

Yale Cancer Center

centerpoint

MAGAZINE

Out of the Lab,
Into the World

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director's letter



Yale Cancer Center was founded in 1974 as one of the inaugural five Comprehensive Cancer Centers in the nation and has a rich history of cancer research and patient care. Last month, our Center received our official notification from the National Cancer Institute (NCI) renewing our Center as a Comprehensive Cancer Center and approving an additional five years of our Cancer Center Support Grant. I am pleased to share that based on the outstanding score on our application, we received a 74% increase in funding compared to our previous funding period.

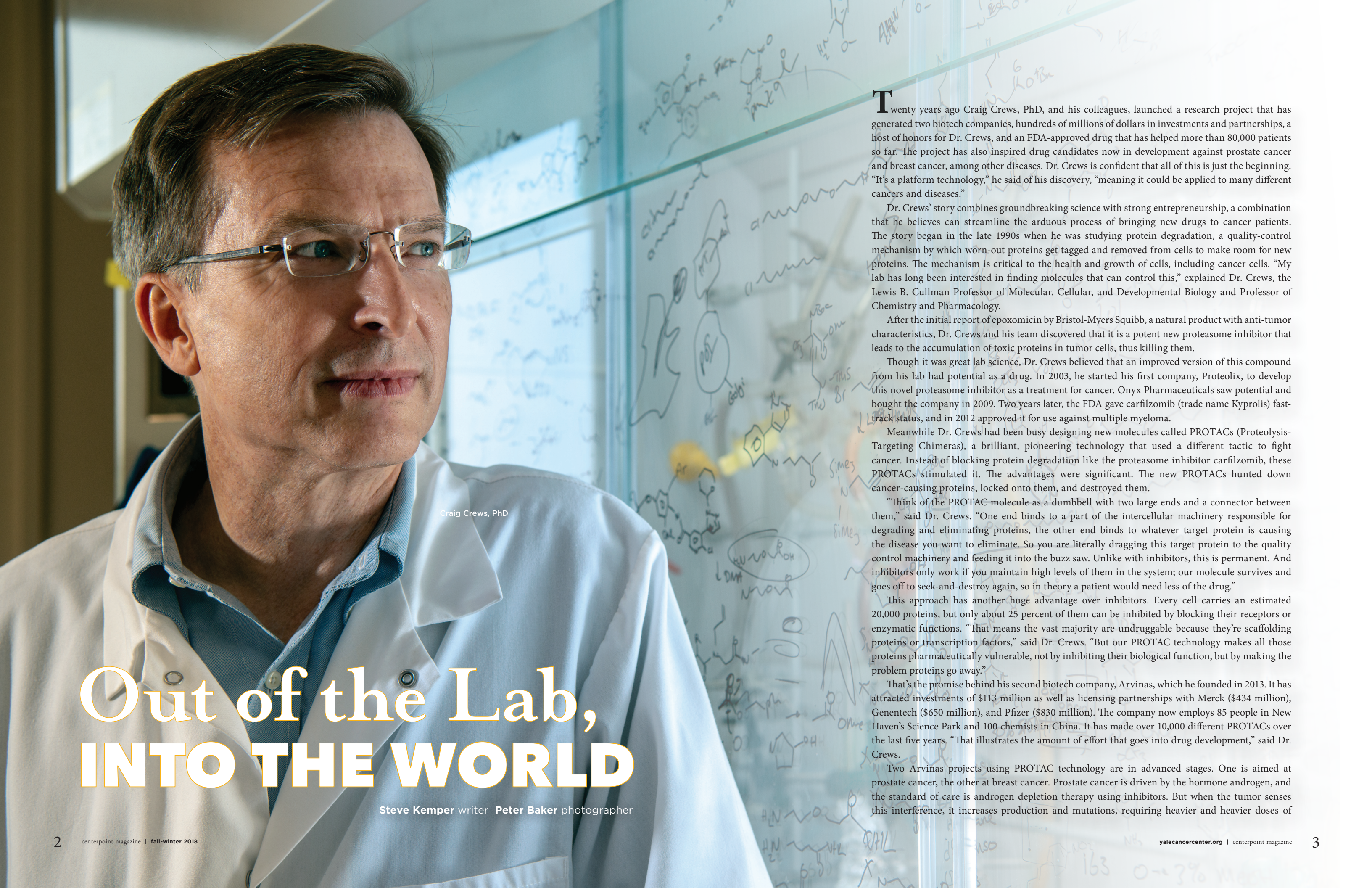
Dr. Craig Crews' story of cancer drug discovery through his chemical biology research is a prime example of the advances that NCI-designated cancer centers can foster through to drug development and, finally, to FDA-approval. As a mentor to countless investigators at Yale Cancer Center, Dr. Crews is a model for moving cancer research from the lab to the clinic in order to benefit cancer patients.

This issue of *Centerpoint* highlights some of the many areas of excellence at our Cancer Center and Smilow Cancer Hospital, including a new research collaboration on the increasing link between obesity and cancer, advances made in bladder cancer through targeted clinical trials, and the new therapy options the expanding field of Interventional Oncology is providing to our patients.

In addition, we are proud of the many accomplishments of our Gamma Knife Center, which is celebrating its 20th anniversary and recently treated its 5,000th patient. Through advanced technologies and research, the Center has led radiotherapy planning and treatment for patients with brain metastases.

I am confident that our increased NCI funding, coupled with our elite science and patient- and family-centered care model at Smilow Cancer Hospital and our Care Centers, will bring many new opportunities to impact research and cancer care in the coming years. On behalf of our entire team at Yale Cancer Center and Smilow Cancer Hospital, we look forward to sharing more stories of success with you in the coming months.

Sincerely,
Charles Fuchs
Charles S. Fuchs, MD, MPH
Director, Yale Cancer Center and
Physician-in-Chief, Smilow Cancer Hospital



Craig Crews, PhD

Out of the Lab, INTO THE WORLD

Steve Kemper writer Peter Baker photographer

Twenty years ago Craig Crews, PhD, and his colleagues, launched a research project that has generated two biotech companies, hundreds of millions of dollars in investments and partnerships, a host of honors for Dr. Crews, and an FDA-approved drug that has helped more than 80,000 patients so far. The project has also inspired drug candidates now in development against prostate cancer and breast cancer, among other diseases. Dr. Crews is confident that all of this is just the beginning. “It’s a platform technology,” he said of his discovery, “meaning it could be applied to many different cancers and diseases.”

Dr. Crews’ story combines groundbreaking science with strong entrepreneurship, a combination that he believes can streamline the arduous process of bringing new drugs to cancer patients. The story began in the late 1990s when he was studying protein degradation, a quality-control mechanism by which worn-out proteins get tagged and removed from cells to make room for new proteins. The mechanism is critical to the health and growth of cells, including cancer cells. “My lab has long been interested in finding molecules that can control this,” explained Dr. Crews, the Lewis B. Cullman Professor of Molecular, Cellular, and Developmental Biology and Professor of Chemistry and Pharmacology.

After the initial report of epoxomicin by Bristol-Myers Squibb, a natural product with anti-tumor characteristics, Dr. Crews and his team discovered that it is a potent new proteasome inhibitor that leads to the accumulation of toxic proteins in tumor cells, thus killing them.

Though it was great lab science, Dr. Crews believed that an improved version of this compound from his lab had potential as a drug. In 2003, he started his first company, Proteolix, to develop this novel proteasome inhibitor as a treatment for cancer. Onyx Pharmaceuticals saw potential and bought the company in 2009. Two years later, the FDA gave carfilzomib (trade name Kyprolis) fast-track status, and in 2012 approved it for use against multiple myeloma.

Meanwhile Dr. Crews had been busy designing new molecules called PROTACs (Proteolysis-Targeting Chimeras), a brilliant, pioneering technology that used a different tactic to fight cancer. Instead of blocking protein degradation like the proteasome inhibitor carfilzomib, these PROTACs stimulated it. The advantages were significant. The new PROTACs hunted down cancer-causing proteins, locked onto them, and destroyed them.

“Think of the PROTAC molecule as a dumbbell with two large ends and a connector between them,” said Dr. Crews. “One end binds to a part of the intercellular machinery responsible for degrading and eliminating proteins, the other end binds to whatever target protein is causing the disease you want to eliminate. So you are literally dragging this target protein to the quality control machinery and feeding it into the buzz saw. Unlike with inhibitors, this is permanent. And inhibitors only work if you maintain high levels of them in the system; our molecule survives and goes off to seek-and-destroy again, so in theory a patient would need less of the drug.”

This approach has another huge advantage over inhibitors. Every cell carries an estimated 20,000 proteins, but only about 25 percent of them can be inhibited by blocking their receptors or enzymatic functions. “That means the vast majority are undruggable because they’re scaffolding proteins or transcription factors,” said Dr. Crews. “But our PROTAC technology makes all those proteins pharmaceutically vulnerable, not by inhibiting their biological function, but by making the problem proteins go away.”

That’s the promise behind his second biotech company, Arvinas, which he founded in 2013. It has attracted investments of \$113 million as well as licensing partnerships with Merck (\$434 million), Genentech (\$650 million), and Pfizer (\$830 million). The company now employs 85 people in New Haven’s Science Park and 100 chemists in China. It has made over 10,000 different PROTACs over the last five years. “That illustrates the amount of effort that goes into drug development,” said Dr. Crews.

Two Arvinas projects using PROTAC technology are in advanced stages. One is aimed at prostate cancer, the other at breast cancer. Prostate cancer is driven by the hormone androgen, and the standard of care is androgen depletion therapy using inhibitors. But when the tumor senses this interference, it increases production and mutations, requiring heavier and heavier doses of

"We're on the cusp of clinical trials at Yale with a compound that was a concept here in Kline Biology Tower 17 years ago."

counteractive therapy. "Basically it's chemical castration," said Dr. Crews. Arvinas has designed an oral PROTAC that eliminates the androgen receptor protein from cancer cells, degrades androgen receptor mutations, and slows tumor growth. Dr. Crews expects clinical trials to begin at Yale and elsewhere later this year.

The PROTAC against breast cancer works similarly. An estimated 80 percent of new breast cancer cases are positive for estrogen receptor alpha (ERα), whose proteins encourage tumor growth. Current therapies try to stop growth in ERα breast cancers by inhibiting the receptor, but many breast cancers become resistant, allowing signals from the receptor to break through and stimulate tumor growth. Arvinas' estrogen PROTAC solves that by eradicating ERα proteins. Clinical trials will begin next year.

Another Arvinas project demonstrates how broadly the PROTAC technology can be applied, said Dr. Crews. When the protein called Tau aggregates, it causes neural death that leads to Alzheimer's disease. Arvinas is working on PROTACs that drag Tau to its death.

Dr. Crews sees the company as the fruit of a partnership between academia and private biopharma. Academia develops the idea and demonstrates its feasibility, but it will die if not handed off to the private sector, which can supply money and professional drug developers to mature the concept into a drug. "And now we're on the cusp of clinical trials at Yale with

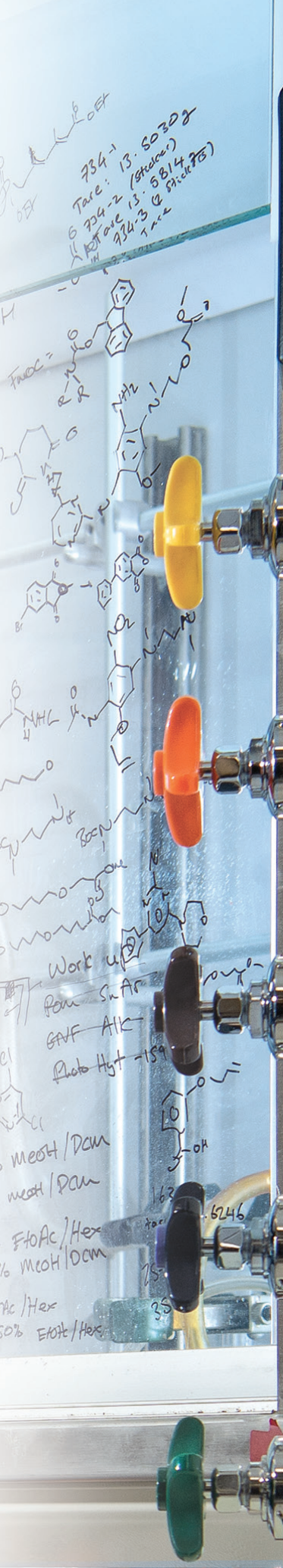
a compound that was a concept here in Kline Biology Tower 17 years ago," said Dr. Crews, "so I'm really very excited by this."

Academics often don't know how to bridge the gap between the lab and private investment. To help them, Dr. Crews started a program called PITCH (Program in Innovative Therapeutics for Connecticut's Health) that he runs through the Yale Center for Molecular Discovery. PITCH is using a \$10 million, three-year grant from the state of Connecticut to help scientists from Yale and the University of Connecticut develop promising biotech ideas to the point where they are attractive to venture capital firms. Over the past two years, PITCH has considered more than 90 projects, and 17 have been approved for further development on Yale's West Campus.

"We have been pitching those 17 to venture capitalists over the last year and there's a lot of interest," said Dr. Crews. "We're hoping that some of these proto-companies will soon turn into real companies. Good science is not enough," he added. "It's not an either/or thing. I hope other faculty can see that I've been able to maintain an active academic lab but also play a role through advocacy and consulting to further the development of real-world applications through these biotech."

He traces his interest in propelling discoveries out of the lab to his father, who worked on materials science at NASA. "He looked at alloys and composite materials for airplane wings, analyzing fatigue and fracture," said Dr. Crews. "He would tell me about plane crashes where engines had failed because the material had been too fatigued due to the pattern of the rivet holes. So it was clear to me early on that my Dad's basic research had practical applications. As a basic researcher driven by my scientific curiosity, I love what I'm doing here, but I'm always asking how we can take what we're learning into the lab and help people."

Right now, Dr. Crews and the 18 members of his lab are investigating leukemia, glioblastomas, lung cancer, and pancreatic cancer. "We're very interested in some of these tough cancers that haven't been easily addressed using the current drug repertoire," he said. "And we're making progress." ☺



Thanks to Targeted Therapy

Eliza Folsom writer Peter Baker photographer

In May 2013, Joe Weber had just dropped his son off at Logan International Airport in Boston and was driving back to Connecticut when he decided to stop for a bite to eat. Before continuing his two-hour trip home, he visited the restroom and noticed an exceptional amount of blood in his urine. This came as a surprise to Joe as he had no indication that something was wrong in the weeks or days prior. He immediately made an appointment with his primary care physician.

His physician referred Joe to a urologist, who diagnosed bladder polyps as the cause of the blood, and recommended outpatient surgical removal. Joe went ahead with the surgery, and would continue to be checked every three months for the next year, only to have polyps recur and be removed in two additional surgeries. After his third surgery, Joe questioned whether the polyps could indicate a larger problem and he sought a second opinion.

It was then that Joe received the diagnosis of muscle-invasive bladder cancer. His new urologist recommended he immediately start an aggressive regimen of chemotherapy to precede surgery to remove his bladder and a portion of his small intestine. As testing continued, it was determined the bladder cancer had metastasized to Joe's lungs, elevating him to a stage IV cancer diagnosis, and surgery was no longer an option. In

consultation with his doctor, they decided to proceed with the standard of care for his bladder cancer, and for the next eight months, Joe received chemotherapy once a week. While his treatment did begin to shrink the tumors in his lungs, the side effects were too challenging and Joe decided to end treatment.

Knowing Joe would not be able to tolerate a return to this treatment regimen, his doctor advised he enter a clinical trial, and referred him to Dr. Daniel Petrylak, Professor of Medical Oncology and Urology, at Smilow Cancer Hospital. Dr. Petrylak is a leader in the development of new drugs to fight bladder cancer, and his success with clinical trials has expanded the treatment options for all patients, including many newly FDA-approved drugs.

Joe first met with Dr. Petrylak in July 2015, and for the next two years unsuccessfully participated in two separate clinical trials. In July 2017, Joe became eligible for a third trial touted as "targeted chemotherapy." This trial combined an antibody targeted at a protein present in bladder cancer cells, with chemotherapy.

After three months, Joe had to again stop the treatment due to side effects, which in this case presented as neuropathy, or weakness and numbness in the feet. Joe paused his treatment for six months, but continued to have scans every eight

“I am not sure whether a cure is in the realm of possibility, but I’m confident that we can arrest bladder cancer with as few symptoms as possible.”

weeks during this break. Remarkably, the results of his scans began to show that his lung tumors were shrinking even while off treatment. It appeared that the three months of the initial treatment had been enough to cause tumor shrinkage.

Joe resumed the targeted therapy in April 2018 when his side effects improved and has completed two more cycles to date, but at a decreased dosage. As a result, his neuropathy symptoms have also subsided, allowing Joe to resume his normal activities - working in the yard, albeit at a less rigorous pace, and playing golf. Joe’s treatment team is thrilled with his progress and he shares their excitement, exclaiming, “Dan is the man!”

Under the care of a palliative care specialist at Smilow, Joe’s medications are managing his bladder symptoms and keeping his neuropathy in check. Overall, Joe feels very normal and is enjoying life as much as possible while looking forward to celebrating the major milestones in the lives of his two children, Michael and Emily. While it was a long road before finally arriving under the care of Dr. Petrylak, Joe is thankful for the opportunity to have had access to three clinical trials and the care of his amazing staff: Kristen Crowley, Ebony Williams,

and Shelby DeCarlo, among others.

“Dr. Petrylak is a world-class expert in research and trials, and the advances he has made in bladder cancer treatment in a few short years is truly amazing,” remarked Joe. “I am not sure whether a cure is in the realm of possibility, but I’m confident that we can arrest bladder cancer with as few symptoms as possible.”

In the meantime, Joe aimed to check off a few big items from his bucket list: 1) to play a round of golf with Dr. Petrylak, and 2) complete a West Coast road trip with his son down the Pacific Coast Highway in California. Number one, Joe is still working on, but number two, he was recently able to complete.

Squeezing in a trip between treatments, Joe and his son started their adventure by spending two days in Denver, Colorado before flying to San Francisco. As luck would have it, Joe’s wife, Maura, and daughter, Emily, were able to join them and for the next three days, they made family memories across the Bay Area including a special trip to Muir Woods National Monument to see the redwood trees. After Maura and Emily headed back to Connecticut, Joe and Michael picked up their convertible and started south to kick off their special trip.

Their first destination was Los Angeles, but not before passing through some of the most scenic vistas in California: Monterey, Carmel, Malibu, and Santa Monica. Up next: San Diego, where they visited the San Diego Zoo and swam in the warm waters of the Pacific Ocean. After San Diego, Joe and Michael drove eight hours east through the Arizona desert to their next stop, the Grand Canyon. After one day of sightseeing, they concluded their trip with an extravagant steak dinner before turning in the convertible and flying home.

After a jam-packed journey of 1,400 miles through three states, Joe can look back and be thankful for these newfound opportunities to explore and enjoy life that did not seem possible a few years ago. But after such a memorable and successful trip that crossed one item off his bucket list, another has taken its place. On the eve of their return to Connecticut, in a conversation with his son at dinner, they realized that Joe has visited 43 of the 50 states. Upon learning this fact, son Michael is now inspired to get his father to all 50 states.

As the famous quote goes, “Life is either a daring adventure or nothing.” And thanks to his second chance at life, Joe can embark upon his daring adventure and continue to work on his bucket list. ☺



A Founding Force Retires from Smilow

Steve Kemper writer Kate Eisemann photographer

Ten years ago Abe Lopman took a risk. He left a prestigious job and a comfortable future at one of the country's great cancer centers, Memorial Sloan Kettering, for an enticing possibility in the small city of New Haven.

"No one then regarded Yale as a powerhouse in cancer," Mr. Lopman remembered. "So it took a few visits and a lot of conversation with some key people—Marna Borgstrom [President and CEO, Yale New Haven Health System], Rick D'Aquila [now President, Yale New Haven Health System], and Bob Alpern [Dean, Yale School of Medicine]. They convinced me they were committed to doing something very different and very right in developing a cancer program at Yale New Haven."

Part of their vision was going up on Park Street in New Haven—a new cancer hospital, still nearly two years away from opening, named after its major donor, Joel E. Smilow. "Very few of us get to finish designing and implementing a 500,000 square foot, half-a-billion-dollar hospital devoted to delivering top-notch care to patients and their families," explained Mr. Lopman.

He seized the opportunity, and in February 2008 began his new job as Vice President of Operations for Yale New Haven Hospital and Executive Director of the half-built Smilow Cancer Hospital. In the last decade, he has played an indispensable role in Smilow's story, a role that ended in October 2018 with his retirement at age 68. Charles S. Fuchs, MD, MPH, Director of Yale Cancer Center and Physician-in-Chief of Smilow Cancer Hospital, called Mr. Lopman "the architect of our great Center," and added that his leadership and vision were instrumental to its growth into a nationally renowned hospital with a network of 12 cancer care centers throughout Connecticut.

Catherine A. Lyons, RN, MS, Vice President of Patient Services and Chief Nursing Officer at Smilow, seconds Fuchs emphatically. She was recruited by him in 2010 to revitalize the nursing and patient care programs. "Smilow would not be Smilow without Abe Lopman," she said. In 2009 when Mr. Lopman teamed up with the newly-arrived Thomas J. Lynch, Jr., MD, the hospital's founding Physician-in-Chief and new Director of the Cancer Center, "It was magic," added Ms. Lyons. "It was a coming together of like-minded people driven to build a world-class organization that took care of patients and families with the utmost compassion. Smilow went from being a place almost no one knew about to a formidable facility."

Mr. Lopman, with Dr. Lynch, Ms. Lyons, and the people they recruited, thought about every aspect of cancer care. That meant discarding the typical staff-to-patient ratio. In some areas, the nursing staff doubled. The medical school and Cancer Center hired more than 125 new faculty members, whose expertise greatly benefited Smilow's patients. While the hospital was still under construction, Mr. Lopman insisted that some spaces be redesigned to minimize stress and noise, and to maximize amenities that might give patients and their families comfort and peace at the difficult times of diagnosis and treatment. "We wanted them to know that we

weren't focused only on the physiological part of it," he said.

For instance, the plans called for flat screen televisions in all the waiting rooms. No, said Mr. Lopman. When a patient and family are waiting to have what may be the most frightening medical conversation of their lives, they shouldn't be forced to listen to a stream of bad news or a screaming talk show. He put in fish tanks instead.

And speaking of those waiting rooms, he added, they're way too big and we're going to shrink them. "Large waiting rooms means you have a flawed system," he said. "We were not going to tolerate waiting. We converted all that saved space to exam rooms and clinical spaces where patients could be seen, and we built systems to make sure patients don't wait long. If they do, we have failed."

He also put his office in the center of the hospital so he could walk through the units and interact with patients and staff, something he says he will greatly miss, along with the people he works with, "The best people by far that I've ever been surrounded by in my 47 years in healthcare."

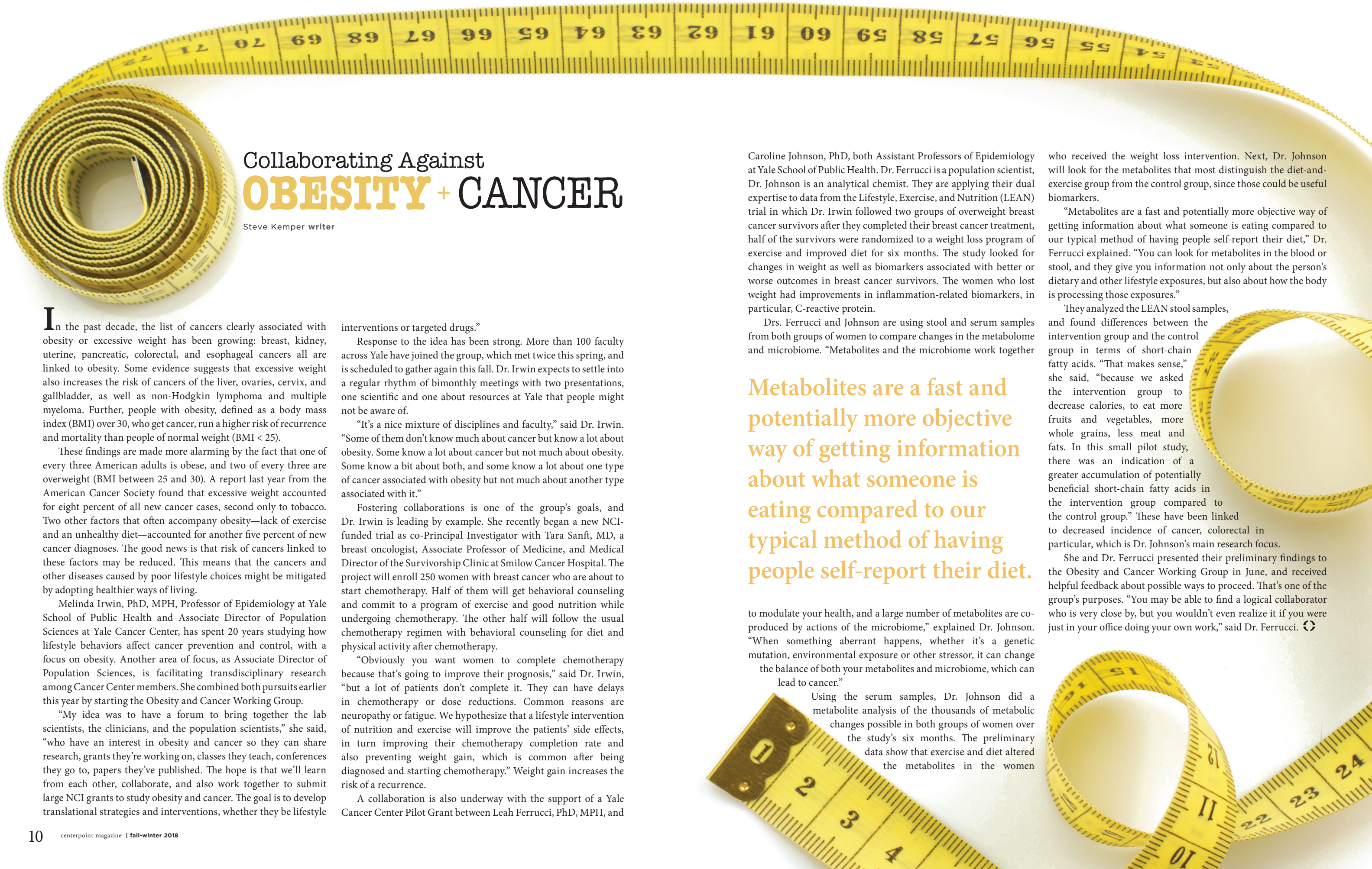
It's clear why Ms. Lyons calls him "the cheerleader-in-chief," and says, "He stretched our capabilities. We had to develop skills we didn't know we had. He's the consummate coach and mentor. He always finds the good, even if you've made a mistake. Even if you're playing golf with him—he's an avid golfer—"if you make a terrible shot and end up in the sand trap, he tells you it's a great position to be in. I'm not sure how he does it, but he turns things around and finds a solution. He is a wonderful human being," she added. "We will all miss him."

Mr. Lopman's parents were Holocaust survivors from Poland who raised him to believe that medicine was "the ultimate and most rewarding thing you could do." He began college at City University of New York expecting to go to medical school or become a medical researcher. Meanwhile he worked part-time drawing blood at a hospital and doing other medical jobs. An administrator at the hospital saw something in him and suggested that he would be good at administration. The idea shocked him at first, but this mentor convinced him to take some training courses.

"That was the beginning of my understanding that I could make an impact in medicine without being a physician," he said. "But I never lost the feeling that medicine was an integral part of me and I was an integral part of it."

Mr. Lopman describes the turnaround over the last 10 years in Yale's reputation for cancer care and research as "unprecedented." Is that what makes him most proud? "No," he said quickly. "That's a byproduct. I am most proud of the care that's afforded to, and available to, three million citizens in Connecticut and beyond. I'm most proud when my wife comes home from volunteering at Smilow, where most people don't know she's my wife, and she tells me stories of how people feel about the place—not about their cancer, but about the place. That's what we set out to do—to change the way cancer care was being delivered in this region. All the rest is a byproduct." ☺

Abe Lopman



Collaborating Against **OBESITY** + CANCER

Steve Kemper **writer**

In the past decade, the list of cancers clearly associated with obesity or excessive weight has been growing: breast, kidney, uterine, pancreatic, colorectal, and esophageal cancers all are linked to obesity. Some evidence suggests that excessive weight also increases the risk of cancers of the liver, ovaries, cervix, and gallbladder, as well as non-Hodgkin lymphoma and multiple myeloma. Further, people with obesity, defined as a body mass index (BMI) over 30, who get cancer, run a higher risk of recurrence and mortality than people of normal weight (BMI < 25).

These findings are made more alarming by the fact that one of every three American adults is obese, and two of every three are overweight (BMI between 25 and 30). A report last year from the American Cancer Society found that excessive weight accounted for eight percent of all new cancer cases, second only to tobacco. Two other factors that often accompany obesity—lack of exercise and an unhealthy diet—accounted for another five percent of new cancer diagnoses. The good news is that risk of cancers linked to these factors may be reduced. This means that the cancers and other diseases caused by poor lifestyle choices might be mitigated by adopting healthier ways of living.

Melinda Irwin, PhD, MPH, Professor of Epidemiology at Yale School of Public Health and Associate Director of Population Sciences at Yale Cancer Center, has spent 20 years studying how lifestyle behaviors affect cancer prevention and control, with a focus on obesity. Another area of focus, as Associate Director of Population Sciences, is facilitating transdisciplinary research among Cancer Center members. She combined both pursuits earlier this year by starting the Obesity and Cancer Working Group.

“My idea was to have a forum to bring together the lab scientists, the clinicians, and the population scientists,” she said, “who have an interest in obesity and cancer so they can share research, grants they’re working on, classes they teach, conferences they go to, papers they’ve published. The hope is that we’ll learn from each other, collaborate, and also work together to submit large NCI grants to study obesity and cancer. The goal is to develop translational strategies and interventions, whether they be lifestyle

interventions or targeted drugs.”

Response to the idea has been strong. More than 100 faculty across Yale have joined the group, which met twice this spring, and is scheduled to gather again this fall. Dr. Irwin expects to settle into a regular rhythm of bimonthly meetings with two presentations, one scientific and one about resources at Yale that people might not be aware of.

“It’s a nice mixture of disciplines and faculty,” said Dr. Irwin. “Some of them don’t know much about cancer but know a lot about obesity. Some know a lot about cancer but not much about obesity. Some know a bit about both, and some know a lot about one type of cancer associated with obesity but not much about another type associated with it.”

Fostering collaborations is one of the group’s goals, and Dr. Irwin is leading by example. She recently began a new NCI-funded trial as co-Principal Investigator with Tara Sanft, MD, a breast oncologist, Associate Professor of Medicine, and Medical Director of the Survivorship Clinic at Smilow Cancer Hospital. The project will enroll 250 women with breast cancer who are about to start chemotherapy. Half of them will get behavioral counseling and commit to a program of exercise and good nutrition while undergoing chemotherapy. The other half will follow the usual chemotherapy regimen with behavioral counseling for diet and physical activity after chemotherapy.

“Obviously you want women to complete chemotherapy because that’s going to improve their prognosis,” said Dr. Irwin, “but a lot of patients don’t complete it. They can have delays in chemotherapy or dose reductions. Common reasons are neuropathy or fatigue. We hypothesize that a lifestyle intervention of nutrition and exercise will improve the patients’ side effects, in turn improving their chemotherapy completion rate and also preventing weight gain, which is common after being diagnosed and starting chemotherapy.” Weight gain increases the risk of a recurrence.

A collaboration is also underway with the support of a Yale Cancer Center Pilot Grant between Leah Ferrucci, PhD, MPH, and

Caroline Johnson, PhD, both Assistant Professors of Epidemiology at Yale School of Public Health. Dr. Ferrucci is a population scientist, Dr. Johnson is an analytical chemist. They are applying their dual expertise to data from the Lifestyle, Exercise, and Nutrition (LEAN) trial in which Dr. Irwin followed two groups of overweight breast cancer survivors after they completed their breast cancer treatment, half of the survivors were randomized to a weight loss program of exercise and improved diet for six months. The study looked for changes in weight as well as biomarkers associated with better or worse outcomes in breast cancer survivors. The women who lost weight had improvements in inflammation-related biomarkers, in particular, C-reactive protein.

Drs. Ferrucci and Johnson are using stool and serum samples from both groups of women to compare changes in the metabolome and microbiome. “Metabolites and the microbiome work together

Metabolites are a fast and potentially more objective way of getting information about what someone is eating compared to our typical method of having people self-report their diet.

to modulate your health, and a large number of metabolites are co-produced by actions of the microbiome,” explained Dr. Johnson. “When something aberrant happens, whether it’s a genetic mutation, environmental exposure or other stressor, it can change the balance of both your metabolites and microbiome, which can lead to cancer.”

Using the serum samples, Dr. Johnson did a metabolite analysis of the thousands of metabolic changes possible in both groups of women over the study’s six months. The preliminary data show that exercise and diet altered the metabolites in the women

who received the weight loss intervention. Next, Dr. Johnson will look for the metabolites that most distinguish the diet-and-exercise group from the control group, since those could be useful biomarkers.

“Metabolites are a fast and potentially more objective way of getting information about what someone is eating compared to our typical method of having people self-report their diet,” Dr. Ferrucci explained. “You can look for metabolites in the blood or stool, and they give you information not only about the person’s dietary and other lifestyle exposures, but also about how the body is processing those exposures.”

They analyzed the LEAN stool samples, and found differences between the intervention group and the control group in terms of short-chain fatty acids. “That makes sense,” she said, “because we asked the intervention group to decrease calories, to eat more fruits and vegetables, more whole grains, less meat and fats. In this small pilot study, there was an indication of a greater accumulation of potentially beneficial short-chain fatty acids in the intervention group compared to the control group.” These have been linked to decreased incidence of cancer, colorectal in particular, which is Dr. Johnson’s main research focus.

She and Dr. Ferrucci presented their preliminary findings to the Obesity and Cancer Working Group in June, and received helpful feedback about possible ways to proceed. That’s one of the group’s purposes. “You may be able to find a logical collaborator who is very close by, but you wouldn’t even realize it if you were just in your office doing your own work,” said Dr. Ferrucci. ☺



PETER BAKER

Interventional Oncology: Moving Cancer Care Forward

Kevin Kim, MD

Often referred to as the fourth pillar of oncology, alongside medical, radiation, and surgical oncology, Interventional Oncology is a young, but rapidly evolving field. Led by Kevin Kim, MD, Professor of Radiology and Medicine (Medical Oncology) at Yale School of Medicine, the Interventional Oncology Program at Smilow Cancer Hospital provides patients with additional treatment options for personalized cancer care.

Interventional Oncology was developed as a subspecialty of Interventional Radiology to provide definitive or palliative treatments of solid tumors using targeted, minimally invasive procedures performed under precision image-guidance. Procedures such as embolotherapy, immunoembolization, chemoembolization, Y90 radioembolization (selective delivery of immunotherapy, chemotherapy and radioactive particles targeted directly to the tumor), and thermal ablation

(microwave ablation, radiofrequency ablation, cryoablation, and irreversible electroporation to heat, freeze or electrocute and destroy cancer cells) can be delivered as primary or adjuvant treatment, as part of a multidisciplinary care plan. Therapeutic options are also used for palliative care, including various therapies for pain relief, particularly for bone, soft tissue, and spine tumors, and are designed specifically to relieve pain caused by primary or metastatic tumors during cancer treatment, and to gain local control of a cancer so that other therapies can be effective.

One of the first programs of its kind in the country and one of the largest, the Interventional Oncology Program at Smilow is committed to treating patients with multiple types of cancers. First explored using liver directed therapies for liver cancers, Interventional Oncology has grown to become an integral part of the Gastrointestinal, Melanoma, Lung, Sarcoma, and Prostate and Urologic Cancer Programs. In addition, as participants of the Multidisciplinary Pain Program at Smilow, Dr. Kim and his team of Interventional Oncologists also offer patients palliative interventions for solid tumors and bone metastasis.

“In my opinion, the field of Interventional Oncology is one of the most fascinating in cancer care right now,” said Dr. Kim. “We are already able to offer top notch care to our patients at Smilow thanks to the expertise in medical, surgical, and radiation oncology, but now we are also able to offer another layer to enhance the potential high impact of treatment with minimal side effects. We can provide more treatment options and clinical trial opportunities for our patients as well.”

After undergoing a grueling regimen of chemotherapy to treat colon cancer that had spread to her liver, Ms. Jo-Anne Gauger was ready

to stop treatment. That is until her physician at the Smilow Care Center in Torrington, Dr. Christina Gomez, suggested she meet with Dr. Kim to discuss new options. Dr. Kim determined that she was a candidate for microwave ablation to treat the metastatic disease on her liver. The results have been life-changing.

“I was able to go to work the next day and have since undergone the treatment again to treat a small spot

are constantly new advances in Interventional Oncology that make existing therapies more effective and limit exposure to non-cancerous tissue. “For both patients and cancer providers, this is truly an amazing time, and what would have once been a major procedure for a patient, can now be done through a small incision that causes no scarring and with little to no recovery time,” said Dr. Kim. “It is not only more convenient

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**What would have once been a major procedure for a patient, can now be done through a small incision.
The benefit for our patients is immeasurable.**

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that remained on my liver,” said Ms. Gauger. “To have a ‘chemo vacation’ as we came to call it, is truly a blessing for patients like me. I had lost fifty pounds and chemotherapy was taking a huge toll on me both physical and mentally. As long as the cancer remains contained to my liver, I can continue to be monitored and treated this way without the need for chemotherapy. I now feel like I did 2 ½ years ago before I was diagnosed with cancer. I just hope that other patients out there realize there are other options.”

Smilow multidisciplinary tumor boards are one way that Dr. Kim collaborates with other oncology experts throughout the hospital to provide the most effective cancer care for patients. As a part of precision image-guided cancer care, there

and comfortable for patients, but it provides enhancements of quality of life and outcomes. The benefit for our patients is immeasurable.”

Dr. Kim’s goals for the Program are to make safe and effective novel interventional treatments more available and accessible to patients, and to find ways to advance cancer care in the clinic via innovative research. He commented that he goes to bed thinking about cancer therapies and wakes up thinking about new ways that these therapies can benefit patients. Indeed, the Interventional Oncology Program at Smilow leads their field with novel research. Working in collaboration with colleagues throughout Smilow Cancer Hospital to enhance treatment for their patients is their top priority. ☺



JOEL CALLAWAY

Recognizing our Nurses

Liz DeLuca

Education has always been important to Liz DeLuca. She and her siblings were the first in their family to attend college, as was her husband, Fred DeLuca. Fred was founder and CEO of SUBWAY® Restaurants. The grants that are given through the foundation he and Liz established, The Frederick A. DeLuca Foundation, typically focuses on young people, helping them with scholarships and tuition reimbursement. “For us,” said Liz, “education was a road to being self-sufficient.”

For Liz, that meant training to be a nurse. After receiving her nursing degree at the University of Connecticut, she completed her clinical work at Yale New Haven Hospital. Then, for five years, she was a nurse in the surgical intensive care unit at the West Haven VA Hospital. “It was really satisfying to work with patients and families going through difficult situations,” she explained.

When Fred was diagnosed with leukemia in 2013, he and Liz particularly appreciated the day-to-day care and comfort they received from the nurses, nurse practitioners, and physician assistants at Smilow Cancer Hospital. Between the long

stays after Fred’s stem cell transplant or short trips for blood transfusions and other tests, Fred was in and out of the hospital for two years, and the couple got a close up view of the dedicated staff at Smilow. Aside from the expertise of the doctors, what struck them most was the empathy and compassion of the nurses. “I think my husband’s life was better because of the care he received at Smilow,” Liz said. “The oncology nurses work with patients who may not have long to live, but they still have to maintain a positive, encouraging attitude,” Liz explained. “I used to think that my experience as a nurse was challenging, but when I saw what the oncology nurses were dealing with, it was just incredible.”

Fred DeLuca agreed, so much so that he told Liz, “I’d really like to thank the people who helped me so much. Let’s think how we can make that happen.”

After Fred’s death, determined to make that happen, Liz returned to Smilow to meet with one of Fred’s doctors, Nikolai Podoltsev, MD, PhD, Assistant Professor of Medicine (Hematology), as well as Catherine Lyons, RN, MS, Vice President, Patient Services, and Chief Nursing Officer, and Lisa Barbarotta, RN, Program Manager, Oncology Nursing Education & Practice. Both Cathy and Lisa were struck by Liz’s affinity for the nursing team. “Liz is a nurse through and through,” said Cathy. “She understands the challenges of trying to provide the best care you can, of keeping the nurses engaged and educated, and what is involved in making sure we have the best and the brightest nurses taking care of our patients.”

Given her nursing background and Fred’s long-time dedication to promoting education, it made sense that Liz decided to direct her generosity in those two areas, asking Cathy Lyons and Lisa Barbarotta in that initial meeting: “What does the

nursing staff need most?”

First on the list of needs for nurses was finding a way to help them educate patients more effectively. “Instead of going over the same information again and again, we wanted a way to transmit information to patients clearly and efficiently,” Cathy said. With Liz’s support, Smilow established a fund for patient education that paid for the development of a patient app about cancer treatment and a video for patients undergoing radiotherapy for cancer.

to the staff rather than have them leave their workplace is huge,” said Cathy.

The DeLuca Foundation’s grants are supporting the professional development of Smilow’s nurses in other ways, too. Beginning in 2016, Liz started funding scholarships and offering extra tuition reimbursement that has made it easier for a number of nurses to pay for their education. The grants have also helped nurses attend national conferences and meetings, and have paid for a professional library

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The oncology nurses work with patients who may not have long to live, but they still have to maintain a positive, encouraging attitude.

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“Now we’re about to make videos for chemotherapy and immunotherapy education. Families can watch them and then we can answer their questions in a more targeted way,” Cathy explained.

But just as key, in Liz’s mind, was furthering education for nurses. One challenge: A far-flung nursing staff. The Smilow network reaches throughout Connecticut, making it difficult for some nurses to get to events and trainings. “There is a simulation center on the main campus in New Haven, with manikins standing in for patients that do all the things that patients do” explained Liz. “The nurses use the manikins to practice for all kinds of situations.”

With the DeLuca Foundation’s financial help, Smilow was able to purchase another manikin—nicknamed the Sim Man—that will be transported to Smilow’s Care Centers. “Being able to take this training directly

on the nursing unit. “In May of 2018, we did our first oncology nursing grand rounds, bringing in a nationally renowned speaker with over three hundred attendees,” said Cathy.

The results of these ongoing efforts will impact nursing at Smilow for years to come. “Beyond the innovative educational instruments for patients and the training for nurses, the downstream effect of Liz’s support is that nurses here feel better about their job,” explained Cathy. “As word gets out, Smilow will become even more of a destination facility for nurses. A single donation can make a world of difference.”

That’s exactly the kind of result Liz and Fred were hoping for. “Fred and I felt it was important to acknowledge and reward the efforts of all caregivers. It is their work that makes a patient’s life better. It is my hope that the Foundation’s support will help in that regard.” 



Elan Gorshein, DO, JD, MPH
Kay Haedicke, MD
Wajih Zaheer Kidwai, MD, FACP
Su Hsien Lim, MD

PETER BAKER

Smilow Cancer Hospital Care Center - Guilford

CENTER AT A GLANCE

- A patient-centered focus on exceptional cancer care
- 50+ staff members; oncology board certified clinicians
- Medical Oncology: Over 900 patient visits and 700 infusion visits per month
- Radiation Oncology: 500+ radiation patient visits monthly
- A Smilow Surgical Specialty Center, including breast surgery
- On site diagnostic imaging, pharmacy, and clinical trials
- Access to supportive care clinicians, including an oncology nurse coordinator, social workers, a dietician, clinical research staff, palliative care, and survivorship planning
- Access to Integrative Medicine services, including massage, Reiki, acupuncture, music therapy, and psychology

YALE NEW HAVEN SHORELINE MEDICAL CENTER
111 Goose Lane, Suite 1300
Guilford, CT 06437
Phone: (203) 453-9192

"The Smilow Cancer Hospital Care Center in Guilford gives our patients access to multidisciplinary cancer care close to their homes on the Connecticut Shoreline. We partner with our colleagues at Smilow Cancer Hospital to offer genomic analysis, personalized treatment plans, and clinical trials, when appropriate."

— Dr. Wajih Zaheer Kidwai
Medical Director

meet the physician

Veronica L.S. Chiang, MD, FAANS

Professor of Neurosurgery; Director, Gamma Knife Center

Our Gamma Knife Center recently celebrated its 20th anniversary and treated its 5,000th patient. Do the same patients benefit from stereotactic radiosurgery today as compared with 20 years ago?

When our Gamma Knife Center opened in 1998, it predominantly treated inoperable or high surgical risk neurosurgical conditions. In its first year, 174 patients were treated using the Gamma Knife. Of these patients, over a third had a pain disorder known as trigeminal neuralgia, a quarter had benign brain tumors, and another quarter had brain metastases. Typically, only one lesion per patient was treated during each Gamma Knife session. Not only has the number of Gamma Knife cases increased to 300-350 cases per year, but our patients have also changed. With improved cancer survival, more patients with brain metastases need Gamma Knife treatment to keep their disease under control. Gamma Knife has become first line treatment for brain metastases.

How has the technology changed over the last 20 years?

While the Gamma Knife technology has evolved, our ability to use the head frame both as a localizer and as an immobilizer during radiosurgical treatment remains. The head frame is the best method to achieve submillimeter precision in the delivery of radiation allowing the Gamma Knife to treat targets less than 5mm in size with guaranteed accuracy. With the original Model C, all the coordinates for treatment targeting were set by hand and only single target treatments were possible. Today, multiple targets can be treated using our Gamma Knife Icon, which is designed so that the patient's head is held in one position and the whole bed moves around to bring the targets into the correct position for treatment. The Icon can also deliver mask-based radiosurgical treatments. When treatments are several hours long, patients can often sleep comfortably in one position for the duration of their treatment.

What are the research priorities for the Gamma Knife Center?

Our team is continually focused on new research to benefit patients with metastatic cancer. Newer cancer treatments, such as targeted therapies and immunotherapies, can cross into the brain and cause unintended consequences. In some cases, the therapies can be helpful in conjunction with Gamma Knife radiation, but many times the interaction can be harmful to the patient. Therefore, our research focuses on new combinations to determine when Gamma Knife should be used. Our physicians collaborate closely with our colleagues in medical oncology at Smilow Cancer Hospital to lead the field nationally in research in this area.

PETER BAKER



Mary Lynne



Joe



Karen



Kaitlin

Read their stories:
yalecancercenter.org/survivors