

Yale Cancer Center

centerpoint

MAGAZINE

Faith, Family,
and a Second Chance

SMILOW
CANCER
HOSPITAL
CELEBRATING TEN
YEARS
OF PATIENT CARE

fall | winter 2021

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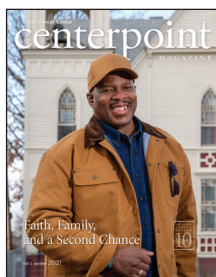


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On the Cover

Walter Pearsall, lung cancer survivor, photographed outside his church, New Light Holy Church in New Haven, CT.

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director's letter

yale cancer center

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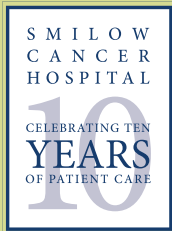
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submit your ideas...

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



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MAGAZINE

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Yale Cancer Center

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The arrival of COVID-19 in Connecticut early in March has sharpened our awareness of many things, but our focus on providing safe, patient-and family-centered cancer care has never wavered. The dedication of Yale Cancer Center and Smilow Cancer Hospital's providers and staff has never shined brighter than over the last ten months, and each day I am truly honored to lead such an inspiring cancer community.

Our research laboratories continued to rise above the challenges of 2020, and closed the year with direct funding of \$107 million, our highest level of research funding ever. Dr. Andre Levchenko's efforts to better understand and ultimately prevent cancer metastasis through collaborations with colleagues in diverse specialties at Yale West Campus Systems Biology Institute will undoubtedly make a positive impact on patients with advanced disease in the coming years. While cancer research will always be our first priority, the study of the SARS-CoV-2 virus, and its impact on our immune system has also become paramount. Dr. Akiko Iwasaki's international leadership and research in this arena will further propel our understanding of the virus.

Stories from patients like Walter Pearsall, who credits Smilow Cancer Hospital and his oncologist, Dr. Anne Chiang, for a second chance at life, provide us all with hope and optimism. Mr. Pearsall received a frightening stage III lung cancer diagnosis and arrived at Smilow for a second opinion after being told he needed surgery. He is now six years out from successful treatment at Smilow and has no evidence of cancer! Mr. Pearsall is grateful to be looking ahead to life with his wife, 13 children, and 22 grandchildren, and he will soon become a Deacon in his church.

2020 challenged each and every one of us, but I truly believe that our entire cancer enterprise emerged stronger as a result. Yale Cancer Center and Smilow Cancer Hospital will continue to push forward with breakthrough discoveries and hope for healing, together.

Sincerely,

A handwritten signature in black ink that reads "Charles Fuchs".

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





Family, Faith, and a Second Chance

Emily Montemerlo writer **Peter Baker** photographer

Back in 2014, Walter Pearsall noticed some blood when he coughed, but he had not experienced any other symptoms or indications that something serious might be wrong. His wife immediately brought him to the local ED where they ran tests and ultimately gave him devastating news, in front of his wife and some of his children, that he had lung cancer and most likely would not survive. He stayed in his local hospital for ten days and the team there confirmed his diagnosis as stage IIIA non-small cell lung cancer (NSCLC) and recommended surgery, but told Walter they would need to remove some of his ribs in order to access the area.

With that knowledge, his wife Lethie suggested they get a second opinion and they soon found themselves in the hands of the Thoracic Oncology team at Smilow Cancer Hospital. The Yale team determined that he was not in fact a candidate for surgery due to several factors including extensive arterial involvement. Walter and Lethie soon met with Anne Chiang, MD, PhD, Associate Professor of Medicine (Medical Oncology) and Chief Network Officer and Deputy Chief Medical Officer of the Smilow Cancer Network. Dr. Chiang specializes in lung cancer treatment, and offered Walter another option that did not require invasive surgery, or a death sentence; a combination of chemotherapy and radiation delivered over five months. For Walter and his wife, this news, and Dr. Chiang, were a blessing. The Interventional Oncology Program team performed a bronchial artery embolization to stop the bleeding that Walter was experiencing so he could begin this curative treatment option.

“We are fortunate that we have a terrific multidisciplinary team that meets weekly to discuss our patients. That way, we can determine very quickly what the best combination of surgery, radiation, or systemic therapy is, and other specialty services that enable us to administer these treatments safely and with little side effects,” commented Dr. Chiang. “Today, we would add immunotherapy to the regimen we offered Mr. Pearsall, which shows how quickly the field is advancing. He is now beyond five years out from treatment and free of disease.”



“*Dr. Chiang is the best doctor there is. She saved my life, and I'm not sure where I would be without that second opinion, but it doesn't matter because I am here, thanks to my family and the wonderful team at Smilow.*”

Starting with his very first chemotherapy session, Walter documented his progress in photos. Six years later and still in remission, Walter has no lasting side effects other than scar tissue from the radiation and some anxiety. After instituting healthy lifestyle changes, Walter is living a full life and spending time with his 22 grandkids. He also joined a support group and makes an effort to encourage other patients. The group is now being held virtually, but Walter continues to benefit and share his story with others to give them hope that yes, they can beat this.

Halley Robinson, Licensed Clinical Social Worker for the Thoracic Oncology Program commented, “I have to admit, when we transitioned the group to Zoom, I worried about whether or not the members would continue participating in the same way, but we have thrived in this platform. We are fortunate to have members like Walter, who have faced the uncertainty of a new cancer diagnosis, undergone the stressors and side effects that are commonly associated with treatment, and now, six years out, are thriving. Walter recognizes and validates the difficult days that one might face with lung cancer, while also offering hope.”

“I won't lie, it was a long, tough road, but the only time I spent in the hospital were those first ten days. I was able to go home after treatment and recover which was so important to me,” said Walter. “I have 13 children and they took turns, along with my wife Lethie, bringing me in for treatment. I am so thankful that I had that support system. I was scared and lost a lot of weight, lost my hair, and was very fatigued. My doctors took excellent care

of my physical needs, and my family and faith took care of me mentally and spiritually.”

The five-year overall survival for stage IIIa disease is roughly 25% and the further out Walter gets, the better his odds, explained Dr. Chiang. “He is doing extremely well, and we have every hope and confidence that he will continue to do well.”

Before COVID, Walter and Lethie loved to travel, and plan to do so again once it is safe. “I come from a military family and have lived all over the world including Alaska and England. I enjoy sharing stories of my childhood with my kids and grandkids,” said Walter. “They were my reason for fighting; they still need me and I was not ready to leave them. People would always say to me, ‘those grandkids are like medicine to you,’ and they were right. They didn't fully understand what I was going through, but the love from them kept me going through the darkest times. In a way, they helped save their ‘Papa.’”

Walter is currently on his way to becoming a deacon in his church, New Light Holy Church in New Haven, and at the age of 63 feels that he has a second chance at life. “Dr. Chiang is the best doctor there is. She saved my life, and I'm not sure where I would be without that second opinion, but it doesn't matter because I am here, thanks to my family and the wonderful team at Smilow. I told my kids not to feel sorry for me, but to pray for me and to treat me like they always had. I am through the storm now and want to be there for others to show them they can get through it too.”



Fresh Eyes on Metastasis

Jenny Blair writer **Peter Baker** photographer

When cancer kills, it's usually because the tumor has spread, or metastasized. Understanding how metastasis works could offer new ways to get malignancies under control. But the process is fantastically complex—more than any one discipline of science can encompass.

To tackle the problem of metastasis, Andre Levchenko, PhD, the John C. Malone Professor of Biomedical Engineering and Director of the Yale Systems Biology Institute at Yale West Campus, connects researchers working in such different areas that they would not ordinarily even cross paths. Thanks to their resulting conversations, he and his colleagues have made several discoveries that could one day lead to effective blocks on cancer spread.

“We consciously put together a group of people who include physicists, mathematicians, chemists, and people who may not even initially have known a lot about cancer,” Dr. Levchenko said. “This very interdisciplinary approach started paying off pretty quickly in new and unconventional approaches.”

To leave their tissue of origin and adopt what Dr. Levchenko calls the “more adventurous lifestyle of invading the surrounding tissue,” cancer cells have to overcome a series of hurdles. The cells first have to stop multiplying, their inner workings prioritizing “go” over “grow.” They must push their way into the circulation, travel, then exit to set up camp in a new place. All the while, they must evade destruction by the immune system and cancer drugs.

THE WAR ON CANCER WAS DECLARED IN THE 1970s. WE'VE MADE A LOT OF PROGRESS, BUT THE WAR IS NOT WON YET. AND I THINK, FREQUENTLY, PROGRESS COMES FROM VERY UNEXPECTED QUARTERS.

Understanding these changes in behavior requires a careful analysis of the many interacting molecules that trigger them, Dr. Levchenko explained. This understanding should be based on careful modeling of the complex tumor niches to permit both scientific exploration and discovery of interventional targets.

One such discovery required the use of biomedical engineering techniques. His lab developed a surface covered with microscopic ridges that mimics the 3-D environment metastatic cells encounter. When the researchers put cells from brain tumors onto these surfaces, surprisingly they observed that the tumor cells allowed them to accurately predict tumor recurrence in the clinic based on individual cells from actual patients with brain cancer.

Another technique emerging from the interdisciplinary approaches at the institute could greatly speed cancer drug development. Efforts by pharma companies are hampered by the fact that many molecules key to cancer progression are “difficult targets”—proteins whose function and chemical activity are not clear, making it difficult to use the conventional drug development techniques.

In a stroke of insight, a team that includes Farren Isaacs, PhD, and Jesse Rinehart, PhD, at the institute used the techniques of synthetic biology, which can create artificial DNA, to change those proteins in small ways. Those proteins whose tweaks made them biologically active could, in turn, be rapidly tested against thousands of molecules that could inactivate them. A molecule that does so—for instance, one that proves able to block a protein crucial to metastasis—could form the basis of the next breakthrough drug. This led to identification of new drug candidates for brain cancer.

Another way to look at cancer spread involves studying not just the bad actors, but the enablers: Nearby non-cancerous cells and proteins that allow metastasis to take place. That line of thinking informed another of Dr. Levchenko's discoveries, which began with a conversation about the placenta. On walks around Yale West Campus, he and evolutionary biologist Günter Wagner, PhD, the institute's previous acting director, began to talk about the fetal organ that allows for nutrient, waste, and gas exchange. Dr. Levchenko recalled noting several eerie parallels.

“The more Günter was telling me about the placenta, the more I was telling him that it looks very much like cancer,” Dr. Levchenko said. “It causes an immune reaction that is suppressed by the mother. It's very invasive, in humans at least. It causes blood vessel growth. If you look at molecules that are involved in placental growth and development,” he added, “they're very much the same molecules you find in tumor growth and invasion of tumor cells.”

But not all placentas behave this way, as it happens. In humans, the placenta invades the uterus far more than it does in many other animals. What's more, researchers have noticed that animals with less invasive placentas are less likely to experience malignant cancers, and vice versa.

“In horses, where the placenta is not very invasive, melanoma—one of the most invasive and metastatic tumors in humans—turns out to be completely non-metastatic,” Dr. Levchenko said.

We still don't know why this is, but Drs. Wagner and Levchenko believe that uterine cells hold a clue. In humans, uterine cells permit placental invasion in much the same way that fibroblasts do. Fibroblasts form the structural framework of our tissues.

To explore this lead, Dr. Levchenko and his colleagues examined differences between cells in cows—which, like horses, are relatively resistant to malignancies—and humans. Those differences, they found, occur not so much in the invasive cancer cells, but in nearby, non-cancerous structural or “stromal” cells. Human stromal cells allow the tumor cells to pass. Bovine stromal cells do not.

Dr. Levchenko compared the situation to an invading army. “Sometimes you have a local population welcoming the army, and sometimes the local population will put up a lot of resistance. In humans, we have stromal cells that are throwing flowers, so to speak, on the invading cells.” In cows, by contrast, “they were putting up walls in the way of these invading cells.”

The researchers teased out which molecules differed between the species, then they tweaked those molecules in human cells in the laboratory. Those changes made the human cells resistant to tumor invasion.

“We learned how to essentially educate the cells to be more resistant to invasion—and so we immediately had some interesting targets for drug development,” Dr. Levchenko explained.

The placenta-metastasis connection “was completely out of the box, an example of how you start thinking about things in an unconventional, orthogonal fashion,” Dr. Levchenko said.

These scientific synergies take place not just within the Systems Biology Institute, but also with researchers at the Cancer Biology Institute and Yale Cancer Center. In fact, Dr. Levchenko said, while his lab research into metastasis has been productive, it is important to stay grounded in clinical relevance, “to make sure that what we do is going to be useful.”

So he and his colleagues—from engineers to computer scientists to physicists to synthetic and evolutionary biologists—also collaborate with cancer physicians who care for patients with tumors like glioblastoma, pancreatic carcinoma, and melanoma.

“The war on cancer was declared in the 1970s. We've made a lot of progress,” he said. “But the war is not won yet. And I think, frequently, progress comes from very unexpected quarters.”



Andre Levchenko, PhD



Akiko Iwasaki, PhD

Understanding Immune System

Jenny Blair writer Peter Baker photographer

A bewildering puzzle of COVID-19 is why the virus affects people so differently. Though older men seem to fare worst in the face of infection with SARS-CoV-2, younger people may unpredictably falter, too. Moreover, many people develop long-term symptoms. We don't yet understand why.

But for Akiko Iwasaki, PhD, the Waldemar Von Zedtwitz Professor of Immunobiology and Molecular, Cellular and Developmental Biology, pieces of the puzzle are emerging. Genetics, gender, and even botched timing on the part of the immune response all appear important. What she learns could help us better predict who is likely to sail through a bout with COVID and who may need targeted lifesaving care.

There's a lot of variation in how the human immune system mounts a defense against coronavirus. For a group of people hospitalized with either moderate or severe COVID-19, Dr. Iwasaki's team recently mapped out those differences in a study that appeared in *Nature*.

Among patients with moderate disease who recovered, proteins involved in tissue healing and repair were relatively abundant. By contrast, among those with worse disease, the cytokines were more mixed, showing up in combinations that are unusual for viral infection. More people died in that group.

Based on these immune signatures, the researchers were able

to distinguish the patients' disease trajectories. Further data from a larger study, Dr. Iwasaki said, could help doctors predict a patient's course of disease and formulate tailored therapies.

One of the immune system's early defenses is a group of proteins called type I interferons. Produced by immune cells in response to viruses, interferons are key to the body's initial, rapid defense against coronavirus. But some people make too much of it, others not enough, and still others neutralize it with autoantibodies—and that makes a difference.

"In the early phase of the infection, if you can generate robust interferon, you will control the virus because interferon will trigger all these antiviral genes," Dr. Iwasaki explained. That is likely how people with asymptomatic or mild disease keep it under control, she added.

On the other hand, if the immune system doesn't create interferon soon enough, the virus can replicate undisturbed. Later, caught off guard by uncontrolled viral replication, the immune system may respond by manufacturing large quantities of interferon.

But by that point, it might be too much of a good thing. Massive amounts of interferon can drive inflammation, which in turn recruits white blood cells to the lung and make disease worse, Dr. Iwasaki described. Patients with more severe

COVID-19 have been observed to have higher levels of interferon. “What I’m hypothesizing now is that the timing of the interferon really matters,” Dr. Iwasaki said.

Another group of people with severe COVID-19 do not mount an interferon defense at all, Dr. Iwasaki and co-author Eric Meffre, PhD, Associate Professor of Immunobiology and of Medicine (Immunology), and a Yale Cancer Center member, explained in a recent commentary in *Nature*.

For example, a recent study of 659 people with life-threatening COVID-19 found that 23 had mutations in genes known to be important in severe viral infection. These mutations left the individuals unable to either produce or to respond to interferon. By contrast, in 534 people with milder cases, only one had such a mutation.

Another study found autoantibodies against interferon in some people with severe COVID, most of them older men. That finding may help explain men’s overall heightened vulnerability to the disease.

Dr. Iwasaki also uncovered another such gender-based difference in work she published in *Nature* with viral epidemiologist Saad Omer, MBBS, MPH, PhD, of the Yale School of Medicine

at Yale Cancer Center and Smilow Cancer Hospital and a member of the IMPACT team, is leading the sample collection from cancer patients with COVID-19.

“This is the only way we could do our research,” Dr. Iwasaki said of the biorepository. Thanks to these patient samples, Dr. Iwasaki, Dr. Herbst, and others are also able to study how cancer status affects COVID-19.

Understanding cancer patients’ experiences with COVID-19 may help us better understand the immune system, Dr. Iwasaki explained. Some types of cancer appear to make people more susceptible to severe COVID-19, while many cancer therapies interact with specific steps in the immune response—an effect that may alter the course of COVID-19.

Cancer immunotherapy has also illuminated the way cytokines can provoke damaging inflammation, Dr. Iwasaki said. For example, the cutting-edge cancer treatment chimeric antigen receptor (CAR) T-cells can lead the immune system to release too many cytokines. A drug called tocilizumab, which blocks a cytokine called IL-6, was tested for COVID-19 patients.

Though it didn’t turn out to be effective, Dr. Iwasaki said, that research was important. “These types of inflammatory responses

Blunders in Response to the Coronavirus

and of Public Health. Men who developed weak, defective T-cell immune responses suffered worse disease.

Autoimmunity could also help explain why so many people experience prolonged illness after a bout with COVID-19. Long after their viral tests turn negative, these people, nicknamed “long-haulers,” can experience months of fatigue, shortness of breath, muscle aches, brain fog, and other symptoms. “We’re trying to find out if there’s any immunological mechanism that can explain long-haulers,” she said. “I raised three different hypotheses, none of which are mutually exclusive.”

One hypothesis is that these patients’ immune systems have turned on them, resulting in long-term autoimmunity. Another possibility is that remnants of virus, such as bits of protein or genetic material, remain to stimulate the immune system. That could result in chronic inflammatory symptoms. A third scenario is that the virus in long-haulers never goes away. Instead, it may hide somewhere in the body, far from the nasal swabs that can detect it, and continue to cause infection.

Studies like these can’t take place without blood and tissue samples. Dr. Iwasaki’s lab contributed to the effort of the Yale COVID-19 Biorepository, which holds samples from hundreds of COVID-19 patients, including those with cancer. The biorepository, named IMPACT for Implementing Medical and Public health Action against Coronavirus (Connecticut, CT), was launched this spring by Albert Ko, MD, Yale School of Public Health’s Chair of Epidemiology. Roy S. Herbst, MD, PhD, Chief of Medical Oncology

that occur in cancer therapy have really shed light on how we might treat an inflammatory viral disease,” Dr. Iwasaki said.

Testing potentially helpful treatments for COVID-19, like tocilizumab, can take a long time. But Dr. Iwasaki’s lab has developed a versatile mouse model that allows for much quicker trials. Normally, mice are not susceptible to SARS-CoV-2 because they lack the ACE2 receptor that the virus uses as its doorway into cells. Mice can be bred to have this receptor, but that takes months. Instead, Benjamin Goldman-Israelow, MD, PhD, an infectious disease fellow in Dr. Iwasaki’s laboratory, devised a way to introduce the receptor into mice of any genetic background by delivering it into the body with a virus called AAV.

“We’re using this mouse model to rapidly get at these questions that people have about the importance of T cells and B cells and antibodies,” she said. “Whatever it is, we can do it very quickly.”

That speed is crucial. As the pandemic continues to rage around the world, clinical trials of therapies and vaccines have had to skip some steps, as Dr. Iwasaki and her co-authors recently explained in the *Journal of Experimental Medicine*. To better understand not only how the virus and immune system behave, but also to study treatments and potential vaccines, they wrote, “good mouse models are urgently needed. This model provides a vital platform for testing prophylactic and therapeutic strategies to combat COVID-19.”



Experts In Training

The Yale Medical Oncology-Hematology Fellowship Program provides promising young physicians a wealth of clinical and research opportunities to advance their careers.

Among the sea of white lab coats at Smilow Cancer Hospital, you'll find the medical oncology and hematology fellows. The eight promising young physicians selected each year for the prestigious Yale Medical Oncology-Hematology Fellowship Program are important members of not only the clinical care teams, but also the research teams of Yale Cancer Center. They're helping drive innovations in cancer care and blood diseases as they advance their flourishing careers in these fast-changing specialties.

"In no other field of medicine does the therapy change as rapidly as it does in oncology and hematology," said Alfred Lee, MD, PhD, Associate Professor of Medicine (Hematology) and the new director of the esteemed fellowship program. He recently took over the reins from longtime director Jill Lacy, MD, Professor of Medicine (Medical Oncology).

**Alfred Lee, MD, PhD,
Director, Yale Medical
Oncology-Hematology
Fellowship Program**

“I graduated from fellowship in 2011, and yet the landscape of therapies we now have in cancer is completely different,” Dr. Lee continued. “A huge number of treatments that we now use every day weren’t even in existence when I was a fellow. They’re changing so quickly because the science in the lab is changing so quickly; it’s a really exciting time to be in these fields.”

The 36-month program grants fellows full access to the vast resources of Yale Cancer Center as they refine their career focus and expand their sizeable skill set. They devote 18 months to clinical practice, split between Yale Cancer Center and the West Haven VA Medical Center. “The two settings are great complements to one another and create a tremendously broad educational experience for the fellows,” Dr. Lee explained.

At the VA Medical Center, fellows work with a veteran population that’s diverse in age, ethnicity, and socioeconomic status. They become well acquainted with a multitude of common blood disorders and cancer types, including lung and prostate cancer. “Our fellows love the VA experience,” said Sarah Goldberg, MD, MPH, Associate Professor of Medicine (Medical Oncology) and a new associate fellowship program director. “They have a lot of responsibility for patient care there, and the faculty teaches them so much about how to care for our veterans.”

After their broad exposure at the VA, the fellows then drill down deeply during their clinical time at Yale Cancer Center. “We have some of the world’s top experts in many disease areas within hematology and medical oncology,” Dr. Lee explained. “The fellows rotate among our clinics and learn from a world expert in each particular disease. Often, they’ll see very specialized and rare conditions they wouldn’t see anywhere else.”

That scientific expertise is paired with valuable bedside experience, too.

“The fellows take care of our Smilow and Yale Cancer Center patients on so many levels: when they’re in clinic, when they’re admitted, when they call the office,” Dr. Goldberg said. “The Smilow patients overwhelmingly appreciate having a fellow involved in their care. They like having another person who can listen to what is going on and help them through their journey.”

The fellowship also provides 18 months of valuable protected research time. A mentorship committee, comprised of core faculty members identified as outstanding teachers and mentors, helps the fellows evaluate their research options and navigate their potential career trajectories. “We really encourage individual exploration,” Dr. Lee said. “Our fellows have complete access to not only every single possible faculty member throughout Yale Cancer Center, Smilow Cancer Hospital, and the VA but Yale School of Medicine and the entire university. Because of that, we tend to attract fellows with wide-ranging interests.”

During her fellowship, Thuy Tran, MD, PhD, worked in the lab of Harriet Kluger, MD, a leader in melanoma research and director of the Yale SPORE (Specialized Program of Research Excellence) in Skin Cancer. SPOREs enable the rapid and efficient movement of basic scientific findings into clinical settings. Currently, Yale Cancer Center is one of the top centers in the country in terms of numbers of SPOREs dedicated to research in specific areas of cancer biology and treatment. “For years, the skin SPORE has been collecting blood and tumor samples from patients with melanoma and has done extensive genetic sequencing of the samples,” Dr. Tran explained. “In Dr. Kluger’s lab, I was working with patient samples for research. But then in Dr. Kluger’s clinic, I got to finally meet these patients and learn their personal stories. It was very meaningful and motivating in terms of

my drive for improving the translational research to help our patients.”

Dr. Kluger’s mentorship helped Dr. Tran navigate not only short-term goals, such as a target number of publications each year, but also her long-term career objectives as well. Since her fellowship ended in 2018, she has secured two prestigious NIH grants and has been appointed to a faculty position at Yale. She continues her melanoma research, still sees patients at Smilow, and is now an instructor in medical oncology.

“We try to bring in fellows who not only excel in patient care and research but also who want to advance the educational mission of Yale as well,” Dr. Goldberg said. “Many of our fellows are interested in teaching; I think that will make our strong program even stronger.”

For Dr. Tran, her fellowship exemplified the academic strengths of Yale and the friendly, supportive meaning of the very word ‘fellowship.’ “From the beginning, everyone was very welcoming,” she said. “It created a sense of family.”

The success of Dr. Tran and other members of the fellowship family inspires Dr. Lee as he and the fellowship leadership team, including Dr. Goldberg, Dr. Michael Hurwitz (Associate Professor of Medicine and a specialist in genitourinary cancer), and Dr. Nikolai Podoltsev (Associate Professor of Medicine and a specialist in hematologic cancers), move the program forward. “It’s so exciting to work with and learn from our brilliant young physicians,” Dr. Lee said. “We recognize that our fellows will soon become the leaders in their field. They’ll emerge from our fellowship with the opportunity to push their fields forward by finding new therapies and new ways to attack these diseases that are even better than when they trained.” ☺



Sterling Memorial Library

A Class Act

The Yale Class of 1961 Cancer Center Endowment provides generous support for some of Yale Cancer Center’s most promising scientists.

The Yale Class of 1961 calls itself “the undefeated class.” That proud nickname stems from the perfect 9-0 record of the 1960 Yale Bulldogs football team, which won the Ivy League that year. In the nearly six decades since graduation, the alumni of the Class of ’61 have shown the same determination and teamwork as their namesake, as they have stayed connected, worked together toward a larger goal, and established their own legacy.

Their legacy is the Yale Class of 1961 Cancer Center Endowment. Established in 2016, the Endowment, which stands at more than \$1.5 million and continues to grow, has honored one Yale Cancer Center faculty member each year since its inception with a \$50,000 grant to support their highly promising cancer research.

“This Endowment is the only gift of its kind to Yale Cancer Center,” explained Julie Parr, Senior Director of Development for Yale Cancer Center. “This is the only class gift that supports the Cancer Center. And it’s one of the few endowments supporting

discovery science. That's important, for it will continue supporting our vital research for years to come."

The Class of 1961's commitment to Yale Cancer Center (YCC) dates back to 2011. The Class is an extremely tight-knit group; members reconnect at a number of "mini-reunions" around the country each year. Several classmates have been personally affected by cancer. As their milestone 50th reunion approached, these close classmates wished to use their class gift to support the tremendous advances taking place at Smilow Cancer Hospital, which had opened just two years earlier. They banded together to raise \$1 million for the YCC Director's Fund to purchase equipment for Smilow. That effort was led by Vincent Teti. An additional \$200,000 was designated for a YCC research fund named The Cantor-Smith Cancer Research Fund, in honor of classmates Ed Cantor and DeForest Smith, who had served as class co-chairmen for 20 years, and their wives.

That seed of a research fund blossomed into a full-blown endowment as the class gathered for its 55th reunion in 2016. "The idea of building it into something substantially bigger, something that could make a more meaningful contribution, really appealed to us," said Ed Cantor. "We felt we could create a legacy for our class. At our age, that word 'legacy' has become very important to us."

Classmate John de Neufville helped lead the effort. As a member of the Yale Cancer Center Director's Advisory Board, Mr. de Neufville has a front row seat on the progress and innovation underway at the Cancer Center. "As a scientist, I'm always very interested in hearing about evolving cancer treatment opportunities," Mr. de Neufville said. "Attending the board meetings is a science holiday for me."

The opportunity to make a real impact on cancer research sparked a flurry of donations; more than 200 classmates, widows, and friends have since given to the renamed Yale Class of

1961 Cancer Center Endowment. "We are extremely grateful to the Yale Class of 1961 for their generous support of the vital, innovative cancer research taking place at Yale Cancer Center," Yale Cancer Center's Director, Charles S. Fuchs, MD, MPH, said.

Classmate Bruce Chabner, MD, Clinical Director, Emeritus, of the Massachusetts General Hospital Cancer Center and Professor of Medicine, Harvard Medical School, helped structure the Endowment's research grants. They're noteworthy in their support of YCC faculty members age 45 and under, and for funding not a specific project but the overall arc of a researcher's work. To select grant winners, YCC leadership reviews each nominee's curriculum vitae, paying particular attention to the published research they have conducted in their labs at Yale and the impact of their work.

"The winners of these prizes are many of our most promising cancer researchers," explained Daniel DiMaio, MD, PhD, Deputy Director of YCC and coordinator of the grant selection process. "Each have emerged as leading mid-career scientists who have already made important contributions to cancer research and have many more years of exciting research ahead of them. This award allows us to recognize their prior contributions and help inspire them to continue on their exceptional trajectory."

Valentina Greco, PhD, the Carolyn Walch Slayman Professor of Genetics, won the grant in 2017. Her lab studies how organs are maintained throughout life, and she uses mouse models to evaluate how skin tissues function in spite of, and perhaps even thanks to, the mutations they carry. "It was a true honor for my lab members' work to be recognized through this award," she noted, "and also incredibly re-energizing to know that your close colleagues value your lab's contributions."

In 2018, the grant was awarded to Katerina Politi, PhD, Associate Professor

of Pathology and co-leader of YCC's Cancer Signaling Networks Research Program. The grant has enabled her lab to use new approaches, including the cutting-edge CRISPR/Cas9 gene editing tool and techniques to study tumors at the single-cell level to gain new insights into drug resistance. "I was honored and thrilled to hear that I had won the Class of 1961 Research Award," Dr. Politi said. "Having started my independent research career at Yale, this award is especially meaningful for me."

Grant winners have shared their gratitude and updates on their research with their benefactors by speaking at recent Class of 1961 mini-reunions. "The Class loves hearing from the researchers," Ms. Parr said. "They can see the fruits of their labor. They're extremely committed to the Endowment, to Yale, and to the Cancer Center."

As their 60th reunion approaches in 2021, the Class of 1961 is doubling down on its support of YCC. Thanks to an anonymous donor, this year the Endowment will award not one, but two research grants each year, the ongoing additional cost of which will gradually be covered by the Endowment as it grows toward its 60th Reunion goal of \$2 million.

"It wouldn't have occurred to me when we started 10 years ago that we would be where we are today," expressed Mr. de Neufville. "Our contributors have been amazingly generous. The whole process of working with my classmates toward a common goal has been extremely gratifying and has deepened my connections to the Class of 1961 in ways that I couldn't possibly have imagined." ☺


CLASS OF '61 GRANT RECIPIENTS:


- 2015 Melinda Irwin, PhD, MPH
- 2016 Susan Kaech, PhD and Joseph Contessa, MD, PhD
- 2017 Valentina Greco, PhD
- 2018 Katerina Politi, PhD
- 2019 Qin Yan, PhD





January 1, 2020 – June 30, 2020

Honors


 **Julius Chapiro, MD**, was awarded a research grant from the **Society of Interventional Oncology** for his project titled, “Molecular Imaging of the Immuno-Metabolic Crosstalk to Guide Combination Therapies of Liver Cancer.”

 The **National Comprehensive Cancer Network** has funded **Cary Gross, MD**, to support a research collaboration with **Elena Ratner, MD**, and **Dena Schulman-Green, PhD**, to develop new approaches to identify patients with unmet social needs and connect them with resources in their own communities.


 **Jeffrey Ishizuka, MD, DPhil**, has been awarded a K08 Award from the **National Institutes of Health** to support his project, “Triggering Innate Immunity in Tumor Cells to Overcome Resistance to Immunotherapy.”


 **Rong Fan, PhD**, and **Jiangbing Zhou, PhD**, have been awarded a Cancer Tissue Engineering Collaborative R01 Award to support their project, “Ex Vivo Analysis of Human Brain Tumor Cells in a Microvascular Niche Model.”


 **Grace Chen, PhD**, has been awarded the prestigious **Rita Allen Foundation Scholar Award**.

 **Roy S. Herbst, MD, PhD** received the **American Association for Cancer Research Distinguished Public Service Award** for Exceptional Leadership in Cancer Science Policy.


 The **United States Department of Defense (DoD)** has named **Sidi Chen, PhD**, as a recipient of its **Era of Hope Scholar Award**.


 The **Society for Immunotherapy of Cancer** announced **Lieping Chen, MD, PhD**, as one of the recipients of the **Richard V. Smalley, MD, Memorial Award and Lectureship**, the Society’s highest honor, for his pioneering research in immunotherapy.


 **Zhengxin (Jason) Cai, PhD**, has been awarded an R03 grant from the **National Institutes of Health**.


 **Caroline Johnson, PhD**, has received a four-year, \$792,000 Research Scholar Grant from the **American Cancer Society**. Dr. Johnson will use the grant to understand metabolic heterogeneity in colorectal cancer.

 **Roy S. Herbst, MD, PhD**, Chief of Medical Oncology, has been elected to the **American Association for Cancer Research** Board of Directors for a three-year term in recognition of his outstanding contributions to cancer research and treatment.


 **Anne Chiang, MD, PhD**, has been named a **Fellow of the American Society of Clinical Oncology**.


 **Valentina Greco, PhD**, was awarded one of only two **Yale Postdoctoral Mentoring Prizes**, as well as the **Department of Genetics Mentoring Award**. Both prizes celebrate the dedication of a faculty member to the growth of their lab members.

 **Dmitry Kozhevnikov, DO, Laura J. Morrison, MD**, and **Matthew S. Ellman, MD**, received the **Rosenkranz Award for Pedagogical Advancement** from the Yale Poorvu Center for Teaching and Learning.


 **Scott J. Miller, PhD**, has been elected to the prestigious **National Academy of Sciences**.


 **Alfred Lee, MD, PhD**, has been appointed to the **American Society of Hematology** Guideline Panel on Use of Anticoagulation in Patients with COVID-19.

 **Jean L. Bolognia, MD, Peter E. Schwartz, MD**, and **Karl L. Insogna, MD**, received the inaugural **Yale Medicine Distinguished Clinical Career Awards**, which recognizes and honors the careers of physicians marked by significant accomplishments, exemplary dedication, and important contributions in advancing Yale Medicine, the overall medical profession, and the community.

 **Kathryn Miller-Jensen, PhD**, and **Marcus Bosenberg, MD, PhD**, were awarded a **Cancer Systems Immunology Grant** from the National Cancer Institute.

 The **National Palliative Care Research Center** awarded **Prasanna Ananth, MD**, a two-year **Kornfeld Scholar Grant**.

 **Xavier Llor, MD, PhD**, was awarded an R01 Grant from the **National Cancer Institute** to study early onset colorectal cancer.

 **Grace Kong, PhD**, received an R01 Grant from the **National Institute on Drug Abuse** and **U.S. Food and Drug Administration Center for Tobacco Products**.

January 1, 2020 – June 30, 2020

Generosity

\$500,000 - \$1,000,000

Anonymous

\$100,000 - \$499,999

American Cancer Society
Bank of America
CureSearch for Children's Cancer
Mr. Chuanwei Dexter Lu
Melanoma Research Alliance
Donald C. Rankin, MD
and Nancy Rankin

\$50,000 - \$99,999

Anonymous
Mr. William L. Bernhard
Mr. and Mrs. Edward E. Madden
Roslyn Milstein Meyer, PhD
and Jerome Meyer, MD

\$25,000 - \$49,999

All American Waste, LLC
Darcy B. Beyer
Mr. Stuart M. Johnson
Kelly and Michael D. Loftus
Marc Lustgarten Pancreatic
Cancer Foundation
Mr. Joseph D. Morris
Pink Aid, Inc.
Dyanne and John W. Rafal
Jordan M. Stitzer
Mrs. Elizabeth Welke
Estate of Ruth M. Wood

\$10,000 - \$24,999

Anonymous
Mr. Eugene P. Beard
The John Treacy and
Darcy F. Beyer Foundation, Inc.
Big Y World Class Markets
Stephanie and Brian Callahan
Connecticut Brain Tumor Alliance, Inc.
Betty and Alan H. Feldman
Mr. and Mrs. Arthur S. Forkos
Ms. Melanie Ginter
Mr. John S. Lapides
Mr. and Mrs. Peter Nadosy
Catharine and David Parsons
William and Angela Shulman
– in memory of Jackie Shulman





KRISTIN HYNES

Smilow Cancer Hospital Care Center at Greenwich

CENTER AT A GLANCE

- A patient-centered focus on exceptional cancer care
- 50+ staff members; oncology board certified clinicians
- Medical Oncology, including chemotherapy and infusion treatments
- Hematology services, available for patients with any type of cancerous and non-cancerous disorders affecting the blood, lymph nodes, and bone marrow
- Radiation Oncology, provided by Yale Cancer Center physician specialists
- A Breast Center with the latest technology and specialists in one location
- Partnerships with Yale surgical specialists, including thoracic surgeons, urologists, gynecologic oncologists, and breast surgeons to provide multidisciplinary care
- Genetic testing, including genomic profiling of certain cancers
- Clinical trials, available only through Yale Cancer Center
- Lab and Pharmacy services on site for patients' convenience
- Access to supportive care clinicians, including an oncology nurse coordinator, social workers, a dietician, clinical research staff, palliative care, and survivorship planning

“The Smilow Cancer Hospital Care Center at Greenwich brings Smilow quality care to our patients from Fairfield and Westchester counties, providing them unique access to a National Cancer Institute-designated Comprehensive Cancer Center and its clinical trials and advances. Our physicians coordinate with our colleagues in New Haven to ensure all treatment options are reviewed through multidisciplinary tumor boards, and each patient receives personalized cancer care.”

— Dr. M. Sung Lee, Medical Director

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Daniela Addeo, MD, MBA, Radiation Oncology
D. Barry Boyd, MD, MS, Medical Oncology
Beverly Drucker, MD, PhD, Medical Oncology
Dickerman Hollister, Jr., MD, Medical Oncology
M. Sung Lee, MD, Medical Oncology

Bruce McGibbon, MD, Radiation Oncology
Francesca Montanari, MD, Hematology
Stephanie Paine, APRN
Daniel Petrylak, MD, Medical Oncology



meet the physician

Pamela Kunz, MD

Associate Professor of Medicine (Medical Oncology)
Leader, Gastrointestinal Cancers Program

You specialize in the treatment of neuroendocrine tumors (NETs), which is a rare diagnosis. What brought you to subspecialize in this field?

During my fellowship in oncology, very little was known about neuroendocrine tumors (NETs) and there were few treatment options for patients diagnosed with NETs. One of my mentors encouraged me to write a review of the field at the time and that research endeavor launched my interest in clinical research and treatment of NETs and quickly concentrated my career. Because it's a small subspecialty, it has enabled me to partner with colleagues from institutions across the country to create broad collaborations to care for patients with NETs, and to best develop clinical trials and other treatment advances for our patients. I am proud of my leadership roles in the National Cancer Institute NET Task Force, the North American Neuroendocrine Tumor Society, and past participation on NCCN's guidelines committee for NETs. I know that together with my colleagues throughout the country we are making an impact for our patients.

How do clinical care and research motivate one another?

How do you balance the two?

One of the reasons I love academic medicine is the constant collaboration and balance between clinical care, research, and education. Our clinic and our lab both go hand in hand, very much informing one another. The intensity of the doctor-

patient relationship in oncology helps us to tackle the questions that matter through research, and our research endeavors help to bring hope to our patients through clinical trials. The entire process is very forward thinking and continually challenges me, both as a clinician and a researcher.

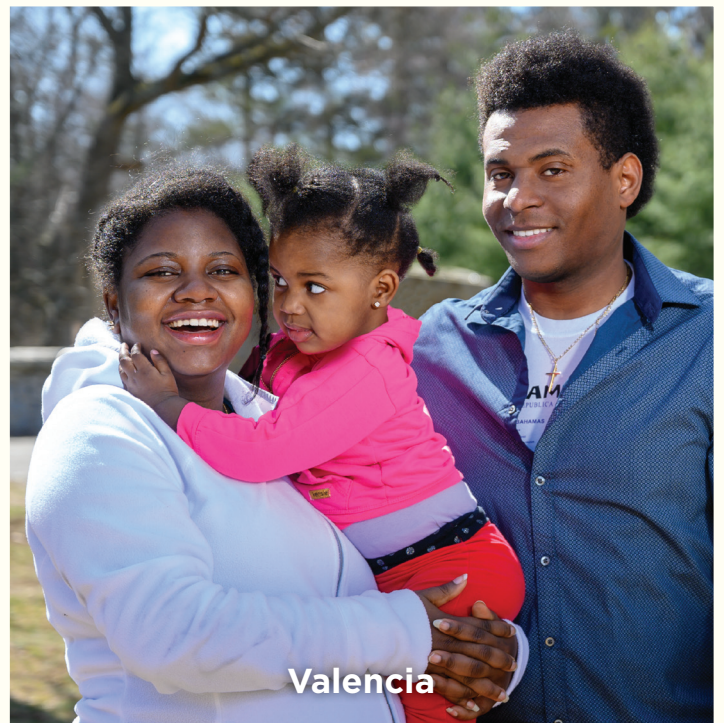
You recently joined Yale from Stanford and are extremely focused on building and mentoring the Gastrointestinal Cancers team. How do you network with your team in the COVID-era?

What principles are you focused on?

I came to Yale with a goal of building a collaborative, respectful, and diverse community focused on gastrointestinal cancers, and quickly had an added challenge of doing this in a virtual environment during the COVID pandemic. My hope is that our team includes everyone that plays a role in the care and research for patients with GI cancers—physicians, basic and translational scientists, advanced practice providers, nurses, clinical research staff, and others. When I first arrived, I began on a listening tour to meet all of the stakeholders and learn more about each area. As a leader, my goal is to ensure that all team members feel that we are part of the same mission—to provide the best care for patients with GI malignancies, educate trainees, and conduct leading research in the field. During the pandemic, I have been trying to build a sense of connectedness and community and hope this will make our Gastrointestinal Cancers Program stronger over time. We have an excellent foundation and I am excited to be part of a team that will do great things.



Roberta



Valencia

Read their stories:
yalecancercenter.org/survivors