

Yale Cancer Center

centerpoint

MAGAZINE

fall | winter 2015



Building the Cancer Biology Institute



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centerpoint MAGAZINE

Centerpoint Magazine is published
two times a year by Yale Cancer Center
to inform the public and the Center's
friends, volunteers, donors, and staff
on current items of interest at Yale
Cancer Center.

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The leadership transition during the summer of 2015 kept our team busy at Yale Cancer Center and Smilow Cancer Hospital at Yale-New Haven, and I am honored to have the opportunity to continue the momentum we have worked hard to achieve under Dr. Thomas Lynch's leadership since 2009. Dr. Lynch left Yale in August to pursue an opportunity at Massachusetts General Hospital and we are proud to wish him the best in his endeavors.

I am committed to building on the strong foundation that Dr. Lynch and our colleagues have created for us over the last 6 years. I truly believe that the best way to honor the hard work we have put forth is to move forward with our strategic plan and to look ahead to identify other areas of opportunity that need attention.

One area that I'm particularly excited to see accelerate is the establishment and building of our Cancer Biology Institute. Earlier this year we welcomed Dr. Mark Lemmon to Yale Cancer Center as Co-Director of the Institute, and I am already impressed with the speed with which he has started recruiting new investigators to Yale and his planning to meet our vision for the Institute. You will read about his goals in this issue of *Centerpoint*.

Smilow Cancer Hospital at Yale-New Haven has emerged as a national leader in oncology pharmacy standards by redefining the way we manage our pharmacies and safely deliver the prescribed drugs to our patients. Last year the team won a national award for its telepharmacy model, which better manages and oversees pharmacy delivery in our 11 Care Center sites. Innovation has continued in 2015, with the development of a new model for monitoring oral chemotherapy prescriptions to ensure compliance and safety at home. In addition, our pharmacists are more prominent in our clinics and available to both our patients and the care teams to answer questions and offer assistance.

As 2015 is coming to a close, we are concluding our 5th year anniversary celebrations for Smilow Cancer Hospital at Yale-New Haven and our 40th anniversary celebrations for Yale Cancer Center. New grant funding, new research advances, new clinical trials, and, most importantly, each and every one of our patients, are inspiring us every day to look ahead to the next 5 years. I look forward to helping Smilow Cancer Hospital and Yale Cancer Center achieve our goals so we have many more advances to celebrate in 2020 during our next anniversary celebrations!

Sincerely,

Peter G. Schulam, MD, PhD
Director, Yale Cancer Center and
Physician-in-Chief, Smilow Cancer Hospital (Interim)

Blessed by Strength and Family

Emily Fenton writer Peter Baker photographer

It wasn't uncommon for Tasha Edens, a manager of a group home, to experience minor bruises while at work, it was part of the job. However, one day in early October of 2012, she came home and noticed deep purple bruising on her legs. She didn't think much of it until a large bruise appeared on her stomach and her husband insisted she go to a walk-in clinic. They drew blood, which later revealed she had leukemia. They could not determine what type, just that she needed to go to the Emergency Department immediately.

It was in the Emergency Department at Yale-New Haven Hospital that Tasha met the Smilow Cancer Hospital Hematology team, first Dr. Alfred Lee, and later Dr. Nikolai Podoltsev. Dr. Podoltsev, Assistant Professor of Medicine (Hematology), was able to confirm a diagnosis of acute promyelocytic leukemia, a rare, quick moving subtype of Acute Myeloid Leukemia (AML) where immature white blood cells accumulate in the bone marrow. This leads to a deficiency of normal blood cells and platelets. Still in shock from the diagnosis, Tasha and her husband were frightened by the sudden urgency with which things progressed.

Dr. Podoltsev explained that the beginning stage of this leukemia subtype is the most dangerous, and in high-risk patients, like Tasha, the risk of death is high. Patients are considered high-risk when their white blood cell counts are 10,000 or over; Tasha's counts were over 20,000 when she arrived.

Tasha began induction chemotherapy in combination with all-trans retinoic acid (ATRA) that day, and was told she would have to stay in the hospital for at least four weeks. This was devastating news for her and her family. "Dr. Podoltsev was wonderful and made it very clear from the beginning that the hardest part about this treatment regimen would be staying in the hospital, and he was right," said Tasha. "I have 7 children, 3 of them biological, ranging in age from 9 to 26, and 2 grandchildren. There was no time to stop and see them or to explain what was happening, we had to move fast."



Tasha (center) with her husband, Marcus, surrounded by their family.

“...I am here, I am alive, and for now I plan to live each day for my children, my grandchildren and for my husband.”

Tasha remained at Smilow Cancer Hospital for 35 days and was monitored for any adverse reaction to the chemotherapy. Previously a disease that was highly lethal, the majority of patients with acute promyelocytic leukemia (APL) are now cured because of the introduction of differentiating agents including ATRA, a vitamin A derivative.

“Coming to an academic hospital, like Smilow, is crucial for high-risk patients like Tasha,” said Dr. Podoltsev. “Things need to move fast to get an accurate diagnosis and begin treatment. With this kind of expertise, cure is almost 90%, which is very favorable for a disease that can be fatal if not identified and treated correctly very quickly.”

One thing that helped Tasha through her hospital stay was the care and knowledge of the staff and doctors. “They never once turned my family away,” said Tasha. “They were comforted and treated with the same kindness that I was. My husband stayed with me every night and went to work in the morning for the Department of Corrections, an already stressful and high-risk job. Then he came home to the kids, the house, and the questions about when mom was coming home. It is a lot of stress for a family.”

diagnosed,” explained Dr. Podoltsev. “Managing such a rare cancer requires a lot of moving parts. Treatment involves inpatient and outpatient care, as well as two years of outpatient maintenance therapy. It takes a lot of understanding on the part of the patient, but the outcome is most often a cure.” Dr. Podoltsev commented that the treatment for AML is a multi-disciplinary effort that includes a nurse practitioner, the nurses in the inpatient and outpatient clinics, and a number of fellows and leukemia service attendings that make the transition between inpatient and outpatient care smoother.

Tasha recently finished 2 years of maintenance therapy, during which she developed Pneumocystis jiroveci Pneumonia (PJP), which is common in patients with a suppressed immune system. She was again admitted into the hospital, this time for 15 days. She now sees Dr. Podoltsev every 3 months for blood work, to make sure there are no signs of a recurrence.

Although physically healthy, Tasha and her family still suffer from the emotional and mental side effects of cancer. She commented that it is always in the back of their minds, what if it comes back and they have to go through all of this again? “My kids are afraid every time I go in for my routine blood work, they think, what if this time mom doesn’t come home again? It is very hard to deal with that.”



Following the induction chemotherapy, Tasha began consolidation therapy, which was given in 3 cycles with a goal of achieving remission and ultimately cure. During this time she was in and out of the hospital for varying durations. A bone marrow biopsy later revealed that the treatment had worked; there was no evidence of disease.

“Tasha’s type of leukemia accounts for only 10 percent of all AML cases. We see about 5 patients a year that are newly

Tasha has learned to listen to her body and if she feels tired, she rests. Something she would not have done before. “I am so blessed to have come through this, and it is thanks in part to my amazing husband who pushed me to focus on my own health for once. It is still hard to put cancer out of my mind and the fear it may return, but I am here, I am alive, and for now I plan to live each day for my children, my grandchildren and for my husband. They are my greatest blessing.”

building THE CANCER BIOLOGY INSTITUTE

Steve Kemper **writer** Peter Baker **photographer**

Yale Cancer Center's Cancer Biology Institute is moving from concept to reality. The Institute was envisioned several years ago by founding Director Joseph Schlessinger, PhD, William H. Prusoff Professor and Chair of Pharmacology at Yale School of Medicine, and a key step in bringing it to life is the recent appointment of Mark A. Lemmon, PhD, as the Institute's new Co-Director and David A. Sackler Professor of Pharmacology. Dr. Lemmon returns to Yale, where he completed his PhD in 1993, from the University of Pennsylvania's Perelman School of Medicine, where he was the George W. Raiziss Professor of Biochemistry and Biophysics as well as Chair of the Department and an Investigator at the Abramson Family Cancer Research Institute.

"We will be building the Cancer Biology Institute from the ground up," said Dr. Lemmon, a biochemist and structural biologist whose research focuses on how molecules work and how cells signal. "It will be a research institute of approximately a dozen faculty laboratories focused on the core science of cancer," he continued, "and will take its place among the burgeoning cluster of new research institutes on Yale's West Campus."

The first question some people have, Dr. Lemmon explained, is why the Cancer Center is planning twelve new labs when so much innovative cancer research is already underway throughout the Cancer Center as well as the greater Yale community? Dr. Lemmon is ready with an answer.

Traditionally, cancer research focuses on a specific type of cancer in a particular organ – pancreas, breast, lung, skin, for example – while trying to understand it and treat it. "It's extremely important to do that, since the treatment and care is of course different in each case. But, as you back up into the science to understand the cellular and molecular basis of these particular cancers," he continued, "you find that ultimately the same core biology is driving all of these cancers – with certain genetic mutations and molecular pathologies being linked to multiple cancers."

The purpose of the Cancer Biology Institute is to study this core biology, with the goal of understanding the common underlying causes of cancer, wherever it appears. Dr. Lemmon believes that the future of cancer research will rely on this type of insight from the basic sciences for the creation of new drugs.

“What we’re really after is a molecular and cellular understanding of cancer and the body’s response to it,” he said. “Each mutated gene encodes a protein that is driving or allowing cell growth, and ultimately we need to understand how all these proteins play together in the big biological system – or biochemical network – that is the cell. Even beyond that, we need to know how the tumor interacts with its environment in the patient. If we can understand these issues when we see a lesion, we can figure out how to attack it pharmacologically – or to help the body attack it.”

For that reason, one of the new labs at the Cancer Biology Institute will focus on understanding genetic changes seen in cancer at the level of biochemical activity. There also will be research labs devoted to non-coding RNAs, epigenetics, cancer metabolism, proteomics, tumor metastasis, DNA repair, signaling networks, chemical biology, cancer immunology, and bioinformatics/computational biology, among other areas.

Dr. Lemmon also wants the Institute to develop mouse models of cancer so that researchers can do animal-based studies that result in new targeted therapies.

Together with Dr. Schlessinger, he has started recruiting scientists to run the Institute’s labs. By the end of this year, in addition to himself and Dr. Schlessinger, he expects to have three more researchers on board, including Kathryn Ferguson, PhD, who studies the molecular mechanisms that regulate signaling. Also a Yale PhD, she is moving her lab from UPenn’s Perelman School of Medicine to join Dr. Lemmon at the Institute. Dr. Lemmon’s next priority is to hire faculty who are experts in epigenetics and in computational biology/bioinformatics.

His goal is to open new labs at the rate of 2-3 per year. By 2020 he expects the Institute to be fully staffed, with 120 people working in a dozen labs. Some of the lab directors will be senior faculty, but most – seven or eight – will be junior people.

“We won’t be hiring people who have already done their best work,” said Dr. Lemmon. “Some of the young researchers starting their independent labs after successful post-docs are most in tune with the latest technologies and are spectacularly good. We want to hire these people as an investment in the future of

cancer research at Yale.”

Dr. Lemmon also emphasizes that the Institute won’t be an ivory tower for basic sciences. “Anyone I hire must be committed to making their research count for cancer,” he said. “We want everything done here to be translational and lead to targeted therapies.” Though he expects the Cancer Biology Institute’s labs to become one of the drivers of basic science at Yale, “they will be driving it based on opportunities emerging from the clinics here,” he said. “I want basic scientists who want to make bridges to the clinical side.”

This bridge, he added, is already in place at the Cancer Center, thanks to the leadership of people such as Thomas J. Lynch, MD, until recently the Director of YCC, Peter G. Schulam, MD, PhD, Director of Yale Cancer Center and Physician-in-Chief of Smilow Cancer Hospital (Interim), and Roy S. Herbst, MD, PhD, Chief of Medical Oncology and Associate Director for Translational Research. Translational Working Groups at YCC are combining basic sciences with clinical research that leads to phase I trials of new drugs. “One of our main goals is to feed that pipeline,” said Dr. Lemmon.

The Institute’s location among other research institutes on Yale’s West Campus, said Dr. Lemmon, is conducive to cross-fertilization and ground-breaking approaches. He expects

productive partnerships with the Chemical Biology Institute, the Systems Biology Institute, the Microbial Sciences Institute, and the Nanobiology Institute. The Cancer Biology Institute also will benefit, he noted, from proximity to the Center for Genome Analysis, with its massive database of information about genetic changes in cancer patients from Smilow Cancer Hospital.

All of these strengths, as well as the chance to build a Cancer Biology Institute with Dr. Schlessinger, lured him back to Yale. “It’s all set up in an ideal way here,” he said. “I also think that as personalized medicine has advanced in cancer, and more and more genetic changes are discovered in cancer, understanding the biochemistry – which is actually the consequence of those changes – has lagged behind. I’m passionate about bringing more biochemistry and functional understanding into personalized medicine – because that’s what we need to figure out in order to develop new drugs to use against cancer.”



Mark A. Lemmon, PhD, Co-Director of the Cancer Biology Institute and David A. Sackler Professor of Pharmacology



ONCOLOGY PHARMACY INNOVATION

Steve Kemper writer Peter Baker photographer

For pharmacists, nothing is more important than providing the correct medicines at the correct dosage. That’s why the highest award given by the American Society of Health-System Pharmacists (ASHP) is for Excellence in Medication-Use Safety. Last year the award went to Yale-New Haven Hospital for an innovative telepharmacy program that uses audio, video, and digital photography to deliver safe treatment to cancer patients receiving IV chemotherapy in Smilow Cancer Hospital’s 11 locations outside of New Haven. No other cancer hospital offers anything like it.

This year the hospital submitted an application for another ASHP award focused on oral chemotherapy. It’s a program aimed at improving the safety, compliance, and monitoring of patients who receive their cancer chemotherapy through oral medicines taken at home.

Both programs are unique to Smilow, where the department of Oncology Pharmacy Services is establishing itself as a trailblazer in the field.

The telepharmacy program came about when Smilow decided to extend its reach in 2011 by integrating a group of private oncology practices with offices throughout the state. The goal was to bring first-rate cancer treatment to patients at Smilow Cancer Hospital Care Centers near their homes instead of requiring them to drive to New Haven. The immediate issue was how to ensure that patients at the new care centers received the same quality of treatment given at Smilow, while also keeping the treatments convenient and seamless for patients, with minimal wait times.

“So we were challenged with a lot of things,” said Howard Cohen, RPh, MS, FASHP, Director of Yale-New Haven’s Oncology Pharmacy Services. “We had to introduce pharmacy and pharmacists into these centers in a very short timeframe, there was a shortage of available pharmacists to hire, and they also needed to be oncology-trained, which made it that much harder.”

Even if such pharmacists could be found, Cohen didn’t want them tied to computers all day, invisible to everyone in the care centers while they compounded drugs. He wanted them available to physicians, nurses, and patients to answer questions and confer about the drugs being used. Not all the new centers were busy enough to need a full-time pharmacist, which added another wrinkle to the issue of personnel.

Cohen and a multidisciplinary committee designed a telepharmacy model. It would allow pharmacists to oversee the mixing of drugs by pharmacy technicians in multiple places, would free pharmacists to interact with providers and patients, and would allow staffing flexibility. But when they asked the state of Connecticut for permission to run a pilot study, they ran into a wall: state law required a supervising pharmacist and pharmacy technician to be located in the same building. Nevertheless the Smilow team convinced the state to allow the pilot. It worked so well that in April 2012 the state legislature passed a new law permitting hospitals to use telepharmacy, under strict conditions.

“I wasn’t sure we could pull it off,” said Catherine A. Lyons, RN, MS, executive director of patient care services at Smilow. “Number one, we had to figure out a way to provide the service given our resource and time limitations, so I wasn’t sure we could meet the commitment to provide the same standard of care to patients in the centers. Pharmacy came up with an incredibly creative way to meet that expectation. And number two; we had to change state law. It’s extraordinary we were able to do that. It’s a groundbreaking program.”

It's also very safe. Here's how it works: a physician writes a chemotherapy prescription, which is entered into Smilow's electronic medical records system. A nurse reviews the script for accuracy, and then sends it to a pharmacist, who reviews it against the patient's labs for both accuracy and appropriateness. Any pharmacist can do this verification on-site or via computer. Next the order goes to a pharmacy technician at the location where the patient receives therapy.

There, in a sterile "clean room," the technician mixes the prescription's drugs, using menu-driven software that requires a step-by-step procedure. The software asks the tech to show the name of the drug, the lot number, and the expiration date, all of which get photographed. If the software says to put five milliliters of a drug into a syringe, the tech must take a photo of the syringe with that exact amount in it before being allowed to continue. The digital photos provide a record of everything done.

A second level of safety comes from bar coding. The tech must scan every drug before mixing it into a prescription. If the drug is incorrect, the software halts the process. This eliminates errors due to what pharmacists call "look-alike-sound-alike" drugs. If the tech skips any instruction or ignores any stop sign, a large X appears on the screen.

In addition, a wide-angle camera in the clean room allows a pharmacist anywhere in the system to observe the tech via computer. If the pharmacist or tech needs to speak, they can do so through a hands-free phone system.

Once the prescription is mixed, the tech puts it in a bag, labels it, and sends it to an area called the sorting cube. A second pharmacist reviews the photos to make sure the prescription was mixed correctly and no steps were missed. Once the prescription is approved, a second label is applied and the medicine is ready to go.

Though most of the care centers now have a pharmacist on site, a pharmacist can do many of these steps remotely. This frees the resident pharmacist to interact with the rest of the team at the care center. "The pharmacist becomes visible," said Cohen. If a pharmacist at a care center needs to be part of the morning huddle to discuss patients, or to consult on medications, or to answer questions from patients, another pharmacist can step in remotely.


"Patients, pharmacists, and technicians all benefit from telepharmacy," said Nancy Beaulieu, RPh, BCOP, Manager of

Oncology Pharmacy Services. "Particularly at the cancer care centers. For the patients, it provides the same level of safety, scrutiny, and oversight as in the hospital, and for the staff, it provides a lot of flexibility and support." For instance, if a care center has a heavy flow of patients scheduled for a certain day, telepharmacy allows another pharmacist to help, even from 40 miles away. "It's like having 10 pharmacists at every site," said Beaulieu.

These days not all cancer patients come into a center for IV chemotherapy. Many cancer medications can now be taken orally at home. For physicians and pharmacists, that's worrisome. "We didn't know anything about what was happening to patients," said Osama Abdelghany, PharmD, BCOP, Manager of Oncology Pharmacy Services. "The physician wrote a prescription, but we didn't know if the prescription was filled, or if the patient could afford the medication, or if patient took it correctly or did well on it, or if they took it all or stopped because of side effects. All of that was a black hole because none of it was documented in our records."

Another multidisciplinary team began developing a program to provide better care to patients using oral chemotherapy. The goals were to standardize the process of prescriptions, to make sure the patient actually filled the prescription, to educate the patient about the medication, and to monitor the patient for toxic side effects and compliance. "Even if they're not in the hospital or our infusion centers," said Cohen, "they're still our patients." The pilot program began in March and has quickly expanded to the care centers. About 200 patients are now participating.

To help track whether patients filled their prescriptions, Smilow opened a specialty pharmacy. So far, about half of the oral chemotherapy patients are using it. Regardless of where the prescription is filled, someone from Smilow calls the patient twice a month to make sure the drug is being taken and taken correctly, and to ask about side effects.

"Other specialty pharmacies just fill the prescription," said Abdelghany, "but we are following every single patient, even if they filled it outside our pharmacy. From a business perspective it's crazy, but it's the right thing to do." All the information goes into the patient's electronic record. "This information was not known before," added Beaulieu, "and now it's documented in a systematic way." 



New Type of Drug Can Target All Disease-Causing Proteins

Nat Chem Biol. 2015 Aug 11.

Current drugs block the actions of only about a quarter of known disease-causing proteins, but Yale University researchers have developed a technology capable of not just inhibiting, but destroying every protein it targets. The new type of drug, called Proteolysis Targeting Chimeras (PROTACs), can also continue to destroy mutant proteins in mouse tumors.

Almost all current drugs are small molecules designed to fit into the folds of disease-causing proteins and inhibit their function. High doses are often needed to ensure that protein function is blocked sufficiently to produce therapeutic results, which in turn can produce harmful side effects.

In contrast, PROTACs engage the cells' own protein degradation machinery to destroy targeted proteins by tagging them for removal and can do so multiple times, meaning it can work at lower doses.

Study Identifies 'Major Player' in Skin Cancer Genes

Nat Genet. 2015 Sep.

A multidisciplinary team at Yale Cancer Center has defined a subgroup of genetic mutations that are present in a significant number of melanoma skin cancer cases. Their findings shed light on an important mutation in this deadly disease, and may lead to more targeted anti-cancer therapies.

To deepen understanding of melanoma mutations, the Yale team conducted a comprehensive analysis using whole-exome sequencing of more than 200 melanoma samples from patients with the disease. The researchers confirmed that a gene known as NF1 is a "major player" in the development of skin cancer.

Additionally, researchers observed that melanoma patients with the NF1 mutation were older and had a greater number of mutations in the tumors.

From Yale, a New Sunblock that Doesn't Penetrate the Skin

Nat Mater. 2015 Sep 28.

Researchers at Yale have developed a sunscreen made with bioadhesive nanoparticles that doesn't penetrate the skin, eliminating serious health concerns associated with commercial sunscreens.

Most commercial sunblocks are good at preventing sunburn, but they can go below the skin's surface and enter the bloodstream. As a result, they pose possible hormonal side effects and could even be promoting the kind of skin cancers they're designed to prevent.

Using mouse models, the researchers tested their sunblock against direct ultraviolet rays and their ability to cause sunburn. In this regard, even though it used a significantly smaller amount of the active ingredient than commercial sunscreens, the researchers' formulation protected equally well against sunburn.

Rare Mutation May Extend Survival in Lung Cancer Patients with Brain Metastases

JCO. 2015 Oct 5.

Most patients with non-small cell lung cancer (NSCLC) that has metastasized to the brain have a dire prognosis. But Yale researchers have identified a subset of those patients with a rare genetic mutation who are living significantly longer than patients without the mutation.

NSCLC accounts for 85% of all lung cancers, with 30%-50% of patients developing metastatic disease to the brain. Typically, patients with this diagnosis die of the disease within seven months. However, patients with the rare ALK mutation, which is found in just 5% of NSCLC cases, are living an average of four years, with the disease controlled in the brain nearly a year after their initial treatment.

Treatment approaches include whole brain radiation therapy, radiation for individual lesions, and surgery, typically for a single metastasis. Since whole brain radiation is associated with significant cognitive effects and the use of additional radiation therapy for progression is common in this population, the Yale researchers suspect that patients with the ALK mutation would benefit from radiation focused on individual metastases.



PETER BAKER

New Technique Spares Women Additional Breast Surgeries

Dr. Anees Chagpar, Director of The Breast Center at Smilow Cancer Hospital at Yale-New Haven and Associate Professor of Surgery

A simple change in how surgeons do partial mastectomies can cut in half the chances that women will need a follow-up surgery, Anees B. Chagpar, MD, MSc, MBA, MA, MPH, FACS, FRCS(C) found in a recent study published in *The New England Journal of Medicine* and presented at the 2015 American Society of Clinical Oncology annual meeting. Dr. Chagpar is an Associate Professor of Surgery at Yale School of Medicine and Director of The Breast Center at Smilow Cancer Hospital at Yale-New Haven.

Between 20 and 40 percent of women who have partial mastectomies will have positive margins, areas of cancer that extend to the edge of the tissue surgeons remove.

In these cases, the women must undergo a second surgery to have more tissue removed once the additional cancer has been identified. Dr. Chagpar found that routinely removing a small additional amount of tissue all around the tumor during the initial surgery substantially decreased the number of cases with positive margins. Taking the additional step only prolonged the initial operation by an average of 10 minutes.

Avoiding a follow-up surgery has an enormous emotional benefit. “When you are faced with a diagnosis of breast cancer, you want that cancer out of you, and you want to go back to your life,” said Dr. Chagpar.

A second surgery may also delay the start of radiation and chemotherapy. Dr. Chagpar is doing more research to look into how the change might alter the course of treatment and whether there is any difference in recurrence among women who had additional tissue removed during initial surgery.

How to approach margins has been a source of controversy among breast cancer surgeons. Some believed the additional tissue removal, known as

cavity shave margins (CSM), would help ensure that all the cancer around the main site was gone. Others, including Dr. Chagpar, thought the CSM practice went too far. After all, surgeons used x-rays to get a good understanding of where the cancer was. Many surgeons were also concerned that removing more tissue could lead to more complications and poor cosmetic results.

Dr. Chagpar is happy to have proved herself wrong. Patients – surveyed before they knew whether they were in

Chagpar said that the findings should be widely applicable, because positive margin rates at Yale are consistent with the national average. Nevertheless, additional study is planned incorporating other sites and asking additional questions.

One of the features of the study was that surgeons would not know whether they were taking the CSM until the last minute. All previous margin studies reviewed cases of surgeons who routinely took shavings versus cases of

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Taking the additional step only prolonged the initial surgery by an average of ten minutes. However, avoiding a follow-up surgery has an enormous emotional benefit.

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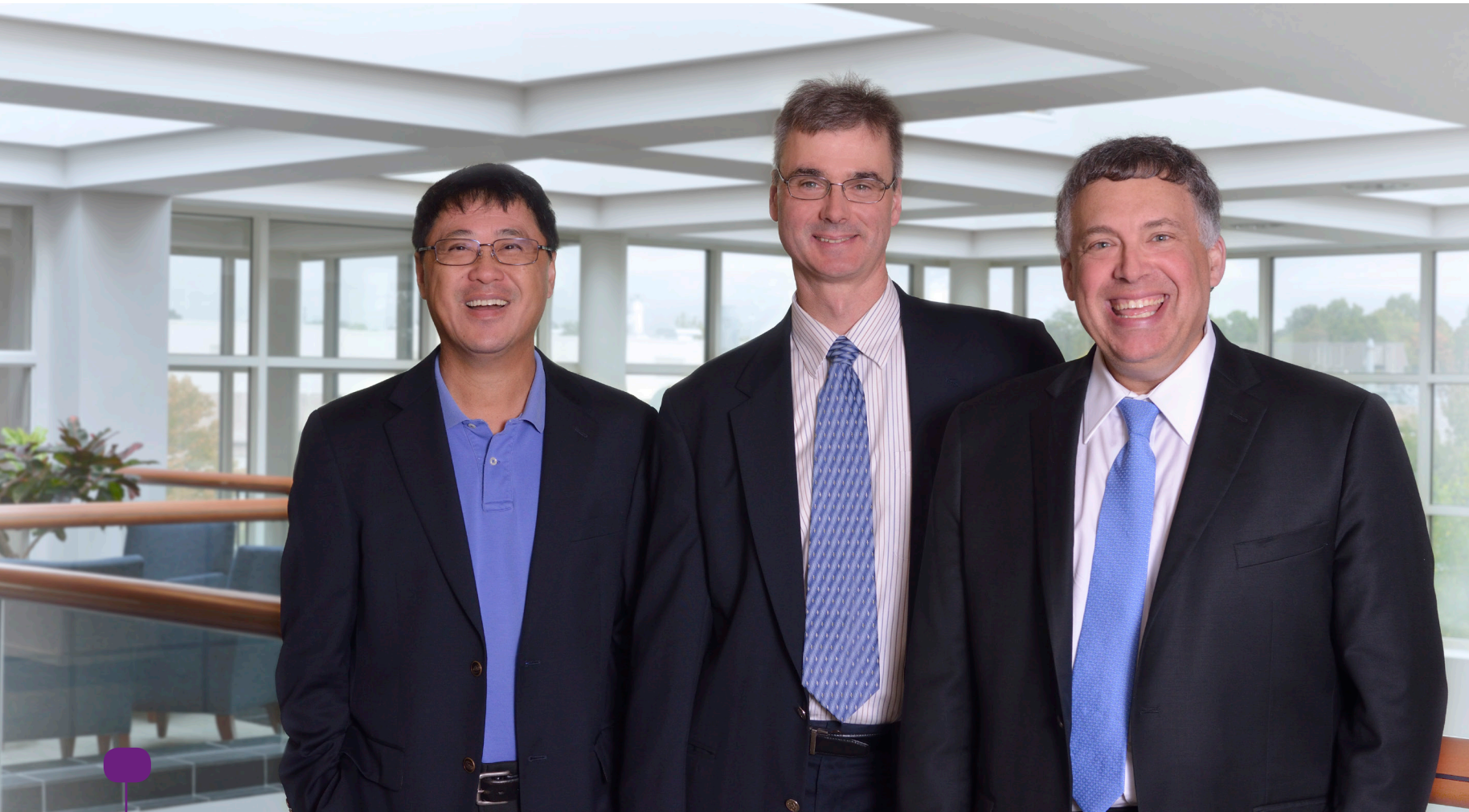
the CSM group or not – were equally happy with the appearance of the breast, regardless of the procedure they had undergone. Dr. Chagpar will continue to follow the women to see if their long-term cosmetic results remain good. The CSM group did not have a higher rate of complications.

“Sometimes I think that we have, what I’m going to call hubris of the medical profession, in that we think we already know the answer,” said Dr. Chagpar. “You never do the study until somebody says: I don’t know the answer.”

The study was conducted at Smilow Cancer Hospital with most Yale breast cancer surgeons participating. Dr.

surgeons who did not. In this study, surgeons were asked to do the best job they could using imaging to get good margins. When the surgeon felt satisfied enough to close, a nurse would open an envelope that would instruct the team to finish the procedure or to take shaved margins. Follow-up studies will use this same protocol.

The response to *The New England Journal of Medicine* paper, published in May, has been enormous, according to Dr. Chagpar, who is scheduled to continue to present on her findings in Japan, Korea, Brazil, and throughout the United States. “This is something that doesn’t solely affect our patients here at Yale,” she said. ☺



PETER BAKER

Building a Powerhouse Team To Tackle Lung Cancer

When Roy S. Herbst, MD, PhD was beginning his career, he did not intend to focus on lung cancer, a disease with few effective treatments. But his mentor, groundbreaking cancer researcher Emil Frei, urged him to reconsider. “This is where your talents are needed,” Dr. Frei said. “There will be advances. You just have to be perseverant.”

Decades later, there still are not enough effective treatments against lung cancer, the leading cause of cancer deaths among adults in the US. Dr. Herbst realizes that he not only needs to persevere against lung cancer – he needs to inspire a team of talented scientists to do the same. He is the lead investigator on a new \$11 million grant from the National Cancer Institute. The highly competitive Specialized

Lieping Chen, MD, PhD, Edward Kaftan, PhD, and Roy S. Herbst, MD, PhD

Programs of Research Excellence (SPORE) grant program involves research scientists and clinicians who work in both labs and clinics. This ensures that advances in laboratory science are rapidly put to work to develop more effective treatments.

Dr. Herbst is Associate Director for Translational Research and Chief of Medical Oncology at Yale Cancer Center and Smilow Cancer Hospital, a role that consistently requires him to do matchmaking between scientists with different specialized expertise that can move a project forward. “You want the best science from the best people, but the

key thing is working collaboratively, translationally,” he said.

The grant will focus on non-small cell lung cancer (NSCLC), the most common form of lung cancer. It will take a two-pronged approach: developing better treatments and finding more effective ways to help people stop smoking. Most, though not all, NSCLC patients are smokers.

One team will study immunotherapy in NSCLC – helping the body’s own immune system to combat tumors. “Twenty percent of lung cancers immediately respond to immu-

notherapy,” said Dr. Herbst. “We want to get that up to 100 percent.” Lieping Chen, MD, PhD who is co-principal investigator for SPORE, will lead basic science work on the project. Dr. Chen is Co-Director of the Cancer Immunology Research Program at the cancer center.

Another project will explore microRNA-based therapies for metastatic NSCLC, which is currently incurable. The team will work with can-

nodule patients. Lung nodules are typically discovered when a patient has a CT scan. People with these nodules are at heightened risk for lung cancer, so helping them to quit tobacco use has a special urgency. The team will study how well specific behavioral interventions and medications work in assisting these people to give up smoking. They will also track changes in biomarkers among patients who succeed.

The new Yale SPORE in Lung Cancer



The only way to approach a problem as big as lung cancer is to have experts in basic, translational, and clinical research working on several fronts taking the research from the lab to the clinic and back again to develop even newer insights.




cer biologist Frank Slack, PhD, now at Harvard. When Dr. Slack was at Yale, he discovered a microRNA that regulates critical oncogenes. His work identified that microRNAs could be both causes of lung cancer and potential therapeutic agents against it.

A third group will explore the Epidermal Growth Factor Receptor (EGFR). Mutations found in the EGFR signaling pathway play an important, though not sufficiently understood, role in lung adenocarcinomas. Additional knowledge could be used to create more targeted therapies and to develop strategies against tumors that become resistant to treatment.

The grant also includes a project to study smoking cessation in lung

will create several resource cores that will help lung cancer researchers from throughout the cancer center with support in administration; biostatistics and bioinformatics; and biospecimen banking, pathology, and genomics. The latter will be critical in banking biological material, what Dr. Herbst calls “those very, very precious patient samples,” to be used in research.

With the award, Yale Cancer Center becomes one of a select group of institutions to be awarded two SPORE grants from the NCI. The cancer center already has a SPORE focused on skin cancer. Dr. Herbst also works to mentor other teams at Yale to facilitate similar programs focused on other cancer types. 



CHRIS VOLPE PHOTO

Closer to Free Ride Celebrates 5 Years

The 5th annual **Closer to Free Ride** on September 12 was a fantastic day of celebration and camaraderie. The ride surpassed all expectations with over 1,250 riders and 500 volunteers and raised over \$2.2 million to support patient care at Smilow Cancer Hospital and research at Yale Cancer Center.

In a day of many inspiring moments, the presentation of the Mark Reitsma Courage Award to Stephen Ackley-Ortiz stands out. In January 2011, he was diagnosed with Stage IV metastatic squamous cell carcinoma in his throat and his neck. A month later, he learned that he also had stage II colon cancer. After searching for care, he found a team at Smilow who told him they could battle both cancers simultaneously. His unique treatment plan was, in his words, “brutal,” but it worked and he immediately wanted to give back. Only a few months after completing his treatment, he rode 25 miles in the inaugural Closer to Free Ride. The next year he rode 100. In 5 years he has raised more than \$75,000 for Closer to Free to celebrate the fact that he is now cancer free! 🚴



PETER BAKER

Q+A

meet the physician

Suzanne B. Evans, MD, MPH

Assistant Professor of Therapeutic Radiology

Your clinical practice is on the care of women with breast cancer. How has the radiation treatment changed over the last decade?

We have seen a huge number of advances in radiation therapy for breast cancer. Probably one of the most exciting has been the recognition that women receiving radiation to the breast alone can be treated with hypofractionated radiation treatment. This shortens a 6-7 week course of radiation down to 3-4 weeks, with the same effectiveness in fighting their breast cancer. There are studies to suggest this treatment results in less fatigue and less skin irritation. This is certainly the experience we have seen with our patients at Smilow Cancer Hospital.

Additionally, there are more advances than ever to avoid treating the heart in women with cancer affecting their left breast. Women can be treated with deep inspiration breath hold technique, where the woman holds her breath for about 15-20 seconds at a time during radiation. The lungs fill with air, and then the heart moves away from the breast. This helps lower the amount of heart tissue that is exposed to radiation from breast treatment.

Much of your research focus is on quality and safety standards to improve patient care. How do hospitals like Smilow Cancer Hospital set the standards nationwide?

Smilow has really taken a proactive attitude towards quality and safety. This is evidenced by the Yale Medical Group's Professionalism Charter, which sets the standards for how we treat each other and those we care for. Smilow cultivates a culture of safety, in which all staff members are heard, and we work collaboratively to improve quality. This is also demonstrated through our commitment to incident learning, in which the institution looks at the processes of care that may not have gone smoothly, and seeks to identify how we can improve our procedures to deliver care flawlessly and with high levels of service.

Are the increasing number of choices for radiation therapy making the decisions for treatment more difficult for patients and providers? What factors are considered?

Certainly there are a number of choices to be made regarding radiation. I am involved in a grant with Dr. Shiyi Wang and Dr. Cary Gross here at Yale to create a decision analysis tool for older women diagnosed with breast cancer. Older women (>70 years) with estrogen positive cancers derive a smaller absolute benefit from breast radiation. This tool will help prioritize the needs and values of an individual woman in her decision as to whether receiving radiation is "worth it" to her. This is exactly the sort of shared decision-making that we want in medicine, with special consideration for the values of our patients.

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by the National Cancer Institute

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