

Yale Cancer Center

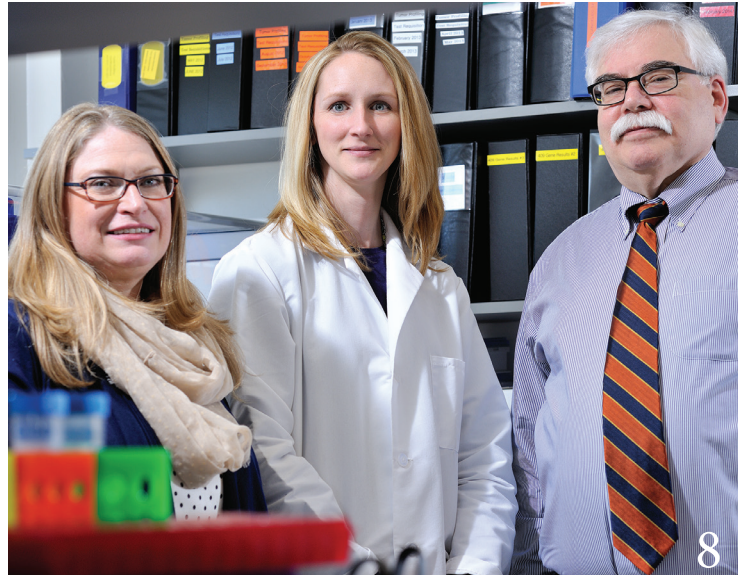
centerpoint

MAGAZINE



From Bench
to Bedside
and Back

spring | summer 2014



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Peter Baker **photographer**

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yale cancer center

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Yale Cancer Center
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MAGAZINE

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Yale Cancer Center and Smilow Cancer Hospital at Yale-New Haven have joined the National Comprehensive Cancer Network (NCCN) with official acceptance into the organization at their annual meeting in March. As many of you know, NCCN is a prestigious group of Cancer Centers who come together to set national guidelines for cancer care and I am pleased that our faculty will now share their expertise on the NCCN guideline setting committees. Our membership in NCCN is a reflection of the outstanding clinical care provided to our patients at Smilow Cancer Hospital and the increasingly fast pace of our translational research efforts from Yale Cancer Center.

April's American Association for Cancer Research (AACR) annual meeting was a great opportunity for Yale Cancer Center to highlight the translational science breakthroughs coming from our laboratories to our clinics. Major research contributions were highlighted at the podium at AACR from Dr. Roy Herbst, chair of the Association's Tobacco and Cancer subcommittee, on tobacco control and the Lung Cancer Master Protocol; Dr. Katerina Politi on EGFR resistance; Dr. Mario Sznol on PD-1 pathway inhibition; Dr. Lieping Chen on harnessing the immune system; and Dr. Lajos Pusztai and Dr. Christos Hatzis on bioinformatics and sequencing analysis. I look forward to updating our readers on the progress of their research in upcoming issues of Centerpoint Magazine.

Patient and family-centered care is a primary focus of the Smilow Cancer Hospital leadership each day. Catherine Lyons, RN, MS, NEA-BC, Executive Director of Patient Care Services, continues to concentrate on our patient satisfaction surveys and makes continuous recommendations and adjustments to our services based on patient responses. Considerable efforts have been made toward improving our patients' experience in our outpatient clinics in Smilow and we are seeing continued improvement in our patient satisfaction results.

Our overall Press Ganey score for all of our outpatient clinics was just reported for the first quarter of 2014 and it is our highest score ever! Even more meaningful, we are now benchmarking our results against 34 other NCI-designated Cancer Centers; our overall score for the period ending March 31 puts our rank at the 65th percentile against this peer group! I appreciate all of the efforts of the physicians, nurses, and staff who continually strive to improve our patients' experience each day.

I look forward to updating you on new research initiatives and translational research developments in the next issue of Centerpoint Magazine. Enjoy the summer season with your families!

Sincerely,

Thomas J. Lynch, Jr., MD
Director, Yale Cancer Center
Physician-in-Chief, Smilow Cancer Hospital

What if YOU were the patient?

Wendell Yarbrough's patient was having a trying day. She saw him for a follow-up appointment after her surgery to remove the cancer in her larynx (voice box), had an imaging procedure in a different building, and finally needed to make her way to the speech pathologist to get a prosthetic to enable her to speak. He spotted her in front of the wrong building shortly before that third appointment. Dr. Yarbrough pushed the patient's wheelchair to the correct clinic. While that solved her immediate problem, he knew that other patients faced similar hurdles.

"We can't expect patients to navigate all this when they are sick," explained Dr. Yarbrough, MD, MMHC, Professor of Surgery and Pathology. Dr. Yarbrough leads the Head and Neck Cancer Program at Smilow Cancer Hospital, whose patients typically encounter a large number of team members both before and after therapy. Dr. Yarbrough met with the program team and leaders in Smilow and they set out to make the logistics of getting all that care simpler. The team redesigned the patient experience using one overarching question: "If you were the patient, how would you want to be treated?"

A variety of innovations in scheduling and communication are now in place to streamline care. The Head and Neck Cancer Program is the vanguard of a larger clinical redesign involving the entire hospital. Making care more efficient will help us care for more patients, according to Rogerio Lilenbaum, MD, Chief Medical Officer of Smilow Cancer Hospital.

As part of a larger multidisciplinary project to improve patient flow, patients began noticing differences as soon as they entered the building. Blood drawing is now centralized to Smilow's fourth floor lab, which patients pass when they enter from the parking garage. More phlebotomists and nurses have been hired to speed the process. An increasing number of patients will be getting their blood drawn at various labs in their own communities before their appointments so that results are ready when they meet with their doctors.

Some appointments take much longer than others. "A visit here is by nature more complex than it is in a private office," Dr. Lilenbaum said. So physicians have been asked to design a

'realistic template' that creates a true picture of how long various patients need. Scheduling according to these templates – rather than to an arbitrary appointment length – should cut down on patient wait times.

Often doctors will be ready to see a patient, but there is no available room, Dr. Lilenbaum said. Smilow has implemented new electronic status boards to notify staff immediately when a room is empty. Another innovation to speed patient care is encouraging oncologists to write chemotherapy orders before the visit. These orders will, of course, be verified before administration, but should reduce the amount of time that a patient waits for his or her chemotherapy to be mixed in pharmacy.

Patient care will also be improved by making better use of nurse practitioners and physician associates, Dr. Lilenbaum explained, and by giving patients the option to go to one of the 8 Smilow Cancer Hospital Care Centers scattered throughout the state.

While trying to make services more efficient for a large volume of patients, services are also being expanded. "We want to offer psychological support for oncology patients who may be in distress," he said. Genetic testing will also be more widely available with more rapid access. Screenings are being increased for various kinds of cancers as well. "We are renewing our efforts to be a leader in patient experience and patient satisfaction," Dr. Lilenbaum said.

Great communication is critical to both. "Patients want to know: Is my spouse going to need a hotel room? Will I know how to take care of the drain when I go home?" Dr. Yarbrough said. The Head and Neck Cancer Program connects each patient with a clinical coordinator, a point person who plays the key role of answering questions and connecting the patient with available services.

Patients with head and neck cancer require care from many providers to assure the best outcomes. The Head and Neck Cancer Program strives to coordinate as many visits as possible into a single day – a major feat of scheduling and space allocation that involved many departments. Getting different professionals to work together has long been seen as critical to effective health care, but it is equally vital to delivering health care that is convenient and patient-centered. ☺

Dr. Rogerio Lilenbaum and Dr. Wendell Yarbrough



PETER BAKER



From **BENCH** To **BEDSIDE** And **BACK**

Lajos Puztai, MD, PhD
and Vikram Wali, PhD
Sophia N. Ononye, PhD

PETER BAKER

The rallying cry at Yale Cancer Center is “translational medicine”—that is, moving research swiftly from the lab to the clinic so that patients can benefit from breakthrough therapies. The scientists and clinicians working on breast cancer at Yale Cancer Center and Smilow Cancer Hospital have enthusiastically embraced this. More than 200 breast cancer patients currently participate in 16 clinical trials that encompass every stage of breast cancer, from benign high-risk lesions to mastectomies, chemotherapies, radiation, and survivorship.

“The breast team leads the Cancer Center in therapeutic clinical trial accrual and accounts for 35 percent of all therapeutic trial accrual here,” said Anees B. Chagpar, MD, MSc, MA, MPH, Director of the Breast Center at Smilow Cancer Hospital at Yale-New Haven and Associate Professor of Surgery (Oncology). “That doesn’t include another five pending trials or our work in non-therapeutic studies. What I’m most proud of,” she added, “is that we engage our patients at every phase of their journey, in every discipline, to get the highest quality of care for them as well as the most data to help us improve treatments and quality of life for other patients down the line.”

Translational medicine depends upon a constant feedback loop between researchers and clinicians. In rare instances,

one person embodies that loop. On the breast cancer team at Yale, it’s Lajos Puztai, MD, D.Phil., Director of Breast Medical Oncology and Co-Director of the Cancer Genetics and Genomics Research Program. “He is a classic example of a physician/scientist with one foot in the lab and another in the clinic,” Dr. Chagpar said, who calls him one of the world’s top five genomics experts.

To understand his translational work, a bit of background about breast cancer is helpful. Fifteen or 20 years ago, breast cancer was classified as a single disease. Genomic analysis has demolished that monotype, replacing it with four broad classifications based on the receptors in breast cancer cells: HER2, ER (estrogen receptor), PR (progesterone receptor), and triple negative, whose cells lack any of the other three

receptors. Triple negative breast cancer is proving to be the most genomically heterogeneous and also the most resistant to chemotherapy. At the moment, all four FDA-approved drugs that molecularly target breast cancer are aimed at HER2.

“There are about 25 or 26 other molecularly targeted drugs approved by the FDA,” Dr. Puztai explained, “but they aren’t approved for breast cancer. They are for diseases like melanoma, kidney cancer, and lung cancer. We find the same abnormalities in breast cancer that our colleagues see in these other diseases, though less frequently. So the obvious question is, if a drug works in lung cancer or melanoma against a particular abnormality, will that drug work in a breast cancer with the same abnormality?”

That’s the idea behind several of Dr. Puztai’s



Dr. Christos Hatzis,
Director of Bioinformatics
for Breast Medical
Oncology

PETER BAKER

projects, including one with David F. Stern, PhD, Professor of Pathology. Dr. Puztai asked Dr. Stern to use high throughput screening to test a wide array of combinatorial therapies on triple negative cell lines grown in the lab—not just the FDA-approved drugs but also another 150 experimental agents now in clinical trials. If anything looks worth pursuing, Dr. Puztai will help Yale clinicians put together a Phase I trial for patients whose breast cancer hasn't responded to the usual first-line treatments.

"It closes the loop, in a way," says Christos Hatzis, PhD, Director of Bioinformatics, Breast Medical Oncology, who has worked with Dr. Puztai for a decade. "We can start with clinical samples, do discovery, go back to the lab and test them, and if the results look promising enough, bring them back to clinicians to be further evaluated in small clinical studies."

An example of this is a project Dr. Puztai calls Map-It (Molecular Analysis Prior to Investigational Therapy), a study for patients with metastatic breast cancer. After radiologists collect biopsies, about 200 genes are subjected to molecular analysis through next-generation sequencing. "We are looking for molecular defects against which there are already FDA-approved drugs or investigational drugs," Dr. Puztai said. For example, a mutation in the EGFR (Epidermal Growth Factor Receptor) gene has been identified as a cause of lung cancer, and FDA-approved drugs that inhibit this receptor have proven effective. Dr. Puztai wants to see if breast cancer patients with this mutation respond to the targeted drug.

On the immuno-therapy side, Dr. Puztai is looking at the PD1 ligand inhibitor, which has shown great promise against melanoma and lung cancer by stimulating the immune system. Dr. Puztai is leading a Phase I study to investigate the

inhibitor's effect on metastatic breast cancer. "Early-stage triple negative breast cancers are much more curable if lymphocytes are present," he said, "and this drug revs them up into super lymphocytes."

Another of Dr. Puztai's projects will help oncologists and breast cancer patients decide how long to continue endocrine hormone therapy, typically given for five years. Several large studies have shown that lengthening this to 10 years decreases recurrence and improves survival—but only by one or two percent, and the therapy itself carries health risks for some patients as well as additional costs.

Dr. Puztai emphasizes that all of these projects depend on the collaborative support of many specialists within the breast team, from surgeons who take tissue samples to radiologists who do biopsies and pathologists who handle the samples, and on to molecular analysts and informaticists. To illustrate, he mentions another new project that requires the participation of the entire team: the creation of a bio-repository.

"Lajos's idea is to develop a database for breast cancer," Dr. Hatzis explained, who is deeply involved in the project. "A doctor will be able to type in the specific mutation and the specific gene, and the database will look for information about that mutation on that gene. If nothing has been reported, the database will aggregate up and look for any mutation on that specific gene. And if it's a very rare mutation, it will aggregate to a higher level and look for any mutations in genes involved in that particular pathway."

Next the database will link to the literature about specific treatments and rank them at different levels of evidence. The doctor can then look on clinicaltrials.gov to see if there are any trials at Yale or elsewhere involving a particular therapy. "It will be a clinically useful tool," Dr. Hatzis added, in quite an understatement. He and Dr. Puztai hope to have a prototype ready for use by Yale clinicians by the end of the summer, with a long-term goal of public access.

Dr. Chagpar notes that breast cancer research at Yale is getting more intricate and more tightly intertwined with the clinic. "We are able to translate from the bench to the bedside and back," she said. "We will no longer treat breast cancer with a broad brush, but will very specifically understand what each person's tumor looks like, how it behaves, and what drugs we can use to treat its mutations." ↻

Most cancer survivors not exercising enough to benefit

AACR; 2014. Abstract 5039.

Despite the benefits that physical activity can offer, a mere 10% of cancer survivors are exercising enough to reap those benefits, according to research conducted by Yale Cancer Center and the Yale School of Public Health. The findings were presented at the American Association for Cancer Research Annual Meeting this spring.

The U.S. Department of Health and Human Services recommends cancer survivors engage in 150 minutes of moderate-intensity physical activity, or 75 minutes of vigorous-intensity physical activity, and two sessions of strength training, every week. The Yale researchers found that among the population of cancer survivors studied in the United States, only 10% met these physical activity guidelines from the government.

Yet, all survivors who said they exercised at recommended levels reported better quality of life (less fatigue, improved mental and physical health, and increased satisfaction in social activities and relationships).

The team reviewed data from the 2010 National Health Interview Survey that included information from more than 19 million cancer survivors. The large sample size of survivors and the inclusion of more than 10 types of cancer were unprecedented in this type of study.

Gene regulator critical for breast cancer metastasis to the lung is identified

Cell Rep. 2014 Mar 13.

Yale Cancer Center researchers have identified a regulator of gene expression that is responsible for the progression of breast cancer and its metastasis to the lung.

In women, breast cancer is the most common cancer, and the second leading cause of cancer-related death. When it metastasizes, it does so primarily to the lung, brain, and bone. Only limited treatment options are available, and scientists are working to identify and test new drug targets for the development of effective therapies.

Recent studies suggest that abnormal gene expression contributes significantly to tumor formation and progression. But the regulators of such changes in metastasis are poorly understood.

The Yale researchers analyzed gene expression datasets of human breast tumors, as well as those of cancer cells, and found that overexpression of the enzyme RBP2 is critical for breast cancer metastasis to the lung. Loss of RBP2, they also found, suppressed tumor formation in mouse models.

The authors say their evidence suggests that RBP2 regulates a critical epigenetic switch that sets the stage for tumor metastasis. They say the enzyme offers a novel target for development of therapies designed to inhibit tumor progression and metastasis.

New prostate cancer treatment convenient, less expensive, but may be riskier

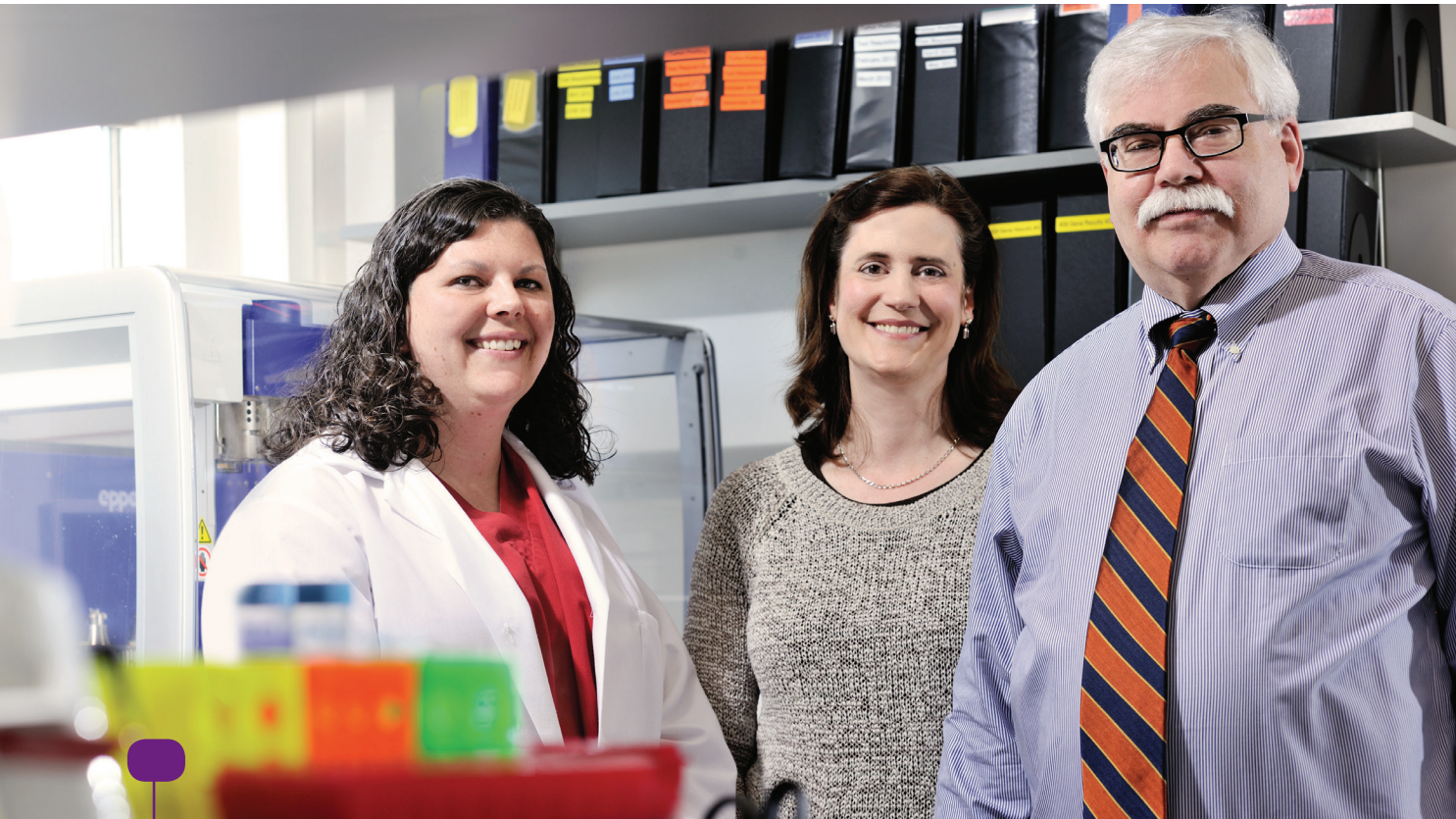
J Clin Oncol. 2014 Apr 20.

A faster and less expensive form of radiotherapy for treating prostate cancer may come at a price, according to a new study by Yale Cancer Center researchers — a higher rate of urinary toxicity or urine poisoning.

The standard therapy for prostate cancer is called intensity modulated radiation therapy (IMRT). Stereotactic body radiotherapy (SBRT) is a newer treatment that delivers a greater dose of radiation than IMRT. Patients receiving SBRT can complete an entire course of treatment in one to two weeks, compared to seven to nine weeks for IMRT. There have been few studies comparing the costs of these treatments, and their toxicity.

The study by researchers at the Cancer Outcomes, Public Policy and Effectiveness Research (COPPER) Center at Yale Cancer Center — compared IMRT to SBRT in a national sample of 4,005 Medicare patients age 66 and older receiving prostate cancer treatment. Participants received either SBRT or IMRT as a primary treatment for prostate cancer during 2008 to 2011.

The team found that the mean per-patient cost to Medicare for a course of SBRT was about \$13,600, compared to \$21,000 for IMRT. The study also revealed that at 24 months after the start of the treatment, there were increased side effects for SBRT compared to IMRT, due to urethral irritation, urinary incontinence, and obstruction. However, even when including the cost of treating complications, the overall medical costs due to SBRT were still lower than that of IMRT.



PETER BAKER

Cancer Center Chosen for Groundbreaking Study

Late last year, the National Institutes of Health chose Yale Cancer Center (YCC) and two other research institutions from among 150 applicants to conduct an extensive groundbreaking study on cancer genomics and experimental drugs. The program, overseen by the National Cancer Institute (NCI), is called MATCH (Molecular Analysis for Therapy Choice).

The study has two phases. First, cancer tissue from about 3,000 patients across the country will be molecularly analyzed to detect their genetic mutations. Yale's Tumor Profiling Laboratory will be heavily involved in this phase, along with the other two institutions chosen, Massachusetts General Hospital and MD Anderson Cancer Center, as well as the NCI diagnostic testing facility in Frederick, Maryland. All are known for expertise in genomic analysis and Ion Torrent next-generation sequencing. This phase is expected to take about two years.

Karyn Ronski, MS, MB (ASCP),
Zenta Walther, MD, PhD, and
Jeffrey Sklar, MD, PhD

In the second phase, 1,000 patients will be matched with clinical trials designed to test new therapies against the patients' specific mutations. The NCI has persuaded about 20 pharmaceutical companies to donate the new drugs, which are ready for clinical trials. The trials will range across cancers and mutational types. Since many of the mutational subsets will be small, it's unlikely that a single cancer center could enroll enough patients to conduct a credible trial, so a patient's participation in a given trial will not be limited by geography. For instance, a lung cancer patient in Chicago with a particular mutation may get linked to a trial being run at Yale; clinicians in Chicago will administer the therapy according to the guidelines of the Yale trial and report the results to Yale clinicians.

Almost all of this is unprecedented in cancer research and medicine. MATCH reflects the NCI's growing commitment, in terms of both funding and focus, to genomics and translational research. All clinical trials sponsored by the NCI, for example, must now include collection of tissue and genomic analysis.

Yale Cancer Center is at the forefront of genomics and translational research, which certainly factored into the NCI's decision to choose it for this prestigious but complex study. "We probably were selected because we've pushed the sequencing technology as far as anybody in the country," said Jeffrey L. Sklar,

MD, PhD, Director of the Molecular Tumor Profiling Laboratory, of Molecular and Genomic Pathology, and of the Molecular Diagnostics Program.

The NCI and the participating research centers are determining standard operating procedures, and also deciding which genes to analyze. About 200 have been selected, and these will be sequenced to reveal mutations.

“To minimize sequencing errors, the NCI will push software manufacturers for constant improvement. As part of the MATCH study, Dr. Sklar’s lab will have access to these evolving technologies.”

Dr. Sklar says it's still unclear what kinds of mutations the NCI wants to match with clinical trials. A growing number of drugs are aimed at specific mutations, and preliminary trials have shown that some of the drugs can be effective. That's one possible category for matches.

Dr. Sklar believes that the NCI is also interested in trials on "cross-tumor mutations." Research has made clear that the same mutations often appear in different kinds of cancers. In lung cancer, for instance, a mutation in the EGFR gene is well known and is often targeted with erlotinib (Tarceva). If that same mutation appears in a pancre-

atic cancer, would that cancer respond to the lung-cancer drug? Or what about a mutation suspected of activating a protein or a pathway? If a known inhibitor exists, would it work on that mutation in a number of cancers? The MATCH study might begin to answer such questions.

Before being selected for MATCH, Dr. Sklar's small lab—three pathologists, two technicians, and an informaticist—was already working at capacity to satisfy Yale's in-house needs for sequencing. The new study will add a huge workload. To handle it, Dr. Sklar bought more equipment and added two technicians, another informaticist, and a case coordinator.

"The new equipment will more than double our potential throughput," he said. He expects the MATCH study to claim 25 to 35 percent of the lab's new capacity. Once the study's first phase is over, Yale researchers will benefit from this expansion.

Dr. Sklar sees other benefits to participating in the study as well. To minimize sequencing errors, the NCI will push software manufacturers for constant improvement. As part of the MATCH study, Dr. Sklar's lab will have access to these evolving technologies. The same will be true for advanced technologies in tissue preparation. And when the clinical phase starts, Yale will almost certainly host several trials.

"So patients who come here potentially could have access to these new drugs, which a nonparticipating center won't have," Dr. Sklar said. "We'll learn early on what's effective and not effective." ↻

Arming the Immune System to Fight Back against Cancer



Bill Brown went to his primary care doctor and a local hospital in 2011 because he had swollen glands in his armpit. At the time, he made no connection between the discomfort he was feeling and the stage I melanoma lesion that his dermatologist had diagnosed and excised ten years prior. Upon the reoccurring diagnosis in 2011, this time stage III melanoma, Bill once again turned to his trusted dermatologist for advice. His advice was 'I want you to get a second opinion from someone who is an expert in the field of melanoma cancer.' He recommended Harriet Kluger, MD, Associate Professor of Medicine (Medical Oncology) at Yale Cancer Center. That day his dermatologist proceeded to arrange the appointment for Bill. Bill attributes the quality of his decade long patient-doctor relationship with his dermatologist to his continued peace of mind, and to saving his life in 2001 and again in 2011.

Bill met with Dr. Kluger and his case was discussed at a weekly Melanoma Tumor Board at Smilow Cancer Hospital. Afterwards, he felt that there was a plan for him and was hopeful that he could fight his diagnosis, being "in the best of care that anyone can possibly wish for." He was initially treated on a clinical trial comparing a new drug, ipilimumab, to another drug used for stage III melanoma, interferon; he was randomized to receive treatment with interferon. Approximately a year later, the melanoma spread to his liver and additional lymph nodes. At that point Dr. Kluger helped Bill participate in a new clinical trial with ipilimumab in combination with an anti-PD1 drug, nivolumab. Both of these are immunotherapy drugs that work by activating the patient's own immune system. Ipilimumab blocks one brake on the immune system, CTLA-4, while nivolumab blocks another brake, PD-1. The hypothesis was that the combination would be a more potent activator of the immune system than either drug alone, potentially allowing it to work against the tumor cells.

When Bill shared the news with his oldest son who was about to graduate with a master's degree in bioscience, his son Ian said, "Dad, I did some research on your clinical trial, and you are about to participate in a truly groundbreaking research trial that will be remembered years from now." Bill further explained, "I was fortunate enough to qualify for the clinical trial I am currently on. It is based on groundbreaking immunotherapy research and the level of care I am receiving is unmatched."

For years researchers have wondered why the immune system does not attack the cancer cells when they begin to invade the body. Yale, in collaboration with colleagues at other

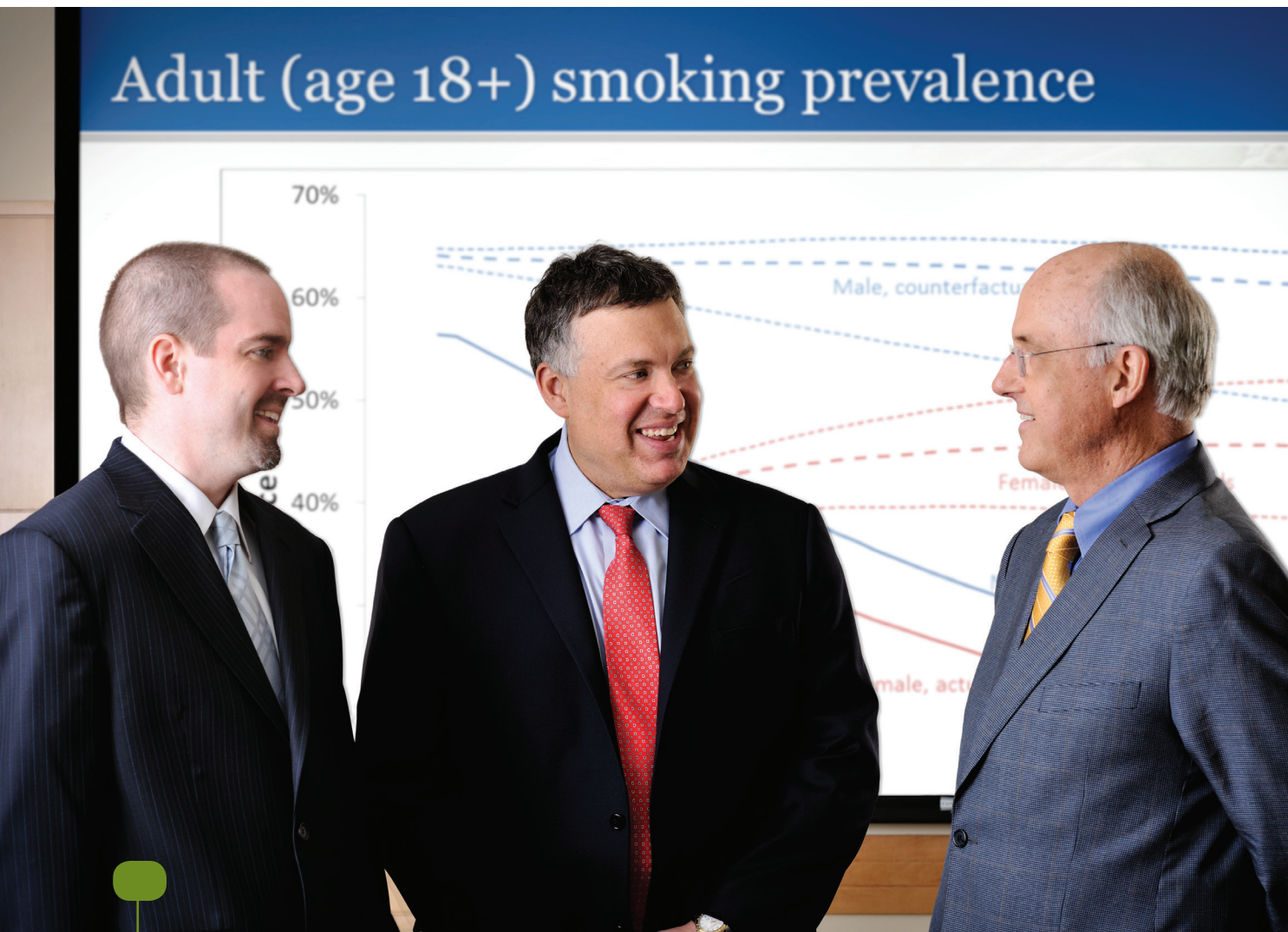
institutions, found that the interactions of certain proteins and receptors allow tumor cells to disable T cells, the immune system's main fighters. Using PD-L1 as a binding partner for PD-1, a receptor on the surface of T cells, cancers inactivate T-Cells. By using an antibody to block either PD-1 or its binding partner, PD-L1, the immune system can be provoked to attack cancer cells. PD-1 and PD-L1 inhibitors are well tolerated and this approach has had excellent results. The June 2013 issue of the *New England Journal of Medicine* noted that this immunotherapy approach to attacking melanoma may be an option for other types of cancers as well.

"When we combined inhibitors of PD-1 or PD-L1 with inhibitors of CTLA-4, we saw unprecedented responses in patients with a variety of tumor types. The results of this trial in melanoma have been dramatic and have led to a national trial comparing the two drugs to either drug alone," Dr. Kluger said. For Bill, the spot on his liver has shrunk significantly, and the lesions on his spleen are gone.

Bill takes great pride in being part of the clinical trial and was recently re-enrolled for 2 more years. He is handling the regimen well and responding without any major side effects. Bill is a firm believer in keeping your mind, body, and spirit strong and remains active and very upbeat. Recently the Smilow nursing team dubbed Bill "the 8th floor mayor" because he seeks out fellow cancer patients to listen to and shares experiences, fears, hopes, and of course a few laughs.

Last year Bill rode 62.5 miles in the Closer to Free bike ride, proudly wearing a homemade banner to honor and thank his melanoma care team on the 8th floor of Smilow. He described the entire team as his second family and wanted to ride for them as a way to express his gratitude for their gifts of talent and devoted care they have given him. "I wanted to ride for the team, to honor them for all that they do, not just for me, but for all patients. Their devotion, talents, expertise, and attitude give one hope and peace that you feel truly cared for by the best. They are a gift to us all."

Bill has already signed up to ride in this year's event on September 6th and is recruiting fellow melanoma "thriller survivors," as he calls himself, to join him. One thing is certain, that Bill will once again 'banner' his passionate gratitude for the Smilow 8th floor team. "There is so much expertise and noble passion at Yale, which is critical when you find yourself confused and fighting for your life. They will do everything in their power to help you get better while finding a cure, and I am well on my way there. Blessings Smilow 8." ☺



PETER BAKER

Millions of lives saved by Surgeon General's Report on smoking But the fight isn't over

Benjamin Toll, PhD,
Roy S. Herbst, MD, PhD,
Theodore Holford, PhD

By the early 1960s, scientists had amassed a significant body of evidence linking smoking to lung cancer. Many were urging President John F. Kennedy to fight tobacco use in America. “He had a lot of other things on his plate: The Cuban missile crisis and civil rights...,” Theodore Holford, PhD, Susan Dwight Bliss Professor of Biostatistics and a member of Yale Cancer Center, explained. “He sort of pushed the issue onto the surgeon general.”

The result was the 1964 Surgeon General's Report on Smoking and Health, a landmark document that brought together scientific leaders to review thousands of studies that demonstrated the dangers of smoking. Surgeon General Luther Terry released the report, which he called a “bombshell,” on a Saturday to maximize coverage in the Sunday newspapers. It was the basis for everything from banning certain types of tobacco advertising to limiting smoking in public places. And it is the reason why so many Americans have quit.

The report has saved 8 million lives so far, according to a study Dr. Holford published in the *Journal of the American Medical Association* on the report's 50th anniversary. National smoking rates have been cut in half. Dr. Holford says that even he was surprised by how successfully lower rates of smoking have extended life, by 7.8 years for men and 5.5 years for women.

He is quick to add that hundreds of thousands of Americans continue to die from smoking-related illnesses annually: “We're not there yet.” His current research projects include evaluations of various anti-tobacco strategies to determine which are most effective.

Roy S. Herbst, MD, PhD, Ensign Professor of Medicine and Chief of Medical Oncology, is researching personalized medicine targeted to deliver more effective anti-cancer treatments to his lung cancer patients, 80 to 85 percent of whom have a history of smoking. “The best way to deal with cancer, of course, is to prevent it before

it happens,” Dr. Herbst said. He chairs the Tobacco and Cancer Subcommittee of the American Association for Cancer Research (AACR).

An estimated 18 percent of Americans smoke today, despite widespread knowledge that smoking is unhealthy and despite measures like high taxes on cigarettes. “Those 18 percent are pretty hard core,” Dr. Herbst said. This means that anti-tobacco measures need to be smarter. Teams of researchers at Yale are examining the best ways to help smokers quit, and their work is having a national impact, he said.

often with little follow-up, according to Dr. Herbst.

Furthermore, tobacco use is often not tracked in patients or study volunteers, he explained, leaving physicians without the information they need to choose the best treatment for a given patient. One of Dr. Herbst's initiatives through AACR is to standardize documentation of tobacco use during clinical trials.

Every patient at Smilow who smokes is offered support to quit. Clinicians will even visit a patient having chemotherapy chairside, according to Dr. Toll. All the services offered by the program, which



Family members want them to quit. So quitting can increase harmony at home. Patients quickly feel better, save money, and don't smell like cigarettes. It's part of a positive package.



Dr. Herbst invited Benjamin Toll, PhD, Associate Professor of Psychiatry and Director of the Smoking Cessation Program at Smilow Cancer Hospital, to join the AACR's Tobacco and Cancer Subcommittee. The two frequently collaborate on research and presentations. One of their goals is to make smoking cessation for cancer patients far more widely available.

Research shows that smoking decreases the effectiveness of radiation, chemotherapy, and surgery, in addition to putting patients at risk for subsequent cancers. Yet a national survey found that only 40 percent of oncologists offer their patients smoking cessation help,

include counseling and medication, are validated by research.

The argument against doing smoking cessation with cancer patients is that quitting is another stress in an already trying time. “Smoking can be stress enhancing,” counters Dr. Toll. In addition to improving the effectiveness of their treatments and preventing recurrences, patients will get immediate, concrete benefits by quitting, he said.

“Family members want them to quit,” he explained. So quitting can increase harmony at home. Patients quickly feel better, save money, and don't smell like cigarettes. “It's all part of a positive package,” he said. ☺



No guts, no glory

High-risk, high-reward fund aims to accelerate cancer research



Mr. Charles Stiefel, inaugural donor to the Discovery Fund

The best scientists think outside the box, but most funding sources favor work that builds incrementally on past research. That slows the pace of innovation in cancer care.

“Although my career was in the pharmaceutical industry, my many friends in academia have often lamented the fact that some of the most promising research projects cannot get funded. They have described a ‘Catch 22’ scenario, whereby a project cannot obtain NIH or academic funding because insufficient data have been generated; yet without any financial support, it is impossible to generate these data,”

said Charles Stiefel, the inaugural donor to the Yale Cancer Center Discovery Fund, designed to support “high-risk, high-reward” research.

Donors to the fund will play an active role in selecting projects for support and are invited to serve a two-year term on the fund’s board along with Yale Cancer Center leadership.

Federal funding for medical research has declined in real dollars since 2009. The National Cancer Institute budget for FY 2013 will be approximately \$4.78

billion, \$293 million less than in FY 2012, a reduction of 5.8 percent. “So if you want to break new ground in your science, you have to find other ways,” explained Thomas Lynch, Jr., MD, Director of Yale Cancer Center.

These cuts come at a time when the potential of cancer research to advance is extraordinary. Yale scientists are doing exciting work in cancer biology

side effects,” he explained.

While the fund takes a venture capital style approach of embracing risk, it rigorously tracks outcomes so that donors can see the impact of their investment. Scientists will not have to spend years on small pilot studies before getting support for a significant project. “I think the faculty are grateful for the opportunity to submit a project idea to a

“Firstly, I have always felt that Yale is a very special place,” Charles Stiefel said. “Secondly, Yale Cancer Center is one of the top oncology centers in the world. And finally, I have a lot of confidence in Tom Lynch, who brings a wealth of experience and a very unique skill set to Yale.”

and genetics, personalized medicine, and other areas that promise substantially new and better treatments.

Charles, of Raleigh, North Carolina, and his wife, Daneen, have made cancer the focus of their philanthropy. “My father, mother, uncle, and younger brother all died of cancer; and my two older brothers and I have successfully battled cancer. I have learned first-hand what a terrible disease this is,” he said.

His experience has also made him keenly aware that the work of developing better treatments needs to move faster. “My little brother died in the early seventies of Hodgkin’s Disease, a cancer that is now highly curable. My dream scenario would be to see higher cure rates for all types of cancer, as well as treatments with fewer and less severe

fund like this,” Dr. Lynch said.

The strength of the Yale Cancer Center faculty was one of the reasons that Charles chose to support the Discovery Fund. He has a long history with Yale, having graduated from Yale College in 1972. “Firstly, I have always felt that Yale is a very special place,” he said. “Secondly, Yale Cancer Center is one of the top oncology centers in the world. And finally, I have a lot of confidence in Tom Lynch, who brings a wealth of experience and a very unique skill set to Yale.”

When the board is complete, investigators will begin submitting proposals. “We’re going to be giving awards that are big enough to really accomplish something,” said Dr. Lynch. “That’s what this is all about – accomplishing something.”



PETER BAKER

Q+A

meet the physician

Steven Gore, MD

Director of Hematological Malignancies

You specialize in care of patients with myelodysplastic syndrome. Can you explain what that is?

Myelodysplastic syndrome is a type of chronic leukemia - at one time it was referred to as "pre-leukemia." It is a low-grade cancer in which the bone marrow stem cells are abnormal. They try to produce normal blood cells, but the blood cells mature abnormally (white blood cells, red blood cells, and platelet forming-cells). In fact, "myelodysplastic" syndrome translates as funny looking bone marrow disorder. So these very abnormally maturing cells somehow recognize that they are not really good for anything and they kill themselves off in the bone marrow and patients end up with very low blood counts.

As myelodysplastic syndrome progresses, how do immature cells impact a patient's health?

The immature cells, called blast cells, start to pile up in the bone marrow. We quantify the amount of blast cells a patient has, and customize treatment based on that determination; as well as to what extent their blood counts are abnormal. Over time, patients may become dependent on red blood cell transfusions, and at times, transfusions

of platelets. Patients may have bleeding problems or frequent infections. Our goal with low-grade myelodysplastic syndrome is always to improve quality of life and to slow down progression of the disease. We arbitrarily change the name of the disease once a patient's bone marrow or blood has 20% blast cells, at which time it is referred to as acute myeloid leukemia with myelodysplastic characteristics. As the blast count increases, our goal shifts from quality of life issues, to improving survival, and cure when possible. Cure requires high doses of therapy followed by a stem cell transplant.

Are there clinical trials available for patients with acute myelodysplastic syndrome?

We have just opened a national trial for transfusion-dependent patients with low-grade myelodysplastic syndrome, and are in the process of opening other trials for patients with more advanced or relapsed disease. We are also engaged in laboratory research trying to understand how our most effective drugs for myelodysplastic syndrome work, so that we can better select patients for such therapies, and develop better treatments.

You recently joined Smilow Cancer Hospital as Director of Hematological Malignancies. What are your goals for the coming year?

Smilow Cancer Hospital provides outstanding care for patients with hematologic malignancies. We have very active clinical services, and our physicians are incredibly busy providing care to our patients. In the coming year, I will be actively recruiting several additional physicians with particular expertise in clinical trial development and execution and with specific clinical sub-specialization. The goal is to have important high impact clinical trials open for our patients with all of the major hematologic malignancies at all disease stages, while maintaining the current level of outstanding personalized care.

Barbara Burtness, MD

Barbara Burtness, MD, has joined Medical Oncology at Yale Cancer Center, and will serve as Co-Leader of the Developmental Therapeutics Program and Clinical Research Program Leader for the Head and Neck Cancer Program at Smilow Cancer Hospital. Dr. Burtness is internationally recognized for her research in head and neck cancer. She chairs the Eastern Cooperative Oncology Group Head and Neck Cancer Committee, and leads national and international clinical trials of targeted therapy in head and neck cancer. She comes to Yale from Fox Chase Cancer Center where she co-led the Developmental Therapeutics Program and was Chief of Head and Neck Oncology.



Caroline Cromwell, MD

Caroline Cromwell, MD has joined the faculty in the section of Hematology at Yale Cancer Center. Dr. Cromwell is a well-known hematologist, specializing in benign hematology, particularly clotting and bleeding disorders, and a major thought leader in this area. Most recently she was an Assistant Professor and Director of the Sickle Cell Program at Mount Sinai School of Medicine.



Jennifer Moliterno Gunel, MD

Jennifer Moliterno Gunel, MD has joined the Department of Neurosurgery and the Brain Tumor Program at Smilow Cancer Hospital. Dr. Moliterno joins us from the department of Neurosurgery at Memorial Sloan-Kettering Cancer Center where she completed a neurosurgery oncology fellowship. She received her medical degree from The University of Florida and completed her internship and residency at Yale-New Haven Hospital. Dr. Moliterno's primary focus is on the surgical management of all types of brain tumors.



Laura Morrison, MD

Laura Morrison, MD has joined our Palliative Care Program under the direction of Dr. Jennifer Kapo and serves as an attending physician on the YNHH Palliative Care Consultation Service. Dr. Morrison has also been appointed to the new positions of Director of Hospice and Palliative Medicine Education and Director of the Yale Hospice and Palliative Medicine Fellowship. The Fellowship is currently accepting applications and will receive its first class of fellows in July 2014.



Brian Shuch, MD

Brian Shuch, MD completed a urologic oncology fellowship at the National Cancer Institute before joining Yale School of Medicine. He is a graduate of the University of Michigan and received his MD from New York University. Dr. Shuch's clinical interest is in the multidisciplinary management of sporadic and hereditary forms of kidney cancer. He will work with the Yale Cancer Center Genetic Counseling Office to care for high-risk renal cell carcinoma (RCC) patients.



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Join the Closer to Free Ride! Saturday, September 6, 2014

Why participate in the **Closer to Free Ride** for Smilow Cancer Hospital at Yale-New Haven? You'll make an impact, since any dollars you raise will directly support patient care and research at Smilow Cancer Hospital and Yale Cancer Center. Join the group of passionate riders and volunteers this year and be inspired at every turn. Learn more at rideclosertofree.org.

