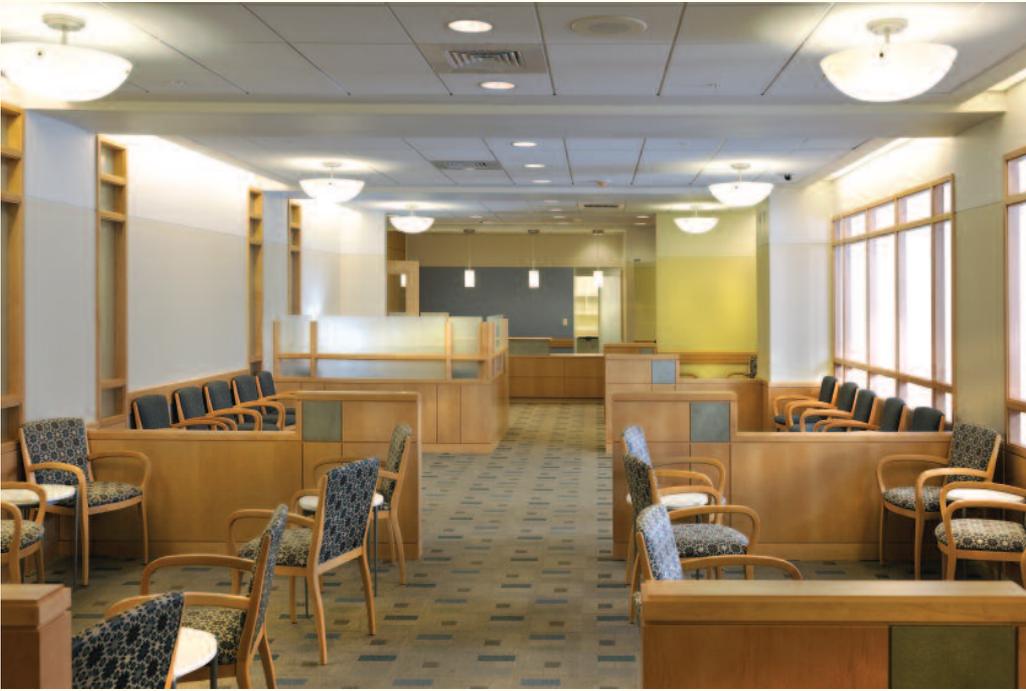
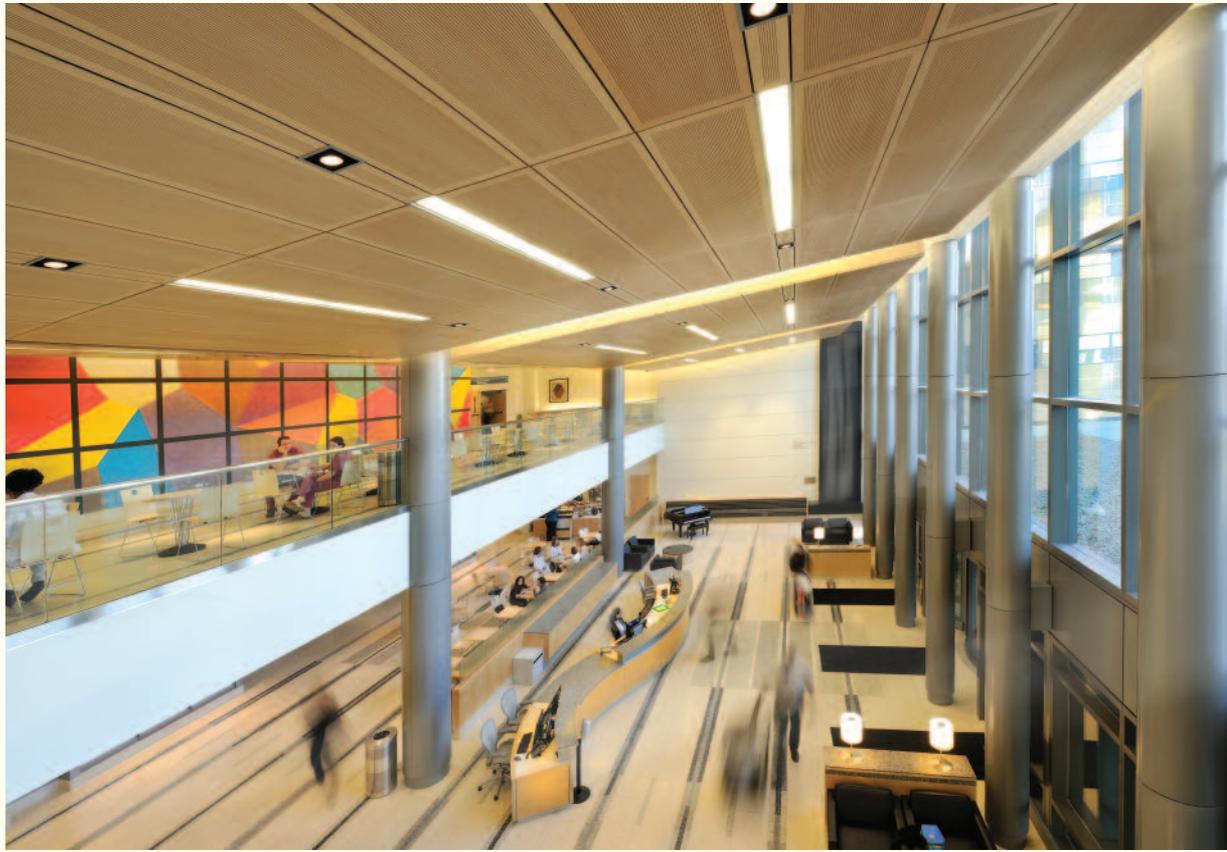
The inclusion of all cancer services at Smilow Cancer Hospital at Yale-New Haven enables our multidisciplinary teams to provide each of our patients with optimal cancer care in a state-of-the-art facility. The 14-story building includes a healing garden, a boutique, 112 inpatient beds, outpatient treatment rooms, expanded operating rooms, infusion suites, diagnostic imaging services, radiation oncology, and a specialized Women's Services Center.

We are pleased to present the new location of cancer care at Yale, as well as expanded services and team care. If you have any questions regarding an appointment schedule or location, please call (203) 785-4191 for assistance. ☺



ALL PHOTOS THIS PAGE PETER BAKER





Chad A. Ellis, PhD Appointed Deputy Director for Research



Yale Cancer Center Director, Thomas J. Lynch, Jr., MD, recently appointed Chad A. Ellis, PhD as Deputy Director for Research. Dr. Ellis joins Yale Cancer Center from the National Cancer Institute (NCI) where he was a Program Director for the Cancer Centers Program.

"We are excited to have Chad's invaluable knowledge from his work with the Cancer Centers Program at the NCI within the leadership group of Yale Cancer Center," Lynch said. "His combination of administrative and research experience in both the public and private sector will strengthen our research organization and help us to advance our basic and translational research initiatives."

Dr. Ellis earned his bachelor's degree in microbiology and cell science from the University of Florida and his PhD in pharmacology from the University of Illinois School of Medicine. He joined the NCI as a postdoctoral fellow in 1999 where he focused on the regulation, activation, and signaling pathways of the *Ras* proteins and identified and oversaw a patent application for the novel protein, *Rig*. Dr. Ellis also spent several years as a research scientist and consultant to private companies, including Rexahn Corporation, FBA, Inc., and Cellectricon Inc.

In his role as Deputy Director for Research, Dr. Ellis will oversee the Center's eight research programs and twelve shared resources. He will also lead the application efforts for Yale Cancer Center's Cancer Center Support Grant from the NCI. ☺

Learning From China's Struggle With Cancer

When Tongzhang Zheng left China in 1984, the rush toward a developed economy hadn't changed everyday life much. People still ate a diet based on vegetables and grains raised by farmers who used centuries-old, natural methods. They bicycled everywhere.

Zheng now heads the Yale School of Public Health's Division of Environmental Health Sciences and returns to China to do research. He literally does not recognize it; Zheng had trouble finding his childhood home among sprawling development. Beijing alone has 4 million automobiles, not to mention a McDonald's in Tiananmen Square. Zheng gets a whiff of pesticides in the tea when he visits rural villages. "They don't even smell it anymore," he said.

Prosperity came with lifestyle changes and pollution linked to cancer, which the Ministry of Health estimates has increased more than 80 percent in three decades. Zheng predicts that by 2020, China will have the world's highest incidence of cancer.

Zheng and other Yale Cancer Center scientists are conducting cancer research with Chinese institutions and inviting Chinese scholars to Yale for training. The primary aim of this work is to help the world's most populous country confront its growing cancer problem.

Increasingly, however, cancer research is an international enterprise, with findings in one country benefitting patients worldwide. China offers unique advantages for research, including a huge population and distinct lifestyles and environmental exposures in various regions.

One fascinating area these collaborations explore is "the fetal origin hypothesis." Some researchers believe genetic changes during fetal development lead to certain cancers. Recruiting a large cohort of pregnant women and following their children for decades will help determine the idea's merit. In addition to taking cord blood and periodic maternal and child blood samples, researchers will record lifestyle factors and environmental exposures.

Yawei Zhang, MD, PhD, an Assistant Professor of Public Health, is interested in the hypothesis in breast cancer, a form of cancer that's rapidly on the rise in China. Though it may take 50 years to see cases of breast cancer in the children born to women in the study, she'll gain valuable information much earlier. For example, a pattern of early puberty in the girls would signal high risk for breast cancer. Girls could be identified for heightened screening. Looking at what their mothers were exposed to during pregnancy will

give clues about reducing risks in future generations.

In some cases, the differences between China and the United States create opportunities. Harvey Risch, MD, PhD, Professor of Public Health, studies the link between *Helicobacter pylori* and pancreatic cancer. These intestinal bacteria are frequently found in prostate cancer patients. In China, colonization by the bacteria is more common, as are smoking and nitrate consumption, also risk factors for pancreatic cancer; yet the incidence of pancreatic cancer is lower in China than in the United States. By looking at cohorts in Connecticut and Shanghai, he hopes to better understand the interplay of genetics and other risk factors.

Risch is collaborating with Associate Professor of Public Health Herbert Yu, MD, PhD, who focuses on how genes and environment interact. Yu suggests that



there may be some protective factor in the Chinese lifestyle, for example, green tea drinking, that keeps pancreatic cancer rates lower.

Traditionally the developing world struggled with infectious diseases resulting from poor sanitation and limited access to healthcare. More developed nations are concerned with chronic diseases associated with a high-calorie, low-activity lifestyle and pollution from industry. With China's rapid development, a switch from infectious to chronic disease occurred. As development spreads globally, we can expect to see that pattern repeated and a worldwide increase in cancer, Yu says.

Can a society have it both ways? Is it possible to conquer diseases like tuberculosis without falling prey to cancer, hypertension, or diabetes? Zhang believes so. When she first came to America, she was struck by how people scrutinized food labels for fat content. There had been little public education about sugar and overall calories, so people still chose foods that made them gain weight. Information is the key to helping people manage whatever risk their lives present, Zhang believes. The scientific discoveries made through these collaborations, she says, must be shared with a global public to have a real impact. ☺