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Left to right Daniel DiMaio, MD, PhD; Joan Steitz, PhD; and I. George Miller, Jr., MD

Peter Baker photographer

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2 A 45 Year Legacy of Research and Collaboration

When Daniel DiMaio, MD, PhD, Joan Steitz, PhD, and I. George Miller, MD, pooled their talents to put together a 400-page application to the NIH back in 1975 on the "Molecular Basis of Cancer Virus Replication, Transformation, and Innate Defense," they never imagined it would became the longest-running program project grant at Yale, and the third longest at the NIH. Today, they celebrate 45 years of its success.

5 Advances for Patients with Sickle Cell Disease

In just under a decade, the Sickle Cell Program at Smilow Cancer Hospital has transformed care for patients and reduced emergency room visits by 60% and hospitalizations by 53%. Dr. John Roberts and Dr. Cecelia Calhoun are committed to continued improvements for their patients.

8 Keeping The Faith

Jeannette Marty is a familiar face at Smilow Cancer Hospital. Her multidisciplinary care team has supported her through many challenges over the last 15 years. Ms. Marty's resolute faith, resiliency, and optimism continually inspire those at Smilow who have traveled alongside her on her long and difficult health journey.

C director's letter

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submit your ideas...

Do you have an idea for a story you'd like to see featured in Centerpoint Magazine? Submit your ideas to: renee.aaudette@vale.edu



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Yale Cancer Center

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Editorial Office

Yale Cancer Center 2 Church Street South, Suite 312 New Haven, CT 06519 renee.gaudette@yale.edu The history of research at Yale Cancer Center is profound. Yale is perhaps best known as the institution where the field of cancer drug development was discovered and the very first cancer drug was administered in 1942. Yale Cancer Center was one of the first National Cancer Institute-designated Comprehensive Cancer Centers when it received approval in 1974, and our research strengths are deeply rooted in the laboratories throughout Yale University.

The longstanding leadership of prominent investigators like Daniel DiMaio, MD, PhD, Joan Steitz, PhD, and I. George Miller, MD, has created legacy programs at Yale Cancer Center that will impact cancer research for generations to come. For 45 years this trio has led a program project grant on the study of viruses, and their implication in cancer. The grant brought over \$50 million in funding to Yale laboratories and resulted in nearly 500 publications, including numerous groundbreaking advances in viral cancers and causes. As they sunset their program project grant, we reflect on the impact the leadership team has made.

One of our clinical initiatives is to improve care for patients with Sickle Cell Disease, which impacts 100,000 Americans, creating devastating pain and leading to frequent emergency department visits and hospitalizations. Since its inception, Smilow Cancer Hospital's Sickle Cell Disease Progam has reduced emergency department visits by 60% and hospitalizations by 53%, and the numbers continue to improve with the leadership of Dr. John Roberts and Dr. Cece Calhoun.



Meanwhile, Dr. Jane Kanowitz is focused on improving care for our older patients by implementing chemo-toxicity calculator assessments into treatment planning for patients over the age of 70. Initial data shows that the use of the tool provides an unbiased assessment of risk and gives patients the information to make an educated decision on treatment. The tool and data were recently presented at the American Society of Clinical Oncology Quality Care Symposium.

Our research and clinical missions continue to evolve at Yale Cancer Center and Smilow Cancer Hospital. Whether we are pivoting from one grant to focus on new areas of research, or we are implementing new clinical programs, our attention remains on improving the care and outcomes for our patients. I am proud of the success our teams achieve, and I know that they will quickly push forward with new breakthrough discoveries and innovative advances in the coming year.

Sincerely,

Nita Ahuja, MD, MBA

Interim Director, Yale Cancer Center

Interim Physician-in-Chief, Smilow Cancer Hospital

William H. Carmalt Professor of Surgery

Chair, Department of Surgery

Surgeon-in-Chief, Yale New Haven Health System



The first year that the National Institutes of Health (NIH) funded a group of Yale scientists to explore links between viruses and cancer, U.S. troops evacuated Vietnam, Gerald Ford was president, and the movie *Jaws* broke box office records. The scientists wrote their 400-page proposal on typewriters and made 20 paper copies on Xerox machines. They put it all into a big box and sent it through the U.S. mail. It was 1975.

Their research pleased the NIH so much that the agency renewed the grant—eight times over 45 years. Entitled

"Molecular Basis of Cancer Virus Replication, Transformation, and Innate Defense," it became the longest-running program project grant at Yale, and the third longest at the NIH. It brought more than \$50 million to Yale labs and resulted in nearly 500 publications, many of them groundbreaking. The grant helped launch the careers of hundreds of scientists who trained under its leadership, including several on the Yale faculty.

Three of the grant's principals are still at Yale: Daniel DiMaio, MD, PhD, Waldemar Von Zedtwitz Professor

of Genetics, Professor of Therapeutic Radiology, Professor of Molecular Biophysics and Biochemistry, and Deputy Director of Yale Cancer Center; Joan Steitz, PhD, Sterling Professor of Molecular Biophysics and Biochemistry; and I. George Miller, Jr., MD, John F. Enders Professor of Pediatrics and Professor of Epidemiology and of Molecular Biophysics and Biochemistry.

"The grant has had a major impact on how we study viruses," said Dr. DiMaio, the principal investigator for the last 25 years. "Otherwise, it wouldn't have lasted



so long. There's lots of competition out there. Every five years the NIH looked at us closely to see if we were still productive and still a good investment. For many cycles of renewal, they decided that we were."

After 45 years, he added, the grant's three leaders decided not to reapply. "We're sun-setting it. It's time to let a new generation take over." It is also time to applaud some of the grant's research highlights.

The human genome was sequenced about 20 years ago, but the first genome

ever sequenced was funded by this NIH grant almost 25 years earlier, when Sherman Weissman, MD, Sterling Professor of Genetics and the grant's first principal investigator described the genetic make-up of a virus named SV40. "He developed some of the earliest techniques for sequencing nucleic acids," said Dr. DiMaio. "That had a profound impact on medicine, and it came from studying tumor viruses."

Before his death in 2020, another biochemist on the grant, Charles M. Redding, MD, Professor of Genetics,

showed how DNA molecules can recombine to alter genes and proteins, which in turn can cause cancer—a crucial discovery. A former member of the program, David C. Ward, PhD, used the program funding to develop a technology called fluorescence in situ hybridization (FISH). It allows researchers to map chromosomes by locating specific DNA sequences and this technology is a standard diagnostic and research tool in labs worldwide.

Dr. Steitz is a founding member of the grant program, which helped fund



66 Their research pleased the National Institutes of Health (NIH) so much that the agency renewed the grant—eight times over 45 years. Entitled Molecular Basis of Cancer Virus Replication, Transformation, and Innate Defense,' it became the longest-running program project grant at Yale, and the third longest at the NIH."

> her landmark discovery of small noncoding RNAs made by viruses. "It turns out that RNAs aren't just messengers," she said, "but are also regulatory elements inside cells, and are important to be able to make an oncogenic virus. We've discovered a lot of noncoding RNAs, and each new discovery brings all sorts of insights into how viruses are able to successfully infect cells."

> "Joan didn't just discover them," added Dr. DiMaio. "She figured out how they work and discovered a lot of new chemistry and structural biology. It opened up a new field."

> Dr. Steitz identified some of those RNAs in collaboration with Dr. I. George Miller, another founding member of the program grant. At the time, scientists knew that viruses caused cancer in animals, noted Dr. Miller, "but nobody believed cancers in people were caused by viruses." Dr. Miller showed that Epstein-Barr Virus (EBV), a human virus, caused lymphomas in monkeys. This was the the first time a human virus had been shown to cause cancer in a primate, providing definitive evidence of its cancercausing activity. Researchers now know that about 15 percent of all human cancers are caused by viruses. The grant also supported Dr. Miller's groundbreaking discovery about how EBV gets activated.

Dr Miller and Dr. Steitz collaborated to characterize a related virus that causes Kaposi sarcoma.

The grant also supported Dr. DiMaio's pioneering research into identifying viral oncogenes, and how turning them off stops cancer cells from growing. More recently, the grant funded his studies about how viruses get into cells. "It sounds simple," he said, "but virus entry is a complicated process with hundreds of cellular proteins involved. We've discovered some cellular proteins that are important for infection, determined how they work to support infection, and learned some new cell biology."

These breakthroughs stemmed from the basic science supported by the grant. "Viruses educate us about every aspect of molecular biology and cell biology and immunology," said Dr. Miller. "We keep on learning things from viruses that are applicable to cancer and to many other problems. If you want to make vaccines, for instance, you have to understand what the virus is doing."

The grant brought together people from many departments. "We all look at virology from different perspectives," said Dr. Steitz. Dr. DiMaio is primarily a geneticist, Dr. Steitz a biochemist, and Dr. Miller a pediatrician. "When we get together," continued Dr. Steitz, "we have people coming in from many different disciplines and it's great."

Their collaborations introduced each other to different approaches and techniques that influenced the direction of their research. Dr. Steitz started with bacterial viruses, then moved into animal viruses after conversations with Dr. Miller. Dr. Steitz helped Dr. Miller understand the advantages of using modern molecular techniques instead of cultivating viruses.

"We've really transferred knowledge back and forth," said Dr. DiMaio. "That's something very special about this grant. We're not working in isolation; we helped each other and molded each other's careers."

In turn, the partners in this program grant have molded the careers of several hundred grad students and post-docs who were trained under them and are now making their own contributions to the field and paying it forward with their own students. "It's a long legacy," said Dr. DiMaio, "like a huge extended family."

"You can see evidence of that legacy in what's happening now with COVID-19," said Dr. Steitz, whose career helped us understand how RNA works. "A lot of work on the immunology of this disease was done here, and the most effective COVID-19 vaccines are RNAbased vaccines."

Advances For Patients With Sickle Cell Disease

Steve Kemper writer Peter Baker photographer

The majority of the 100,000 Americans who suffer from Sickle Cell Disease, an inherited blood disorder, are diagnosed at birth. Patients with sickle cell disease (SCD) grow up spending far too much time in hospitals and emergency rooms, debilitated by the severe pain that typifies the disease.

Newly approved drugs, like crizanlizumab a monoclonal antibody medication that reduces pain crises from reduced blood flow caused by SCD, are helping. Patient pain is much easier to manage at home and patients find they can once again participate in their daily family and work activities. "With advances like crizanlizumab, patients who respond may not be in the hospital again for years," said John D. Roberts, MD, professor of internal medicine and medical director of the Adult Sickle Cell Program at Smilow. "That's really gratifying."

When Dr. Roberts began his medical training in the late 1970s, children with SCD usually died from infections before age five. That dramatically improved after two innovations in the 1980s and 1990s: daily doses of penicillin for young children with SCD, and vaccination against pneumococcus.

"Now more than half of our patients are adults," said Dr. Roberts, "but people still die prematurely—between 45 and 55 in the United States, decades short of normal life expectancy."

Dr. Roberts was recruited to Yale in 2012 after the hospital committed itself to revamping its haphazard but typical approach to SCD. He built a new program that benefited patients in need of consistent services and a streamlined approach to care. The hospital's commitment was reaffirmed in July with the arrival of Cecelia Calhoun, MD, MPHS, MBA, Assistant Professor of Medicine, to direct Smilow's new Adolescent-Young Adult Sickle Cell Program. "Part of the gift of being here," said Dr. Calhoun, "is that people are really excited about ensuring our hospital is a welcoming to patients with sickle cell disease."

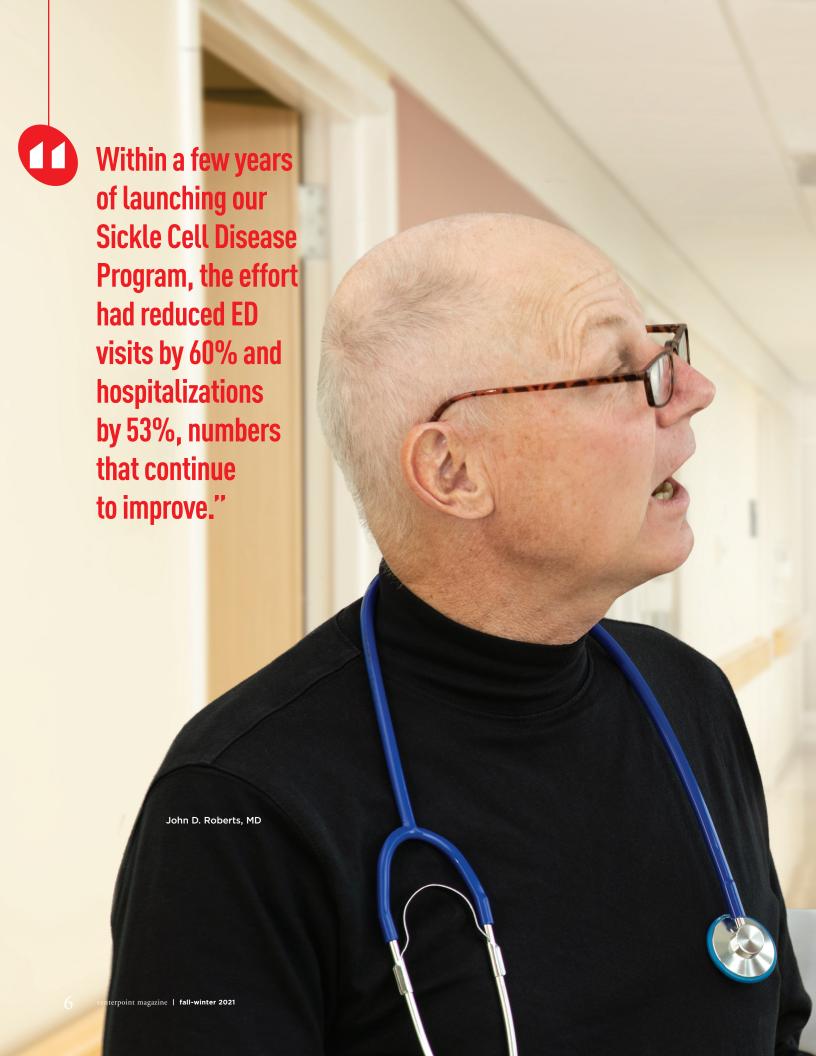
That isn't the case everywhere. The disease is often misunderstood, even by medical providers. Drs. Roberts and Calhoun listed some of the reasons. SCD is relatively rare, so providers encounter it infrequently and clinics dedicated to it are uncommon. Its main symptom is pain, both chronic and acute, and the best treatment is opioids, typically administered in an emergency department (ED). Inevitably, a small percentage of SCD patients become addicted, which has stigmatized the disease

"The main misunderstanding about SCD is that patients are just seeking pain medicine," said Joanna Cole, APRN, FNP-BC, a nurse practitioner who has cared for SCD patients at Smilow since 2012. "That's just not true. This is a legitimate disease with no cure, and our patients who come in are in pain. Some female patients describe it as worse than childbirth."

The misunderstandings are exacerbated by two related issues—race and poverty. In the United States, most patients are Black; most are also poor. The consequences are discrimination and poor access to healthcare. At Smilow, 80 percent of the SCD patients are on Medicaid, a reimbursement category avoided by many healthcare institutions.

Smilow Cancer Hospital leadership and Dr. Roberts wanted to change all that by replacing inconsistent episodic care in the ED or hospital with long-term outpatient care. Smilow opened a clinic devoted to sickle cell patients and staffed it with advanced practice professionals like Ms. Cole who were experienced to care for patients with SCD and opioid use. To help patients manage the social and psychological issues that accompany an incurable disease and constant pain, the clinic also includes social workers and a psychiatrist. The program's goals were to cut down on ED visits and hospitalizations by teaching patients to manage their pain at home.

It worked. Patients felt understood and more autonomous. Within a few years the new program had reduced ED visits by 60 percent and hospitalizations by 53 percent, numbers that have continued to improve. "In a typical year," said Dr. Roberts, "around 85 percent of our adult patients are not admitted to the





hospital." These days, if an acute episode sends a patient to the emergency room, the provider can look at the patient record for the recommended dose of opioids, and can reach out to the dedicated SCD providers.

The program cares for about 200 adults and 200 children, seen in side-by-side clinics at Smilow. Dr. Roberts is excited by the arrival of Dr. Calhoun, whose priority is to make sure those patients transition smoothly into adult SCD care.

Taking responsibility for one's healthcare is challenging for any young adult, noted Dr. Calhoun, but SCD adds the complication of a chronic disease. Young adults with SCD may find the healthcare system intimidating or may avoid the hospital because they feel stigmatized as drug-seekers. They may also be unsure how to navigate insurance

or a job or admission into college. Many young SCD patients are fatalistic and expect little in terms of a career or family.

"And it's just not true," said Dr. Calhoun. "We need to get them excited about their future while they're young. They can have a full life. We can't control things outside of the hospital, but we can reach out and wrap our arms around them to help them through those things at a pivotal time. It's a life's work for me."

The future does hold promise. Opioids remain the best option for acute episodes, but several other drugs, like crizanlizumab, now help patients with SCD manage their pain. And though the only current cure for SCD is a bone marrow transplant from a sibling who is also a complete genetic match, other curative innovations are on the horizon.

Drs. Calhoun and Roberts are excited by the prospect of bringing such trials to

Yale. Dr. Calhoun is confident that the personal relationships built between Yale's SCD providers and patients have formed the trust necessary to enroll participants in trials. She wants to expand that relationship into the community, to educate people about SCD.

"Awareness is such a critical part of making things better," she said, "especially for young people trying to fit in. As we get new therapies and we learn how to treat sickle cell better, it's important for them to be able to say, 'Yeah, I have sickle cell disease and sometimes I have bad pain but I'm still able to do what I want.' How empowering is that? It's not an overnight thing. It takes a consistent and continuous investment, but it has tremendous returns. When you can help people stay alive, what better return is there?"



Antisynthetase syndrome is a rare chronic autoimmune condition that affects multiple parts of the body. For Ms. Marty, it has been linked to diagnoses of both breast and cervical cancer. It has caused myositis, a painful inflammation of the muscles used to move the body, especially her legs. It has affected her esophagus, making it difficult to swallow, and impacts her liver and lymph nodes. It has made her highly susceptible to infections from even minor things, such as a bug bite or cut on her finger. And it has especially impaired her lungs. She has been on oxygen for eight years and has been pursuing a double lung transplant for even longer.

"My diagnosis is difficult because I don't fit in anywhere," she said. "There are support groups for specific cancers or autoimmune diseases, but I have a multitude. I'm grateful that Yale and Smilow have been able to treat me for all of them."

A COMPREHENSIVE CARE TEAM

Ms. Marty's care team spans multiple specialties: immunology, pulmonary, liver, oncology, and pain management. Hari Deshpande, MD, Associate Professor of Medicine (Medical Oncology), was among the earliest members of Ms. Marty's care team. In fact, his initial consult with her predated the opening of Smilow Cancer Hospital by three years. "Unfortunately, Jeannette's condition doesn't have a cure, so we're trying to slow the disease down and stop it from progressing as long as we can," he explained.

Chemotherapy has been part of her treatment regimen from the beginning. However, after many failed trials of various chemotherapy treatments, the combination of the immunotherapy IVIG and chemotherapy rituximab is the regimen that finally helped stabilize her condition. "It helps me function and be able to do things with my family," she said. With her portable oxygen concentrator in tow, she has hiked in New Hampshire and visited friends in New York City and Puerto Rico. She was able to take her dream trip, a Caribbean cruise, with her husband, Angel, and their three children. "I orchestrated adventures for them to have together," she said, "and I found a nice corner in the spa where I could just sit and stare at the ocean. I felt very much alive."

But when her condition flares, it can be too painful to even get out of bed. "My muscles get so inflamed that my legs feel like lead pipes," she explained. At times, she has needed to use a wheelchair to get around. Andrew Putnam, MD, Assistant Professor of Medicine (General Medicine), has long been the pain specialist on Ms. Marty's care team. He has worked with her over the years to find the right medications to reduce her pain. "Jeannette has persevered through major disappointments and hardships and continued with good humor," said Dr. Putnam. "She never gives up and is always hoping that something better is coming around the corner."

FAITH THROUGH LIFE'S STORMS

As a pastor, Ms. Marty credits her faith in God as the anchor that helps her "rise above the ongoing raging life storms," as she wrote in a reflection that she contributed to a Yale New Haven Health publication titled, *Spirituality Through Our Struggles: Patient Stories, Reflection and Prayers*.

"With a poor prognosis like mine, it feels like a clock is over your head saying, 'Time is ticking.' There is so much uncertainty," she said. "It's important to keep living in spite of all of that and to have faith, because without faith the alternative is bitterness, anger, and frustration."



Ms. Marty and her husband had already discussed a future that she might not be a part of. But then the greatest storm yet raged into her life: Angel died suddenly in January 2019. Ms. Marty's care team rallied around her. "They cried with me, which is very telling," she said. "People can offer empathy, but to have someone cry with you and step into that pain with you is beautiful."

She found tremendous support from Dwain Fehon, PsyD, Chief Psychologist for Psychiatric Services at Yale New Haven Hospital and a longtime member of her care team. "With Dr. Fehon, I have a place and person where I can share my emotions," she said. "He has been such a big help to me."

"Jeannette is an amazing person," Dr. Fehon said. "She has such a generous spirit, to give of her time so that others can understand and be more knowledgeable and empathetic with their own patients."

Ms. Marty continues to receive a combination of immunotherapy along with chemotherapy while looking for more resources to remain stable or halt progression. Every time she enters Smilow, she's comforted knowing that familiar faces are there to greet and treat her. "The support I receive at Smilow is a gift. I would not have come this far without this team."

forefront



A Chemo-toxicity Calculator for Older Patients

he powerful toxins delivered in chemotherapy are designed to kill cancer and save lives. But for older patients, those toxins carry a higher risk and may be intolerable. On the other hand, age alone is not a trustworthy indicator of risk, nor does a healthy appearance necessarily mean that an older patient has the physical and mental ability to endure a full regimen of chemotherapy. Oncologists faced with these risks and unreliable markers may be reluctant to offer chemotherapy to older patients who could benefit from it, or may offer it in dosages that do more harm than good.

The Cancer and Aging Research Group (CARG), a national association of geriatric oncology researchers, has developed a validated tool to help physicians and patients make informed decisions about chemotherapy for patients over the age of 70. CARG's "chemo-toxicity calculator" was recently tested in a six-month study at 15 Smilow Cancer Hospital Care Centers as part of an American Society of

Jane Kanowitz, MD, consults with her patient at the Smilow Cancer Hospital Care Center in North Haven.

Clinical Oncology Quality Initiative. The team that designed and ran the study expects the tool to change the way chemotherapy is managed for older patients throughout the Smilow Cancer Hospital Network.

The tool consists of eleven questions asked before a patient over 70 first receives chemotherapy. The provider and patient complete the form together in about five minutes. Some questions are factual: the patient's age, cancer type, levels of hemoglobin and creatinine, and the proposed treatment schedule (doses and type of treatment). Other questions address the patient's ability to function: hearing, balance (how many times has the patient fallen in the past six months?), mobility (can the patient walk one block?), autonomy (can the patient self-administer medicine?), and limitations on social activities caused by physical or emotional difficulties. The tool then calculates the patient's risk on a scale from 0 to 23.

"The tool predicts the risk of toxicity, the risk of hospitalization, and the need to either lower the dose of chemotherapy or change the treatment plan," said Jane Kanowitz, MD, Principal Investigator of the study and Assistant Professor of Clinical Medicine (Medical Oncology) and Medical Director of the Smilow Cancer Hospital Care Center in North Haven.

The tool also neutralizes unconscious biases that can affect treatment. "Oncologists who have been in practice for decades have come to rely on their clinical judgement and were surprised by the calculator's predictive risk in some patients," said Paula Pike, RN, BSN, MSN/A, MBA/HC, NE-BC, Clinical Program Manager for the Smilow Cancer Hospital Network, and a member of the project team. "Some participants were really surprised at what the tool stated for predicted risk."

The medical literature suggests that physicians overestimate or underesti-

mate how well someone will do on chemotherapy about a third of the time. "That's substantial," said Dr. Kanowitz. "I've been using this tool for years and I'm still sometimes surprised when someone is predicted to do better or worse than my perceptions of them. The tool filters out those biases so we don't overtreat or undertreat people."

"Oncologists have been ingrained with the certainty that prescribing chemotherapy is better than doing nothing," she noted. The CARG calculator is intended to provide a more nuanced view. "It also gives patients and their families a better understanding and allows them to make educated decisions for themselves," Dr. Kanowitz said. "For instance, 'I might live longer but I'm not going to live better, and I'm not sure that's what I want." The tool also makes it easier to have the difficult conversation about treatment, added Dr. Kanowitz, because the risk calculation is based on objective information, not on the opinions of the doctor or patient.

The team is still analyzing data from the study, but using the calculator clearly altered treatment plans. Half of the patients in the study received a lower dose or a different treatment following use of the tool. In a few cases, very high scores led to a mutual decision to forego chemotherapy for palliative care. Ms. Pike recalled a case where an oncologist had been certain that a patient was too frail for chemotherapy, but the tool predicted low risk. The oncologist prescribed the full dose and the patient tolerated the treatment well.

The project team also surveyed Smilow's oncologists about the tool. About 80 percent called it valuable for making decisions about treatment, and 75 percent said it helped them discuss the risks of chemotherapy. Dr. Kanowitz and Ms. Pike expect the final data to make a definitive case for using the CARG calculator despite the additional few minutes it adds to a patient visit.

"I think the data will show that using the tool can keep people out of the hospital," said Ms. Pike, "and also puts the patient at the center, which helps us learn what's important to them and to prepare a treatment plan that meets their goals of care." ()

"I've been using this tool for years and I'm still sometimes surprised when someone is predicted to do better or worse than my perceptions of them.

The tool filters out those biases so we don't overtreat or undertreat people."

–Dr. Jane Kanowitz





Giving Traction to Great Ideas

F

or Andy Morse, Yale College Class of 1968, his pride in his alma mater and a lifelong curiosity about scientific research led to admiration and support of the vital work of Yale Cancer Center.

Managing Director of the Morse, Towey & White Group at Hightower Investments, a wealth management firm in Manhattan, Mr. Morse has travelled widely during his finance career. He sits on the Board of Governors of the Weizmann Institute of Science in Rehovot, Israel.

The Institute's mission to advance science for the benefit of humanity mirrors that of Yale Cancer Center.

"Yale is one of those magical places, and there aren't many of them, that has tremendous intellect and heart, which are strikingly evident at its Cancer Center," said Mr. Morse. He serves on the Cancer Center's Advisory Board, a group of volunteers who

Iris and Andy Morse

"When I first started talking with the Center's staff, I was bowled over by their sense of urgency for the mission and extraordinary devotion to both research and clinical care."—Andy Morse

assist the Center in achieving its goals and objectives.

He applauds the Center's unwavering commitment to patient care and science, citing its move at the pandemic's beginning to relocate Smilow Cancer Hospital patients to other Yale hospital facilities to accommodate patients with COVID-19 in need of care.

"When I first started talking with the Center's staff, I was bowled over by their sense of urgency for the mission and extraordinary devotion to both research and clinical care," said Mr. Morse. "They are not just smart men and women; they are decent, astounding people from countless countries and walks of life. The Center's urgent response was both elegant and seamless."

Yale Cancer Center, laser focused on its mission and abiding desire to help people, inspired Mr. Morse and his wife Iris, a long-time cancer survivor. The couple established the Iris and Andrew Morse Fund for Cancer Research.

Driven by Mr. Morse's interest in the microbiome and Mrs. Morse's desire to support the life sciences, in its first year, the Fund will focus on Yale Cancer Center researchers investigating the microbiome's role in cancer development, growth, and treatment.

Host to bacteria, parasites, fungi and viruses known as microbiota or microbes, a healthy microbiome helps the human body function and develop immunity against disease. Recently, a growing body of research has begun exploring the impact of the microbiome—often considered an organ because it is so essential for certain diseases and their treatment, including cancer.

"We're seeing that trillions of bacteria and other microorganisms throughout our body may stimulate cancer formation," said Yale Cancer Center Deputy Director, Daniel DiMaio, MD, PhD, Waldemar Von Zedtwitz Professor of Genetics and Professor of Molecular Biophysics, Biochemistry and of Therapeutic Radiology. "In addition, the microbiome clearly affects the effectiveness of treatments like immunotherapies and chemotherapies on certain cancers for certain people."

In Fall 2021, the Morse Fund will support two to three internal pilot grants for studies on the interplay between the microbiome and cancer. "This is a relatively new area," said Dr. DiMaio. "Yale has a few people working on it, but we're really at the starting line. Andy and Iris's support will jumpstart new areas of research."

In science, funding at the earliest stages of investigation is vital to springboard new discoveries. The National Institutes of Health and other large institutions typically fund studies when they are more well developed—

when, Dr. DiMaio said, essentially many of the answers are already known. The Morses wanted to go where larger funders traditionally don't.

"Andy asked from the beginning what would be most useful," said Dr. DiMaio. "And the pilot funding is always vital. A lot of really good ideas have difficulty gaining traction because they are risky. When we have flexible funds, we can try risky things that may someday lead to important breakthroughs."

On Mr. Morse's part, his comfort with such risks goes back to curiosity and trust in people and process: "With any great advance or discovery, you've got to give people room to make it happen. The Yale Cancer Center team has a strong sense of virtue and commerce. They want to develop breakthrough drugs for cancer. They make no bones about it, and it's all for a good reason. This is the type of risk I am proud to get behind. I always encourage my Yale classmates to approach giving in the same way."

Said Dr. DiMaio of Mr. Morse's perspective, "Andy is successful because he is a risk taker, a visionary. He's a fantastic example of how one person can influence a broader understanding of cancer and lead to better treatments and outcomes."



January 1, 2021 - June 30, 2021

- Valentina Greco, PhD, received the 2021 Momentum Award from the International Society for Stem Cell Research.
- O Joan Steitz, PhD, was named a Wolf Prize Laureate in Medicine
- Chrystal Starbird, PhD, a postdoc in the Cancer Biology Institute laboratory of Kathryn Ferguson, PhD, has won one of the inaugural Rising Black Scientist Awards from CellPress.
- Stephanie Halene, MD, PhD, was awarded a 2-year, \$250,000/ year grant by the Vera and Joseph Dresner Foundation entitled "Exploiting DNA repair defects in IDH mutant MDS via combination therapies."
- Ranjit Bindra, MD, PhD, received a grant for \$150,000 from The Andrew McDonough B+ Foundation to support his team's research on targeting NAD metabolism in pediatric brain tumors.
- Laura J. Morrison, MD, FAAHPM, received the 2021 American Academy of Hospice and Palliative Medicine Gerald H. Holman Distinguished Service Award.
- Prasanna Ananth, MD, MPH, was awarded a K08 Career
 Development Award from the National Cancer Institute to support
 her research project, "The Pediatric Advanced Cancer Experience
 (PACE): Measuring Quality of End-of-Life Care for Children with
 Cancer."
- Lieping Chen, MD, PhD, was elected as a Fellow of the American Association for Cancer Research Academy.

- Michaela Dinan, PhD, was awarded a Research Scholar Grant from the American Cancer Society to fund her research project, "Development of Cancer Survivorship Risk Models to Inform Pathways of Care."
- Nikolai Podoltsev, MD, PhD, and Xiaomei Ma, PhD, received a generous three-year award from The Frederick A. DeLuca Foundation. Other collaborators include Caroline Johnson, PhD, Andrew DeWan, PhD, MPH, and Rong Wang, PhD.
- FRCS(C), were named Fellows of the American Society of Clinical Oncology (FASCO).
- Thomas Prebet, MD, PhD, received a UM1 Supplement from the National Cancer Institute to fund his research project, "Integration of single cell sequencing as a biomarker of PARP inhibitor response for IDH1 and IDH2 mutated AML and MDS."
- Maryam Lustberg, MD, MPH, received a grant from the Alliance for Clinical Trials in Oncology to support her proposal, "PIN ALLIANCE: Power in Numbers using Harmonized GWAS and Toxicity Data."
- Pershing Square Sohn Prize for Young Investigators in Cancer Research, a prestigious award from the Pershing Square Sohn Cancer Research Alliance.

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\$1,000,000 and above

Jeremiah M. Bogert and the Milbank Foundation Louis and Debra Chênevert The Frederick A. DeLuca Foundation

\$500,000 - \$999,999

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Smilow Cancer Hospital Care Center at Waterbury

CENTER AT A GLANCE

- A patient-centered focus on exceptional cancer care
- Over 1,200 patient visits per month in medical oncology
- 900 infusion visits per month
- 40 staff members
- Oncology Certified Nursing Staff
- Multidisciplinary clinics with Smilow Cancer Hospital surgeons specializing in lung cancer and gynecological cancers
- Nutritional Counseling, Genetic Counseling, Social Work, Palliative Care, Tobacco Cessation, Patient Navigation, Healing Garden

The Smilow Cancer Hospital Care Center *in Waterbury partners with community* physicians to provide oncology care to our patients. We offer full access to clinical trials through Yale Cancer Center, the only National Cancer Institute designated comprehensive cancer center in Connecticut, and multidisciplinary cancer care with support from our dedicated patient care team.

— Dr. Anamika Katoch, Medical Director

SMILOW CANCER HOSPITAL CARE CENTER AT WATERBURY

1075 Chase Pkwy, Suite B Waterbury, CT 06708

Phone: (203) 755-6311

Victor Chang, MD Frank Detterbeck, MD Anamika Katoch, MD **Dmitry Kozhevnikov, DO** Elena Ratner, MD Kert Sabbath, MD Karen Hammond, APRN Stacey LaRosa, APRN, AOCNP



Bohdan Pomahac, MD

Professor of Surgery Chief, Plastic & Reconstructive Surgery

You are a pioneer in the field of plastic & reconstructive surgery, most notably having performed the first face transplant in the United States and the first bilateral upper extremity transplantation in the Northeast. For patients cared for at Smilow Cancer Hospital, what current research will bring new innovation to our operating rooms?

There are many areas of cancer reconstruction where innovation is leading care. New indications, new technologies, and new problems all translate into plastic surgery practice and drive innovation in our field. To name one, soon Smilow Cancer Hospital will launch a new program in lymphatic surgery to help patients who have developed lymphedema as a complication of their cancer treatment. In addition, our plastic surgeons are here to support new programs, such as the oncologic spinal surgery team. We are an active part of the multidisciplinary teams taking care of patients with cancer. Whether it is a new clinical trial or a new technology, we are here to support the care of our patients throughout their treatment.

There are many options available for women needing breast reconstruction. How do you help your patients determine the best type of reconstruction for them?

There are many options and as I tell my patients, there is typically no one right or

There are many options and as I tell my patients, there is typically no one right or wrong choice. Everyone has to decide based on their personal preferences and stage of their life, and we as physicians can provide insight from the perspective

of future cancer treatment, patient's body physique, and other factors. Smilow Cancer Hospital has organized webinars to provide updates on breast cancer treatment and care, including reconstructions, and we are organizing pre-operative information sessions to connect new patients with those that went through the process in the past.

The final plan for each patient is a result of dialogue between the patient's physicians and the patient, where both sides learn more about the other one's perspective. Patients should feel well informed prior to making their final decision.

Planning for reconstructive surgery is a multidisciplinary effort. How do you and your colleagues integrate into the team of medical, surgical, and radiation oncologists and other specialists delivering patient care?

This is where Smilow is truly unique. Most of the time, our entire multidisciplinary team is in the same location during patient appointments and evaluation, and communication and conferencing together occurs in real time. We are working on an even better and more seamless system for the near future. COVID has put some restraints on our physical space, but as the pandemic is diminishing, our ability to bring our teams back together will improve. Our multidisciplinary team is growing in all disciplines, including plastic surgery. We are focused on the diversity of our faculty to reflect the diversity of the patient population we help to take care of. Patients are in good hands at Smilow!

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