Yale Cancer Center

centerpoint

MAGAZINE

Striving to Improve Outcomes

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Yale Cancer Center centerpoint MAGAZINE

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

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In combination with our commitment to basic scientific discovery and novel therapeutics, a laser focus on cancer outcomes is a recurrent theme throughout Yale Cancer Center and Smilow Cancer Hospital. Our cancer research and clinical care efforts continually strive to improve outcomes for our patients, through prevention, treatment, and clinical care.

One such effort, the Yale Cancer Outcomes, Public Policy, and Effectiveness Research Center, or COPPER Center, is an integrated, multidisciplinary research team that concentrates on a broad portfolio of research projects to study optimal cancer practices and improve cancer care models. Many of the research findings from our COPPER Center ultimately affect cancer treatment and policy practices worldwide. One example is a recent finding by Dr. Cary Gross who discovered that Caucasian women are more likely to receive tumor profiling than African American or Hispanic women for hormone receptor-positive breast cancer. The study highlights a disparity that needs attention and, when addressed and mitigated, will improve accessibility and options for all women with breast cancer.

A large component of our Population Sciences Program is devoted to the study of diet and lifestyle and their impact on cancer, led by Dr. Melinda Irwin. Dr. Irwin's career has focused on the growing field of lifestyle factors and chronic diseases. Her research over the past 15 years has focused on randomized trials looking at the effects of exercise and weight loss on biological markers, treatment side effects, and quality of life in cancer patients and survivors. For example, one trial tracked nearly 5,000 women with breast cancer and found that three hours of brisk walking a week was linked to a 46 percent decrease in mortality. Even when women began exercise after decades of sedentary living, mortality fell by as much as 33 percent.

Similar research is discussed in this issue of *Centerpoint* Magazine regarding colon cancer patients. Along with my colleagues, I have focused my research efforts on pinpointing links between diet and lifestyle choices and their impact on colon cancer outcomes. We have identified many links, including the positive impact of exercise and aspirin, vitamin D, and nut intake on decreased recurrence and mortality.

As healthy lifestyles and diets continue to demonstrate both decreased cancer incidence and improved outcomes for our patients, it is essential that the important message of good health is reiterated at all levels of healthcare: from primary practice and specialty care, to cancer care. Every physician and caregiver has the responsibility to remind our patients of the consequence of a healthy diet and regular exercise, along with their prescribed cancer care, to enable us to have a positive impact on our patients' lives.

Sincerely,

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

Marissa's Journey

Emily Fenton writer **Peter Baker** photographer

Marissa Antonio, and her daughter, Alexis

It was apparent from the start that Marissa Antonio's case was unique. She was just 39 and a new mother when an MRI revealed a 19cm tumor in her liver, and unlike with most cases, she did not have any complicating disease in the liver, such as cirrhosis. Marissa knew something was not right when she started having pain on her right side and was more tired than normal. At the time she was working nights as a nurse and assumed that was the cause of the fatigue. When she started noticing blood in her urine and couldn't keep any food down, she knew it was time to visit her doctor.

At the visit, her doctor immediately sent her to the Emergency Department where doctors did a biopsy and the next day she received the news; she had hepatocellular carcinoma (HCC), or liver cancer. Marissa was not only devastated, but also shocked that this could happen to her. Her daughter was just 19 months old and knowing she had a long road ahead, she requested to be seen by doctors at Yale.

"My husband and I had been trying to conceive for almost five years, and our daughter finally was here and I was too sick to take care of her. It was two years before I felt well enough to do so. I am so thankful to my husband and my father for stepping up to care for her when I could not," said Marissa.

For any patient with HCC it is important to be referred to a medical center that has a multidisciplinary program and is able to offer a range of treatment possibilities. Marissa first met with medical oncologist Dr. Stacey Stein and with hepatologist Dr. Tamar Taddei, and after discussing the case at the multidisciplinary tumor board, they explained her treatment plan. She started a treatment regimen known as chemoembolization to shrink her tumor before surgery could be scheduled to remove it. Despite suffering various side effects, Marissa was able to complete the treatment and her tumor decreased by over 90 percent.

Before her surgery was scheduled, an MRI was ordered to assess the location and involvement of the tumor. It revealed that there were major veins involved and the cancer was spreading towards her heart. Therefore, surgery was deemed too risky. Marissa woke up every day just thankful she was alive. She planned a trip to the Philippines to reconnect with family and continued to be monitored. When she returned from her trip, another scan was done and this time her cancer was receding instead of growing as they had expected. It was still considered risky, but Drs. Sukru Emre and Ronald Salem decided to take advantage of the small window offered and attempt the surgery Marissa so desperately needed.

After eight and a half hours Marissa awoke to good news; her surgeons were able to remove all of the tumor with no complications, and she would not need a liver transplant.

The newly formed Liver Cancer Program at Smilow Cancer Hospital, led by Mario Strazzabosco, MD, PhD is dedicated to diagnosing liver cancer early, when treatment is optimal. "Marissa's case illustrates the complexities around the management of HCC and how the application of a multidisciplinary approach to care can lead to success against any odds," commented Dr. Strazzabosco. "The success of Marissa's case is the result of a profound knowledge of the standard of care and the ability to think out of the box when needed."

Marissa's care team followed her closely and never stopped exploring new options for her. This continued, and a year after surgery a scan of the chest revealed a growth on the left lower lobe of her lung; the HCC had returned. Thoracic surgeon, Dr. Frank Detterbeck, was able to remove the lesion, along with a benign lesion that had been discovered earlier, but a later scan showed two more small growths. These were also resected, but she experienced complications from the multiple surgeries, and suffered a lung collapse. When more growth was found in the lung, another surgery was not an option and a clinical trial had proved too toxic for her body to handle. That is when they turned to radiation oncologist, Dr. Kimberly Johung, at Smilow Cancer Hospital.

Marissa continued to work while receiving radiation therapy and subsequent tests showed that her Alpha-fetoprotein (AFP), a tumor marker to help detect and diagnose cancers of the liver, had dropped to a safe level. Marissa herself works as a radiology nurse in the Yale New Haven Health System. She shares her story and patients trust that she understands what they are going through. "I feel like God has put me here to be with these patients as they go through a similar journey," said Marissa. "My faith played a crucial role in my recovery, and helped me through the dark times. I hope that I can be that support for someone else." Marissa also attributes her recovery and renewed health to the healthy eating habits she implemented into her everyday life.

While visiting the Philippines, Marissa discussed the family's history of liver disease, which she had always assumed was from alcohol use. However, due to the presentation of Marissa's case, it is suspected that her mother was a carrier for Hepatitis B and unknowingly passed it to Marissa during pregnancy or childbirth. Hepatitis B is a known cause of liver cancer, as are metabolic syndromes and alcoholic liver disease.

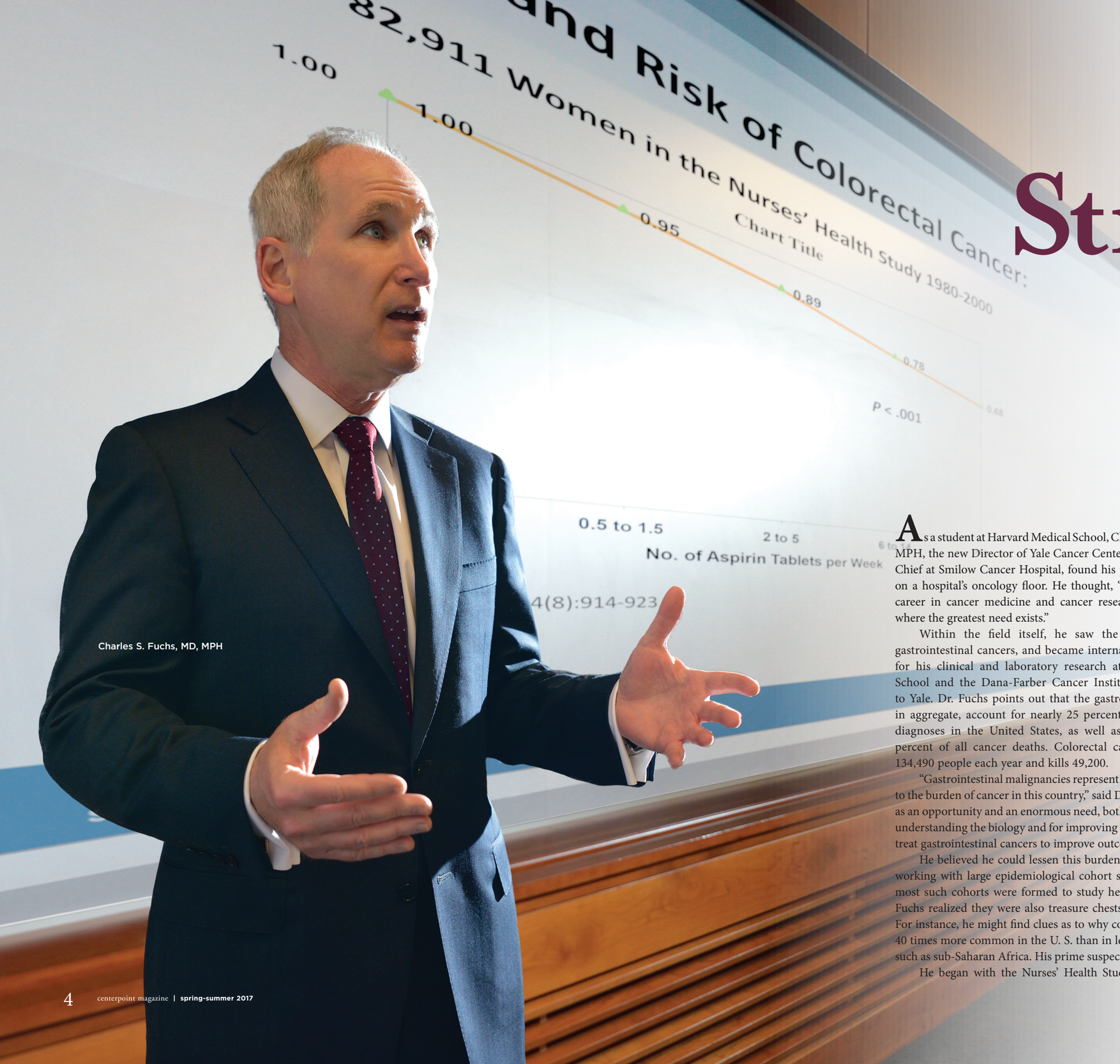
Marissa will continue to be treated with antivirals and followed closely for any signs of recurrence by her hepatologists at Smilow. Her daughter, Alexis, is now seven years old. She grew up with her mother constantly going to doctor's appointments and spending time in the hospital, but with the support of family they have both made it through a difficult journey. Marissa commented that she feels as though Alexis knew when she was finally feeling better.

"She had never been one to ask me to carry her before, but one day she looked up at me and begged for me to pick her up. It was a very special moment. I show her pictures of when I was sick, mommy with no hair, and she knows what I have been through and that I plan to be here for her for a long time," said Marissa. "This was a long journey for all of us, full of obstacles and setbacks. I always tell people that I was treated at the best hospital, with the best doctors. They never gave up on me, and I am so thankful that they kept believing my life was worth saving."

Steve Kemper writer **Peter Baker** photographer

Striving to Improve

Outcomes in Colon Cancer



Charles S. Fuchs, MD, MPH

As a student at Harvard Medical School, Charles S. Fuchs, MD, MPH, the new Director of Yale Cancer Center and Physician-in-Chief at Smilow Cancer Hospital, found his path while working on a hospital's oncology floor. He thought, "I want to pursue a career in cancer medicine and cancer research, because that's where the greatest need exists."

Within the field itself, he saw the greatest need in gastrointestinal cancers, and became internationally renowned for his clinical and laboratory research at Harvard Medical School and the Dana-Farber Cancer Institute before coming to Yale. Dr. Fuchs points out that the gastrointestinal cancers, in aggregate, account for nearly 25 percent of all new cancer diagnoses in the United States, as well as approximately 30 percent of all cancer deaths. Colorectal cancer alone affects 134,490 people each year and kills 49,200.

"Gastrointestinal malignancies represent a major contributor to the burden of cancer in this country," said Dr. Fuchs. "I saw this as an opportunity and an enormous need, both for fundamentally understanding the biology and for improving ways to prevent and treat gastrointestinal cancers to improve outcomes for patients."

He believed he could lessen this burden most effectively by working with large epidemiological cohort studies. Historically, most such cohorts were formed to study heart disease, but Dr. Fuchs realized they were also treasure chests of data on cancer. For instance, he might find clues as to why colon cancer is about 40 times more common in the U. S. than in less developed areas, such as sub-Saharan Africa. His prime suspects: diet and lifestyle.

He began with the Nurses' Health Study, which collected extensive health and medical data on 121,700 registered nurses every two years starting in 1976. Dr. Fuchs received permission from the study to do molecular analysis on tissue samples of colon cancers. Then he looked for links between tumor characteristics, risk factors associated with diet and lifestyle, and outcomes.

"We learned a lot," he said. For instance, a diet high in red meat, carbohydrates, and refined grains increases the risk of colon cancer, as do common byproducts of such a diet, including obesity and diabetes. By contrast, a diet high in fruits, vegetables, legumes, fish, poultry, and whole grains decreases cancer risk. A sedentary lifestyle was associated with greater risk of cancer, while regular exercise decreased risk. So did a daily aspirin and high levels of vitamin D. These findings have been confirmed many times by other studies, and have greatly influenced opinions on colon cancer risk and prevention. He practices what he researches—he exercises, eats a healthy diet, and takes a daily aspirin and vitamin D.

Next, Dr. Fuchs turned to a related question about these risk factors: after a patient is diagnosed with colon cancer, do diet and lifestyle continue to matter in terms of a patient's recovery, survival, and the chances of cancer recurrence? "Despite great interest in this question, there were no studies that adequately offered any answers," explained Dr. Fuchs. He created cohorts of newly diagnosed colon cancer patients and followed them to assess whether their diet or lifestyle or use of supplements influenced their long-term survival, independent of the other cancer therapies that they received.

In the 18 years since, Dr. Fuchs and his colleagues have studied thousands of patients and identified many factors that clearly influence the outcomes of colon cancer patients. For instance, aspirin: Dr. Fuchs found that even after patients were diagnosed with colon cancer, those who took aspirin had a much lower risk of recurrence. The result was so clear that he launched a clinical trial to determine if adding aspirin-like compounds to standard therapies might improve outcomes for these cancer patients.

Dr. Fuchs is highly dubious about most supplements that claim to fight cancer, but he makes an exception for vitamin D. "It affects what genes are turned on or off in a cell," he said. "Colon cancer cells actually possess receptors for vitamin D, and if you expose colon cancer cells to vitamin D in the laboratory, it inhibits their growth." Based on a simple blood test, Dr. Fuchs learned that colon cancer patients with higher levels of vitamin D have much better outcomes, even if they begin taking the vitamin after diagnosis.

Something similar is true for marine omega-3 polyunsaturated fatty acids, more commonly called fish oil, which have been associated with lower risk of colorectal cancer. Dr. Fuchs recently found that patients diagnosed with colorectal cancer have a lower risk of dying from the disease if they increase their consumption of marine omega-3s. If other studies replicate this, the finding could have implications for future treatment regimens.

Other factors associated with the risk of colon cancer can have consequences even after a diagnosis of the disease. For instance, Dr. Fuchs found that patients who exercise are more likely to be cured, even if they don't begin an exercise regimen until after their diagnosis. Conversely, obese people, already at greater risk of getting colon cancer, are more likely to have a recurrence after being diagnosed.

Dr. Fuchs and his colleagues wondered why obesity and sedentary lifestyles increase the likelihood of a relapse of colon cancer. The answer may be insulin, a hormone that manages blood sugar. Obese and sedentary people overproduce insulin, but often not enough to keep blood sugar levels in check. The consequence is type 2 diabetes (also called adult-onset diabetes). "Why is that relevant?" asked Dr. Fuchs. "Because, in the laboratory, insulin can promote the growth of colon cancer."

Next, he looked to see if type 2 diabetics are more likely to have poor outcomes from colon cancer. "The answer was yes," said Dr. Fuchs. "They have a much higher risk of cancer recurrence."

Then he posed the same question by looking at diet. All food increases blood sugar levels; the increase varies with the food. Carbohydrates, for instance, drive up blood sugar and also cause weight gain. When a person's total intake of food and its effect on blood sugar are measured, the result is called the dietary glycemic load. A high glycemic load diet has been linked to obesity, heart disease, and cancer.

Dr. Fuchs wanted to understand if a cancer patient's ability to be cured was affected by such a diet. Again, the answer was yes, with a higher risk of either recurrence or death from the cancer. "Then we went to the heart of it," said Dr. Fuchs. "We measured insulin levels in colon cancer patients at the time of diagnosis, and followed them. We found that those with higher insulin levels in their blood were more likely to die from their cancer."

He followed the implications of these findings farther. Since colon cancer patients with type 2 diabetes tend to have worse outcomes, they concluded that any risk factor for type 2 diabetes would be bad for colon cancer patients. Dr. Fuchs tested this idea against a well-known risk factor for type 2 diabetes, heavy consumption of sugary drinks. He found the expected correlation: colon cancer patients who drank lots of sugar-sweetened beverages were more likely to have a recurrence or die from their cancer.

He noticed in the medical literature that coffee-drinkers were less likely to get type 2 diabetes. This made him wonder, given his previous research, if coffee-drinkers were also less likely to get colon cancer. The answer, again, was yes. Further, patients diagnosed with the disease lessened their risk of a recurrence if they drank more coffee.

"So, it's an interesting series of studies that speak to potential dietary interventions that could augment the benefits of treatment," explained Dr. Fuchs, "and moreover, they offer potential clues in biology."

He intends to continue these investigations at Yale. "The opportunity to lead an outstanding center is a phenomenal opportunity," he said. "And beyond my motivation to lead the Cancer Center, the ability to collaborate with the great scientists here and access Smilow Cancer Hospital to test our findings will further advance our research."

"It's an interesting series of studies that speak to potential dietary interventions that could augment the benefits of treatment, and moreover, they offer potential clues in biology."

Ranjit Bindra, MD, PhD and Peter M. Glazer, MD, PhD

Steve Kemper writer **Peter Baker** photographer

A Counterintuitive Breakthrough in Brain Tumor Therapy

Ranjit Bindra, MD, PhD, was puzzled. His patients were not responding as expected to a heralded new drug, enasidenib, for brain tumors, which targeted a mutation in the IDH gene, implicated in gliomas. When combined with chemoradiotherapy,

enasidenib was supposed to improve outcomes for people whose brain tumors carried the mutation. But in the clinic, Dr. Bindra, Assistant Professor of Therapeutic Radiology and Pathology, found that patients with the mutation who didn't receive enasidenib were responding more strongly to chemoradiotherapy than the patients who received the targeted drug. Enasidenib did perform as advertised, blocking IDH mutations. So why the discrepancy in responses between patients who did and did not take the drug?

Dr. Bindra and Jennifer Garbarino, a second year PhD student.

It seemed counterintuitive, but Dr. Bindra wondered if IDH mutations somehow made brain tumors more susceptible to chemoradiotherapy. He explored this hunch in his lab by creating a model cell line and making it IDH-mutant. In the summer of 2015, his lab screened 3,000 cell lines. "We tested whether the mutation induced sensitivity to radiation chemotherapy," he said, "and that's exactly what we saw."

This was the first discovery. To Dr. Bindra, the next counterintuitive implication was clear: instead of blocking IDH mutations, exploit them. But how?

His lab began testing drugs on the mutated cell lines, looking for something that increased the mutation's sensitivity. In January 2016, a research fellow in his lab named Nathaniel Robinson, MD, told Dr. Bindra that the drug screen had turned up only one hit, on a drug called olaparib that was approved against ovarian cancer. The surprise: olaparib was a PARP inhibitor.

"That was the big aha moment," said Dr. Bindra. "We realized that we were on to something that could be clinically significant."

PARP—poly (ADP-ribose) polymerase encompasses a group of proteins crucial to the continuous process of repairing damaged DNA. Regardless of whether a cell is normal or cancerous, if its faulty DNA isn't mended or removed, it will die. PARP inhibitors block one of the main pathways by which cells fix damaged DNA. Olaparib potently kills cancer cells with BRCA1 and BRCA2 mutations, known to cause ovarian, breast, pancreatic, and prostate cancers, because BRCA proteins are important for a second pathway of DNA repair. The cancer cells cannot survive the effect of olaparib on DNA repair when the BRCA-related DNA repair pathway is also defective.

Dr. Bindra's discovery excited him because if IDH mutations resemble BRCA mutations and respond similarly to a PARP inhibitor, new possibilities opened for treating brain cancer. The discovery also called into doubt the current standard of care for treating patients with IDH mutated gliomas.

Though Dr. Bindra had established that IDH mutations respond to a PARP inhibitor, he did not know how and why. He turned to colleagues at Yale, beginning with Peter M. Glazer, MD, PhD, Robert E. Hunter Professor of Therapeutic Radiology and Professor of Genetics, and Chair of the Department of Therapeutic Radiology. A decade earlier, Dr. Bindra had been a PhD student in Dr. Glazer's lab. More recently, in 2012, Dr. Glazer recruited Dr. Bindra away from Memorial Sloan Kettering to start his own lab at Yale. Dr. Bindra's former mentor became his partner.

Dr. Glazer immediately saw the importance of Dr. Bindra's discovery. He assigned a graduate student, Parker Sulkowski, to dig into the biological mechanisms involved. Mr. Sulkowski, along with Chris Corso, MD, PhD, a resident in Dr. Bindra's lab, did the animal work critical to providing proof of principle. Important additional assistance came from the labs of Stephanie Halene, MD, PhD, Associate Professor of Medicine, Hematology; and Murat Günel, MD, FACS, FAHA, Nixdorff-German Professor of Neurosurgery and Professor of Genetics and of Neuroscience, and Chief of Neurosurgery at Yale New Haven Hospital.

Previous research had established that mutated IDH pumped out a mutant metabolite called 2-Hydroxyglutarate (2HG) at abnormally high levels. "If a mutation is making something that it shouldn't be making," explained Dr. Bindra, "the first and easiest thing to say is, 'Let's make it stop.' That's the typical pharmaceutical paradigm." In this case the result was enasidenib, developed by Agios Pharmaceuticals.

"We argue that metabolites in this subset of cancers should not be shut down or blocked, but instead should be exploited."

But Drs. Bindra and Glazer thought enasidenib solved the wrong problem. "They are correct that 2HG makes a tumor," said Dr. Bindra. "Where they went wrong was to say, 'We have to close this door because we know this mutation opened it.' Think of it like a horse in a barn. That first mutation likely broke the lock on the door, and the horse started running. So by the time they closed the door, the horse was long gone."

That is, the initial mutation creates a malignant cell, but the real problem comes later, as unrepaired DNA triggers lots of other mutations. "By then, stopping the metabolite doesn't do much to help you on the malignant phenotype," said Dr. Glazer. "Instead, let the metabolite be made and then exploit the vulnerability it creates."

That insight came out of Dr. Glazer's lab in the summer of 2016. "There are six or seven DNA repair pathways identified in human cells," he said. "The metabolite 2HG inhibits one of them (the one related to BRCA mutations), so the cell has a deficiency in DNA repair. As with BRCA-deficient cancers, when the PARP inhibitor inhibits another DNA repair pathway, the cancer cell is even worse off."

Much worse, Dr. Bindra, Dr. Glazer, and their colleagues found that the combination of the IDH mutation and the PARP inhibitor increased the death of brain cancer cells 50-fold.

In February, they published their findings in *Science Translational Medicine*. The paper created a stir among researchers, physicians, and patients. A small phase I trial is underway at Yale Cancer Center. A larger phase II trial has been approved by the National Cancer Institute and is planned to launch at the end of summer, with about 50 patients at 35 cancer centers.

Recent research has found IDH mutations in many cancers, including melanoma, acute myeloid leukemia, gastric cancer, colorectal cancer, liver cancer, cholangiocarcinoma, and others.

"We argue that metabolites in this subset of cancers should not be shut down or blocked, despite the knee-jerk desire to do it, but instead should be exploited," said Dr. Bindra. "So the implications are profound. We may need to re-evaluate and take a completely different route when the conventional pharmaceutical approach suggests one way but the biology says to go 180 degrees the other way." Drs. Bindra and Glazer are now researching whether 2HG can function as a biomarker for selecting tumors treatable with PARP inhibitors.

"It's a testament to following the biology," said Dr. Bindra. "It's also a testament to translational science at Yale. I can't think of another institution where we could have gone so seamlessly from the clinic to the lab and back to the clinic."

PETER BAKER

A Critical Mission: Preserving Fertility

Pasquale Patrizio, MD, Director of the Yale Fertility Center

Once a week, Pasquale Patrizio, MD sets off across the Yale campus to Smilow Cancer Hospital. As Director of the Yale Fertility Center and Fertility Preservation Program, Dr. Patrizio is at Smilow with a mission: to raise awareness of fertility preservation options among Smilow's patients and practitioners, and to make it more convenient for patients to incorporate those options into their treatment plans.

"Every year, 700,000 women are diagnosed with cancer," said Dr. Patrizio. "About 10 percent of these women are under the age of 40 and still of reproductive age." Fertility was long considered an unfortunate casualty of cancer treatment. The damage to reproductive organs that can result from chemotherapy and radiation significantly reduce or end a patient's chances of conceiving if fertility is not preserved.

An internationally known and respected reproductive endocrinologist and infertility specialist, Dr. Patrizio has helped advance procedures that can preserve fertility for both men and women and keep alive the possibility of having a family down the road. "When we talk to patients, many are surprised to hear they have options for fertility preservation and happy that they don't need to be concerned about future fertility if they choose to pursue those options," he explained.

Timing is crucial. For the best outcomes, Dr. Patrizio strives to consult with patients before any chemotherapy or radiotherapy begins. He evaluates key medical factors such as a patient's age, type of cancer, recommended course of treatment, and dosage of medications.

For male patients, the options are fairly straightforward. Sperm cryopreservation is the most common procedure, but in rare instances doctors can freeze testicular tissue as well. The frozen sperm preserved, even in very low quantity, can later be used for in-vitro fertilization (IVF).

If a female patient can postpone starting her cancer treatment for two weeks, it can open the door to the two most common procedures for preserving her fertility: embryo cryopreservation and oocyte, or egg cryopreservation.

"There has been such progress in the field of fertility preservation," Dr. Patrizio said. "Before, we were locked into a four- to five-week timeframe for completing a cycle of ovarian stimulation to harvest eggs. Now, we can accomplish this in two weeks, no matter where a woman is in her menstrual cycle. Also, over the past three years the process of egg freezing has improved substantially. Thanks to a new technique called vitrification, the results are much better in terms of egg survival, fertilization, and possible success of a future pregnancy."

> **"Fertility is an important part of quality of life after cancer. We want patients to know what their options are to preserve their fertility at the start."**

A patient's relationship status can influence which of those two procedures is the best match. "If a patient has not yet found a stable partner, she can freeze eggs that can be used in the future," said Dr. Patrizio. "For a woman with a stable partner, embryo freezing is more successful and generally preferred to egg freezing. But even in these instances there are some couples that may opt for egg freezing because of their moral concerns about leaving embryos behind if the patient doesn't survive her cancer."

If a female patient must start her cancer treatment immediately, a different option is available. Ovarian tissue is harvested by laparoscopic surgery and frozen. After the patient recovers from cancer, the ovarian strips are implanted back to the ovary to stimulate function and egg production. For women with gynecological cancers or cancers requiring radiotherapy to the pelvic area, another option is ovarian transposition, which moves the ovaries out of the field of radiation with the intent of limiting harm and preserving as much function as possible.

The range of fertility options can seem overwhelming, especially for a patient already reeling from a cancer diagnosis. That's why Dr. Patrizio has brought his expertise directly to Smilow Cancer Hospital. "The notion of establishing a fertility clinic in a cancer hospital is a pioneering concept that I am sure will soon be replicated by others," he said. "It not only lets us see the patients on a quick referral basis, but it creates a great spirit of collaboration among our fertility team and Smilow's oncologists, hematologists, and gynecologists. Fertility is an important part of quality of life after cancer. We want patients to know what their options are to preserve their fertility at the start so there are no missed opportunities and no regrets after the fact."

PETER BAKER

A New Pathway for Patients

Cara Henderson, RN, BSN, CMSRN, Patient Service Manager and Saral Mehra, MD, MBA, FACS, Assistant Professor of Surgery

Free flap surgeries are among the most complex for patients with head and neck cancers. In these reconstructive procedures, tissue from one part of the body is transplanted to another site, where the new tissue gets reconnected to the blood supply through intricate microsurgeries. Recovery is difficult for patients.

"Many patients will have a tracheotomy, a feeding tube into the nose, a number of drains and wires," said Saral Mehra, MD, MBA, FACS, Assistant Professor of Surgery (Otolaryngology), who specializes in free flap reconstructions. "They find it hard to communicate because of the tracheotomy. We're operating all over their bodies, sometimes their legs, their back, their arms, in addition to the head and neck region, because we're transferring tissue to reconstruct their jaw or their tongue or part of their throat."

Until recently, these patients would spend several days in the hospital's intensive care unit (ICU) before moving to the 15th floor of Smilow Cancer Hospital for further care and rehabilitation. Dr. Mehra and Patient Service Manager, Cara Henderson, RN, BSN, CMSRN, saw an opportunity. "Patients were getting hung up along the post-operative path by going to the ICU," Dr. Mehra said. "Their heart and lungs are fine, so they don't need ventilators, complicated medications, and all the things the ICU is great at handling. They just need high-intensity, nursing care."

Dr. Mehra and Ms. Henderson put together a multidisciplinary team of nurses, nurse practitioners, surgeons, coordinators, and administrators to design a new clinical care pathway for patients recovering from free flap surgery. The plan sent them straight from the OR recovery room to the 15th floor of Smilow, where they would be cared for by a dedicated team of nurses. Beginning in May 2015, 40 patients were assigned to the new pathway, and their outcomes were compared with those of 81 patients who took the normal course of care through the ICU.

The results were impressive. Patients on the new pathway left the hospital an average of two days sooner—8.9 days compared to 11.2 days. The 30-day readmission rate dropped from 13.6 percent to zero. Bypassing the ICU didn't affect other outcomes either, such as surgical complications. The pathway is now standard procedure for free flap patients at Smilow.

Dr. Mehra sees several reasons for its success. Instead of staying bed-bound in the ICU for several days, patients are up and walking almost immediately on the 15th floor. Second, the nurses and care coordinators begin planning for the patient's discharge on the first day instead of waiting until after the patient arrives from the ICU. "Patients are learning from day one how to manage their wounds and their tracheotomy tubes," said Dr. Mehra. "A lot of readmissions are from a lack of education."

Aside from the obvious cost savings, cutting two days from a patient's stay is medically significant. "Spending less time in the hospital reduces a patient's exposure to hospital-acquired infection," said Ms. Henderson, who put together the teams of nurses that made the pathway successful. She agrees with Dr. Mehra that early ambulation is key. "Getting patients out of bed, even one day sooner," she said, "can ensure better outcomes by preventing pneumonia, blood clots, and deep vein thrombosis. All of these early interventions improve outcomes."

> **"Getting patients out of bed, even one day sooner, can ensure better outcomes."**

Cutting two days from the stay also has psychological benefits for patients. "They are quite frustrated after surgery," said Dr. Mehra. "Our patients are often slowly re-learning functions that most of us take for granted, such as speech and swallowing, they have many scars, and they just want to be at home with their families as they continue their recovery."

Each patient is assigned a dedicated team of nurses, which Dr. Mehra and Ms. Henderson both cite as critical, because it ensures consistency of care and clear communication between nurses and physicians. Ms. Henderson also believes that having a dedicated team of nurses gives patients a psychological lift.

"These surgeries can be disfiguring," she said. "That causes a tremendous amount of stress and impairs their self-esteem. So making a connection with the same people over and over gives a patient a feeling of family and support, as opposed to having to reestablish a connection with someone different."

To keep this pathway smooth takes a lot of skill, communication, and coordination. Ms. Henderson's team of 35 nurses and 16 patient care associates received special training to handle the intensive care needed by free flap patients, especially in the first 24 hours when the tissue graft is taking hold and the patient's head must remain relatively immobile. The patient's room has to be fully furnished beforehand with all the special equipment necessary to start immediate care. The nurses also monitor the patient's vital signs every hour rather than the usual four hours.

"It's more work for the nurses on that floor," said Dr. Mehra, "so there could be some reticence at doing a program like this. But everybody got together and made it happen, to make patient care better."

PETER BAKER

A Tradition of Giving Helps Further Prostate Cancer Research

Mr. Bill Reese

A rare book dealer for over 40 years, Bill Reese is used to looking into the past for answers, but a recent significant gift to Daniel Petrylak, MD, Professor of Medicine (Medical Oncology) and Urology, has him focused on the future. Bill specializes in the literature of the early history of the Americas and travels and voyages. In 1975, he launched his career as a sophomore at Yale University (class of '77) by selling a rare map of the Valley of Mexico from 1563 to the University, thus cementing a long-lasting relationship.

In 2013, when Bill was diagnosed with prostate cancer, he took a page from his own work and began a search for the best care possible. After consulting with doctors at Johns Hopkins in Maryland, where he is originally from, Bill realized his treatment would be complex and he would prefer to be closer to his home in New Haven. This led him to Dr. Petrylak and his team at Smilow Cancer Hospital. It was great news for Bill to hear that he could receive the care he needed, near his home.

Bill has a long history of supporting research, having funded over 200 research fellowships on historical topics at 13 institutions. He has always recognized the power of research and the impact it can have on future generations, which is why it was a natural step for him to extend this thinking to the medical field and the transformative research in Dr. Petrylak's lab. His gift will support translational research in prostate cancer and help to improve personalized medicine.

Dr. Petrylak has directed several groundbreaking studies over the years, most notably his trial that demonstrated a survival benefit for docetaxel-based therapy in men with advanced prostate cancer. This trial led to the approval of docetaxel for hormone refractory prostate cancer by the FDA, which until recently was the only approved treatment available. However, in the last few years, there has been immense progress.

"The progress we have seen lately only happens because science is supported by people like Bill, who realize research is the future. We are constantly looking for ways to improve treatments for our patients," said Dr. Petrylak. One of the main goals, commented Dr. Petrylak, is the formation of a SPORE (Specialized Programs of Research Excellence) in Prostate Cancer, which would support multidisciplinary research and help to quickly translate laboratory discoveries to patients. "Gifts like Bill's support pilot trials that help us build our program and move the process forward."

Two of the treatment modalities Bill received did not exist when he was first diagnosed, including treatment with Radium 223, which shows improved overall survival in men with advanced prostate cancer that has spread to the bones. Bill was also tested, and found to carry the BRCA gene, which researchers are discovering is related to more and more cancers other than just breast cancer. In fact, twenty percent of all prostate cancers are related to the BRCA gene.

"In my opinion, an optimistic view is the best view to have when facing cancer," said Bill. "There is reason to hope. The pace and development of new therapies is amazing, and we must keep it moving forward. The wonderful thing about Smilow is the ability to establish relationships not only with your doctor, but other staff as well. It is a large enough center that they can offer you advanced treatment with cutting-edge technology, while at the same time being small enough that you don't get lost in the shuffle. It is truly the best of both worlds here."

Since his diagnosis, Bill has written and published three books, continues his work as a rare book dealer, and remains an active runner. He lost one sister to breast cancer, and watched his other sister undergo treatment for the disease. For him, gifts like this are insurance for the future and he feels fortunate to be able to support Dr. Petrylak and his research. For someone focused on travels and voyages from the past, Bill has come a long way himself in his journey towards a brighter future for patients with prostate cancer.

Along the way, Dr. Petrylak has followed Bill's progress closely, and has been able to incorporate the latest treatment advances into this care. "Despite how far we have come, we still have a long way to go. Patients like Bill, who are so involved with their care, are inspiring and keep us moving forward in more ways than one."

> **"The progress we have seen lately only happens because science is supported by people like Bill, who realize research is the future."**

Debra S. Brandt, DO and Thomas Skoczylas, PCA

PETER BAKER

Smilow Cancer Hospital Care Center - Torrington

PRACTICE AT A GLANCE

- Outstanding teamwork and patient-centered focus on exceptional cancer care
- 900 patient visits per month
- 550 chemotherapy treatments per month
- 40 staff members
- Clinical trials, social work, nutrition, complimentary services (Reiki, yoga, massage, hypnosis), pharmacy, and support groups all offered on-site

"I'm proud of our entire team at the Torrington Care Center. We offer outstanding services to our patients, consistent with the care they would receive at our main hospital, including access to innovative clinical trials and the latest treatment options, with easy access in Litchfield County."

— Dr. Debra Brandt, Medical Director

SMILOW CANCER HOSPITAL CARE CENTER AT TORRINGTON
200 Kennedy Drive, Torrington, CT 06790
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PETER BAKER

meet the physician

Brigid Killelea, MD, MPH, FACS

Associate Professor of Surgery (Oncology)

You care for women with breast cancer, and others seeking preventive surgery. How have the options expanded for women over the last several years?

So much has changed, particularly in the fields of genetics and genomics. Today we are able to tailor medical treatment for each individual patient, depending upon what type of breast cancer they have. For example, many women with early stage breast cancer do not require chemotherapy, and are treated with endocrine therapy, which is a pill. For others, who have more aggressive types of breast cancer, we will often give chemotherapy before surgery, in order to shrink the tumor and see how it responds to treatment. This can also mean that less surgery will be required.

On the surgery side, we are often able to offer less invasive procedures, which means shorter recovery time and the potential for fewer complications. I do a lot of oncoplastic surgery, which means using plastic surgery techniques during surgery to completely remove the tumor and get the best cosmetic result. We are also more selective about which patients need to have all of their axillary lymph nodes removed, which means that fewer patients are at risk for arm swelling.

How do women weigh their options for breast surgery? When do you feel they know they are making the right choice for them?

This can be a hard decision. I feel that my job as a physician is to provide my patients with all of the tools that they need to make the best and most informed choice for surgery. Ultimately though, the decision is up to them. Everyone approaches the diagnosis from a unique perspective, and different patients have different reasons for the type of surgery they choose. Sometimes hearing so much information and dealing with the shock of a cancer diagnosis can be overwhelming, and I understand that. Many patients need a little time to think things over, and discuss with others before we decide together how best to proceed. I always encourage patients to take a few days and come back to talk with me some more if they need to.

You also participate on the Cancer Committee for Smilow Cancer Hospital's American College of Surgeons Cancer Program accreditation. What challenges do you see hospitals facing in the coming years, and how are we preparing at Smilow?

We take the accreditation process very seriously and have a terrific group of physicians, nurses, pharmacists, social workers, and leadership that participate in our quarterly meetings. One challenge that many cancer centers are currently facing is how best to address the changing needs of those who successfully complete their treatment and survive their cancer. This is a great problem to have. We are fortunate to have a strong survivorship program at Smilow, led by my colleague Dr. Tara Sanft. In this clinic, patients are able to spend time addressing concerns that are very different than those who are at the very beginning of treatment.

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Smilow Cancer Hospital

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A Comprehensive Cancer Center Designated by the National Cancer Institute

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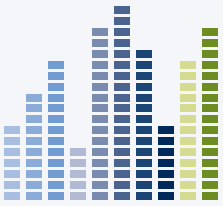

YALE CANCER ANSWERS

Yale Cancer Answers is celebrating 10 years! The weekly program provides listeners with information on the range of options for cancer treatment, prevention, screening, and supportive care. Hosted by cancer specialists from Smilow Cancer Hospital and Yale Cancer Center, each show features a cancer expert to discuss myths, facts, and advances in cancer diagnosis and treatment.

Yale Cancer Answers is consistently ranked in the top three rated podcasts on cancer on iTunes. To listen, visit iTunes or listen live on Sunday evenings on WNPR.

yalecancercenter.org/patient/answers