breakthroughs

YALE CANCER CENTER
SMILOW CANCER HOSPITAL

THE YEAR IN REVIEW

yale cancer center

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> *Generations from now, 2020 will long be remembered as our finest hour and I am honored to have had the privilege to have worked side by side with so many heroes who brought care and hope to countless patients and families.*

As we look back on the past year, we reflect on the fact that 2020 was a year like no other. The global pandemic has profoundly affected our lives and our work and, since early March, the physicians, scientists, nurses, and staff at Yale Cancer Center and Smilow Cancer Hospital have all worked tirelessly to advance our mission in the face of unprecedented challenges. Their collective determination and dedication have truly made the difference for our patients and clinical care, and the continued advancement of our science.

Our clinical teams have redesigned cancer care and research protocols, moved patient floors in a day, redeployed staff across the entire system, and, through it all, remained steadfast to our patients. Our transformation teams are continuing to capitalize on that momentum to transform and adapt Smilow Cancer Hospital for the future through enhancements to patient care, which will further revolutionize our clinical operations.

Our research enterprise has similarly met the challenge and closed the year with direct funding of $107 million, our highest level of research funding ever. In 2020, Yale investigators led multiple new cancer therapies approved by the U.S. Food & Drug Administration. Moreover, we continue to expand our outreach, education, and training programs, and no less importantly, we are redoubling our commitment to embracing diversity, equity, and inclusion throughout our enterprise.

Yale Cancer Center and Smilow Cancer Hospital developed new understanding and delivered hope throughout the COVID pandemic, and we all grew stronger together.

As we highlight the accomplishments of 2020, there is no denying that it was one really difficult year for cancer centers and hospitals throughout the United States. Generations from now, 2020 will long be remembered as our finest hour and I am honored to have had the privilege to have worked side by side with so many heroes who brought care and hope to countless patients and families.

Sincerely,

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

HOW COVID-19 IS TRANSFORMING SMILOW CANCER HOSPITAL FOR THE FUTURE

When COVID-19 surged in the spring of 2020, the physicians and staff who work in ambulatory care at Smilow Cancer Hospital and the Smilow Cancer Hospital Network were forced to respond with lightning speed, creating temporary spaces that would allow for social distancing, beefing up technology for relatively novel telehealth visits, and rethinking patient care to keep everyone safe. But the pandemic necessitated deeper changes, too, changes that have reaped some silver linings during the worst of times.

WORKING TOGETHER IN A WHOLE NEW WAY

Radical change does not simply happen, even in an emergency situation like a pandemic. To make sure things ran smoothly in the new world of COVID-19, the Smilow campus in New Haven and all of its community locations had to think out of the box and create new processes, "almost from the ground up," said Anne Chiang, MD, PhD, Associate Professor of Medicine; Chief Integration Officer and Deputy Chief Medical Officer, Smilow Cancer Network. The results will continue to reap rewards on many different levels, including patient and staff safety, convenience, and faster access to care, to name just a few benefits.

"We have tapped about two hundred people throughout the Smilow Network to get involved in Ambulatory Transformation workgroups. They have in turn reached over 700 stakeholders using interviews, focus groups, and surveys to understand everyone's most compelling

needs and to develop best practices across the system," Dr. Chiang explained. As all the moving parts began to talk to one another, North Haven to New Haven, Torrington to Trumbull, "I've had doctors and staff say, 'Oh, wow, I've communicated with this person via email, but now I really know them and how they work.'" Typically, the Smilow Care Centers tended to be separate from one another—or "siloed" as Dr. Chiang puts it—solving problems on their own, in their own way, rather than routinely sharing solutions. "As an example, you'd have a situation in Torrington, say, with insurance pre-authorizations, and the staff in that office might do a little project to figure it out and fix it." Now, she says, everyone is benefitting from the knowledge each office gleans. "We have a structure where we can think more globally, connecting our network's best practices, thinking about how one patient's experience in Torrington can help another patient in Greenwich. "That process will extend into the future," said Dr. Chiang. "And that's really powerful."

TAKING TELEHEALTH TO ANOTHER LEVEL

By now, almost a year into COVID-19, most people have had at least one telehealth visit with a healthcare provider, but in the beginning, Zoom-style interactions were still relatively new. That changed quickly at Smilow: "In April of 2020, in ambulatory care, we were doing 380 remote visits a week," said Dr. Chiang. "In May, visits shot up to 2,500 a week across our network; we'd never used the technology on that scale."

And while Dr. Chiang and Ms. Major Campos both emphasize that telehealth visits are not meant to replace in-person physician visits, "What's great about it is that we can reach patients with questions or concerns, quickly address any side effects they might be having, say from chemotherapy treatments, or offer follow-up educational sessions for new patients that they would once have had to travel for," explained Ms. Major Campos. That could include such services as nutritional counseling, social work sessions, and even getting a patient evaluated for a clinical trial. "Increasingly, these things will be done remotely," said Ms. Major Campos.

With telehealth, they can do follow up sessions at their convenience via videoconference, with a nurse or another provider. "This is going to be a really important platform moving forward," said Ms. Major Campos. "We know from studies that at the time of diagnosis, patients are only able to take in about 20 percent of what their doctor is saying, but when they're scheduled on another day for a follow-up discussion, they can retain more information."

> "THE PAST YEAR HAS TRULY BEEN GALVANIZING, LEADING TO NEW CONNECTIONS AND RELATIONSHIPS AND MORE CREATIVITY."
>
> - DR. ANNE CHIANG

Another telehealth advantage may be especially appreciated by patients who have been newly diagnosed with cancer. Through efforts of a Patient Access Committee led by Sarah Mougalian, MD, Chief Ambulatory Officer for Smilow Cancer Hospital, and Lisa Shomsky, MBA, BSN, CNML, Regional Director for the Smilow Cancer Hospital Network, newly diagnosed patients are now provided next day appointments with a provider through several Smilow locations and programs. Next day appointments are available in person or via telehealth and quickly connect new patients with a Smilow provider to discuss their diagnosis and next steps.

"Patients often say that the time immediately following a new diagnosis of cancer is the most difficult. The waiting can seem endless—waiting for test results, biopsy results, doctors' appointments—there are so many unanswered questions and so much uncertainty. Quickly introducing our patients to the team of clinicians who will guide them through the process can help allay some of the anxiety that they may be experiencing," said Dr. Mougalian. Patients appreciate the timely response, with a 92% satisfaction rate following the first appointment, and one patient commenting, "The waiting is the worst. A next day appointment was huge for me."

NEW WAYS OF CREATING SPACE TO KEEP PEOPLE SAFE

By now, the term "social distancing" has become part of our everyday lingo—but even after this pandemic passes, the days of crowded medical waiting rooms may be behind us. Necessity is the mother of invention, as Ms. Major Campos puts it, and the ambulatory care team at Smilow has found innovative ways of protecting vulnerable people from potential infection, whether COVID-19 or something else. "I think the pandemic has taught us how important it is to be mindful of patient volume in our clinics, and the close proximity in which we all work," she said. To tackle pressing space issues, for instance, Smilow put a number of new measures into place, including getting patients in and out of waiting rooms more efficiently by doing pre-visit screenings over the phone instead of in person to avoid bottlenecks. "Instead of patients just showing up, we can have a plan ahead of time," explained Ms. Major Campos.

Smilow also started making use of its Network locations outside of New Haven to gain more breathing room for ambulatory patients, relocating physicians in specialties that were formerly available only in New Haven, like surgical oncology. "One hundred or so doctors in our Network moved to different locations—surgeons, medical oncologists, and more—and we did it in a seamless way," said Dr. Chiang.

Because why shouldn't a patient be able to go to one location and get nearly all their care in their own backyard, or closer to it? "No one was sure we'd be able to make it happen, but thanks to the efforts of our amazing teams, we did," said Ms. Major Campos. "It's been an amazing journey, and I'm grateful that we endured together."

The truth is, sometimes, it takes a crisis of unimaginable proportions to show everyone—doctors, staff, patients, what we are truly capable of. "The past year has truly been galvanizing, leading to new connections and relationships and more creativity," said Dr. Chiang. "We are taking advantage of this crisis to transform how we deliver cancer care."


HOPE

A Pressing Need for New Id

"Try to think: What can I learn today?" Nita Ahuja, MD, MBA, FACS, often tells her students.

Dr. Ahuja, William H. Carmalt Professor and Chair of Surgery, takes her own advice as she searches for better ways to combat pancreatic cancer in her own lab. She is relatively new to Yale, having arrived in 2018, and since that time Yale Cancer Center has recruited a team of researchers who have formed the Yale Pancreatic Cancer Collaborative (YalePaCC) to create a collaboration of team science using the tools and expertise of various disciplines to improve success against pancreatic cancer—a mission they see as urgent.

Pancreatic cancer is currently the third leading cause of cancer deaths in the U.S. and is expected to soon become the second deadliest malignancy, surpassing colorectal cancer. In 1977, the five-year survival rate in pancreatic cancer was 2-3%. Today, it is only 10%, underlining the need for rapid progress.

Pancreatic cancer is so dangerous, in part, because it is often not detected until it is at an advanced stage. In addition, it does not respond as well as many other cancers to common treatments like chemotherapy. Dr. Ahuja has already discovered a biomarker that supports earlier detection of pancreatic cancer, and her search is not over. "Translational epigenetics and other forms of basic science research continue to advance our understanding of pancreatic cancer. Our laboratories are on the frontlines of cancer research into biomarkers that could translate into precision diagnostics and therapeutics," she said.

Despite poor outcomes nationally and internationally, patients do better when they receive treatment at places like Smilow Cancer Hospital, which is recognized by the National Pancreas Foundation as a Center of Excellence in pancreatic cancer, and where surgeons specialize in and treat a large number of these cancers. After completing a fellowship at Memorial Sloan Kettering Cancer Center, John Kunstman, MD, MHS, returned to Yale where he had done his surgical internship and residency. He was drawn back to New Haven to work with a former mentor, Ronald Salem, MD, FACS, FRSC (Ed), FRCS(C), MBChB, Lampman Professor of Surgery and "one of the most technically profound pancreatic surgeons I know." Dr. Kunstman had a second reason for choosing to return: "Because it's Yale Cancer Center, because it's enmeshed in the university, which has an obviously outstanding research tradition and unparalleled research resources. I know as a clinician-scientist that it's impossible for me to have success without collaborators across disciplines."

In addition to his clinical work as a surgical oncologist, Dr. Kunstman conducts research in a number of areas. He is the principal investigator of the Yale Gastrointestinal Cancer Biorepository, which supports research projects throughout the cancer center (see related story). He also studies premalignant cancerous lesions called intraductal papillary mucinous neoplasms (IPMN). "We know very little about why some develop into cancers and others never do," Dr. Kunstman explained. His lab is currently working to develop cell lines that will make more IPMN research possible.

Like Dr. Kunstman, Luisa Escobar-Hoyos, PhD, came to Yale in part to work with other great scientists. "Yale is the Mecca of RNA biology," she said. She is undertaking projects with renowned researchers Joan Steitz, PhD, Sterling Professor of Molecular Biophysics and Biochemistry, who has made groundbreaking discoveries about RNA, Karla Neugebauer, PhD, who directs the Yale Center for RNA Science and Medicine, and Susan Baserga, MD, PhD, who is making foundational discoveries connecting ribosome biogenesis to cancer.

For Dr. Escobar-Hoyos, who recently welcomed her first child, the fact that these world class scholars are also women, matters. "They understand how to continue your career, to have a life, and be a mom," she said. Dr. Escobar-Hoyos' research has uncovered the role of aberrant RNA splicing in immune response in both pancreatic and lung cancers. Her lab is currently testing a novel therapy, Splicing-Hit Oligonucleotide Therapy (SHOT), which aims to correct those splicing errors. The hope is that SHOT will be effective in tumors that are currently resistant to therapy, as tumors in the pancreas frequently are.

eas for Pancreatic Cancer

Procedures are already established to fix a splicing defect in the lab, but no one has solved the problem of delivering the therapy directly to a tumor cell. Dr. Escobar-Hoyos is now planning collaborations with Drs. Peter Glazer, Robert E. Hunter Professor of Therapeutic Radiology and Professor of Genetics, and Donald Engelman, Eugene Higgins Professor of Molecular Biophysics and Biochemistry, who invented technology to deliver mRNA therapy to cells.

This kind of cross disciplinary collaboration is a key strategy of the YalePaCC, according to its Director Mandar Deepak Muzumdar, MD, Assistant Professor of Genetics and Medicine (Medical Oncology). Scientists highly trained in their individual disciplines need to learn to "speak a common language" in order to make these partnerships fruitful, he said. The collaborative helps to develop that capacity by hosting a seminar series together with the Center for Gastrointestinal Cancers, which hosts leading researchers from around the world to present their research in the fight against pancreatic cancer.

"Our unique ability to bring together clinicians and scientists focused on pancreatic cancer from throughout Yale and Smilow, and host regular concentrated discussions will propel the research endeavors and success in pancreatic cancer from Yale Cancer Center. I am proud of the collaborations already formed through YalePaCC and look forward to new advances from the team in the coming years," said Pamela Kunz, MD, Director of the Center for Gastrointestinal Cancers at Smilow Cancer Hospital and Associate Professor of Medicine (Medical Oncology). The Center for Gastrointestinal Cancers provides a foundation for the research efforts in all gastrointestinal cancers, including pancreatic cancer, and facilitates additional collaborations throughout the Cancer Center and Smilow.

Our unique ability to bring together clinicians and scientists focused on pancreatic cancer from throughout Yale and Smilow, will propel the research endeavors and success in pancreatic cancer from Yale Cancer Center.

Successful team science also requires a grant structure that supports collaborative work. "At Yale Cancer Center we have funding mechanisms in place to promote team science. As a result of the collaborative work, not only is positive progress seen in our surgical and clinical outcomes for pancreatic cancer, it is also evident in the abundance of federal funding for research and high impact publications which routinely come from Yale Cancer Center investigators," said Dr. Ahuja.

The imperative to pool the clinical and intellectual resources of the Cancer Center, Smilow, and the university are obvious. In addition, patient involvement in research is essential. "I cannot be more grateful to the patient advocates," said Dr. Escobar-Hoyos. Through her involvement in the Pancreatic Cancer Action Network, she has met many patients, whom she credits with working to increase federal funding. Those patients motivate her, she said, to find better treatments.

"The type of folks that generally care for patients with pancreatic cancer are those that enjoy a challenge but are also persistently curious," said Dr. Kunstman. "I think we all wake up in the morning hoping that our career will substantially improve, not just the outcomes for our individual patients, but for all the patients who suffer from pancreatic cancer."

"After the experiences of this year and seeing those disparities laid bare once more, we cannot unsee it, we cannot go back to where we were."

Paving The Way for Cancer Health Equity

Since Marcella Nunez-Smith, MD, MHS, joined the faculty at Yale in 2006, her passion and research has focused on promoting health and healthcare equity for structurally marginalized populations. She and her team advocate for people and communities facing social and economic barriers to things such as housing, education, and employment. These health and social inequities reveal themselves in many forms, but none so evident as in one extremely vulnerable population; cancer patients.

With Dr. Nunez-Smith's recent appointment as Director of the newly formed Center for Community Engagement and Health Equity (CEHE) within Smilow Cancer Hospital and Yale Cancer Center, the mission of ensuring cancer health equity and improving outcomes with an emphasis on traditionally marginalized communities, has begun to take shape. Nationally, Dr. Nunez-Smith also serves as Chair of the COVID-19 Health Equity Task Force for the Biden-Harris administration and previously served as co-chair of the Biden-Harris Transition COVID-19 Advisory Board.

Originally from the U.S. Virgin Islands, Dr. Nunez-Smith's leadership roles have much significance to her personally, as she saw inequities in healthcare play out firsthand. "My father had his first stroke in his 40s and was left paralyzed. I learned there was a term for what we were: an underserved community, marginalized by place and by race," she said. As Chair of the Task Force, Dr. Nunez-Smith is working to confirm that COVID-19 testing, treatment, and vaccines are distributed equitably and is committed to making sure everyone has the information they need to make an informed decision about the vaccine. President Biden has said that her role will ensure "that fairness and equity are at the center of every part of our response."

Realizing the opportunity she has, Dr. Nunez-Smith commented, "I could not have imagined any of this. It's not about me. It's never been about me. This is about the work that needs to be done. I look into the eyes of my three young children and find courage to create something better for them moving forward."

In a study published recently by the American Association for Cancer Research, it was reported that Black Americans have the highest overall death rate from cancer of any racial or ethnic group in the nation. This is one daunting statistic the CEHE at Yale Cancer Center and Smilow Cancer Hospital seeks to change. Locally, Dr. Nunez-Smith is propelling efforts to improve the understanding of and reduce health disparities relevant to cancer care. In addition to access to quality cancer care, there is an overall lack of education and understanding of screening to overcome.

The CEHE builds on Yale Cancer Center's longstanding commitment to high-quality, expert, and patient-centered cancer care, screening, and prevention across the state of Connecticut. The Center leverages a wide range of approaches to community-engaged research, community outreach, education, policy and advocacy, and access to clinical care. The CEHE team has spent their initial focus on creating partnerships with community-based organizations to address the barriers to accessing cancer prevention and healthcare services, and working to bring community perspectives to current cancer research projects.

Charles Fuchs, MD, MPH, Director of Yale Cancer Center and Physician-in-Chief of Smilow Cancer Hospital commented, "Working with the talented research community at YCC and SCH, I am confident the Center will push to expand cancer research that addresses the unique needs of the residents of Connecticut and will have far-reaching effects beyond our state."

As CEHE continues to develop and expand, the team is focused on addressing the social and structural barriers to cancer prevention and care and ensuring that research from Yale Cancer Center is serving the interests of all communities. The hope is that the Center's research and programs will not only benefit patients in New Haven, but worldwide, and improve the understanding of, and ultimately eliminate, cancer health disparities.

Reflecting back on 2020, Dr. Nunez-Smith has accomplished a lot, but also realizes there was a lot to pause and reflect on, and acknowledges the remaining work to be done. "After the experiences of this year and seeing those disparities laid bare once more, we cannot unsee it, we cannot go back to where we were. So I expect an acceleration, quite frankly."

For men with newly-diagnosed prostate cancer, numerous initial options are available. These include formal treatment options as well as a growing interest in active surveillance, a period of close observation. Studies have shown that utilizing a tissue-based genomic test can provide important insight into whether a localized tumor is slow-growing or aggressive, thus enhancing the ability to offer active surveillance to patients, or to potentially tailor the intensity of treatment. Despite their growing availability, little has been known about how these types of tests have been utilized. Recently, Yale researchers performed a large national study to understand patterns of national utilization of genomic testing.

In a study published by *JAMA Oncology*, Michael Leapman, MD, Assistant Professor of Urology at Yale School of Medicine and Clinical Program Leader of the Prostate & Urologic Cancers Program at Smilow Cancer Hospital, and colleagues explored national trends in the use of prognostic genomic tests. They looked at regional patterns of testing, particularly focusing on regions that shared similar trajectories of testing uptake. With new technologies in cancer care coming available at a rapid pace, the Yale research team sought to understand potential facilitators and barriers to use.

Using data from Blue Cross Blue Shield Axis, the largest source for commercial insurance claims in the United States, claims were reviewed for commercially-available, tissue-based gene expression testing in the six-month period following a new diagnosis of prostate cancer. The researchers used a form of statistical growth modeling to uncover trends in the use of genomic tests and the proportion of tested patients within regions. The primary regional unit used in the study was the Hospital Referral Region (HRR), areas that tend to share distinct referral patterns for complex surgical care.

The study cohort was comprised of 217 qualifying HRRs with more than 90,000 men and an average age of 60 at prostate cancer diagnosis. Dr. Leapman and colleagues found that while there was overall increasing use of tests, there was very striking geographic variation. For example, many HRRs show little to no use of genomic testing while testing was much more common in others. Furthermore, the study revealed geographic regions which adopted genomic testing at faster rates possessed higher education levels, median household incomes, access to prostate cancer resources, and prostate cancer screenings.

"Little was known about how genomic testing was used in routine clinical care," said Dr. Leapman. "While we anticipated higher rates of test utilization over time, we were surprised at the extent of how early use of genomic testing with prostate cancer varied based on region."

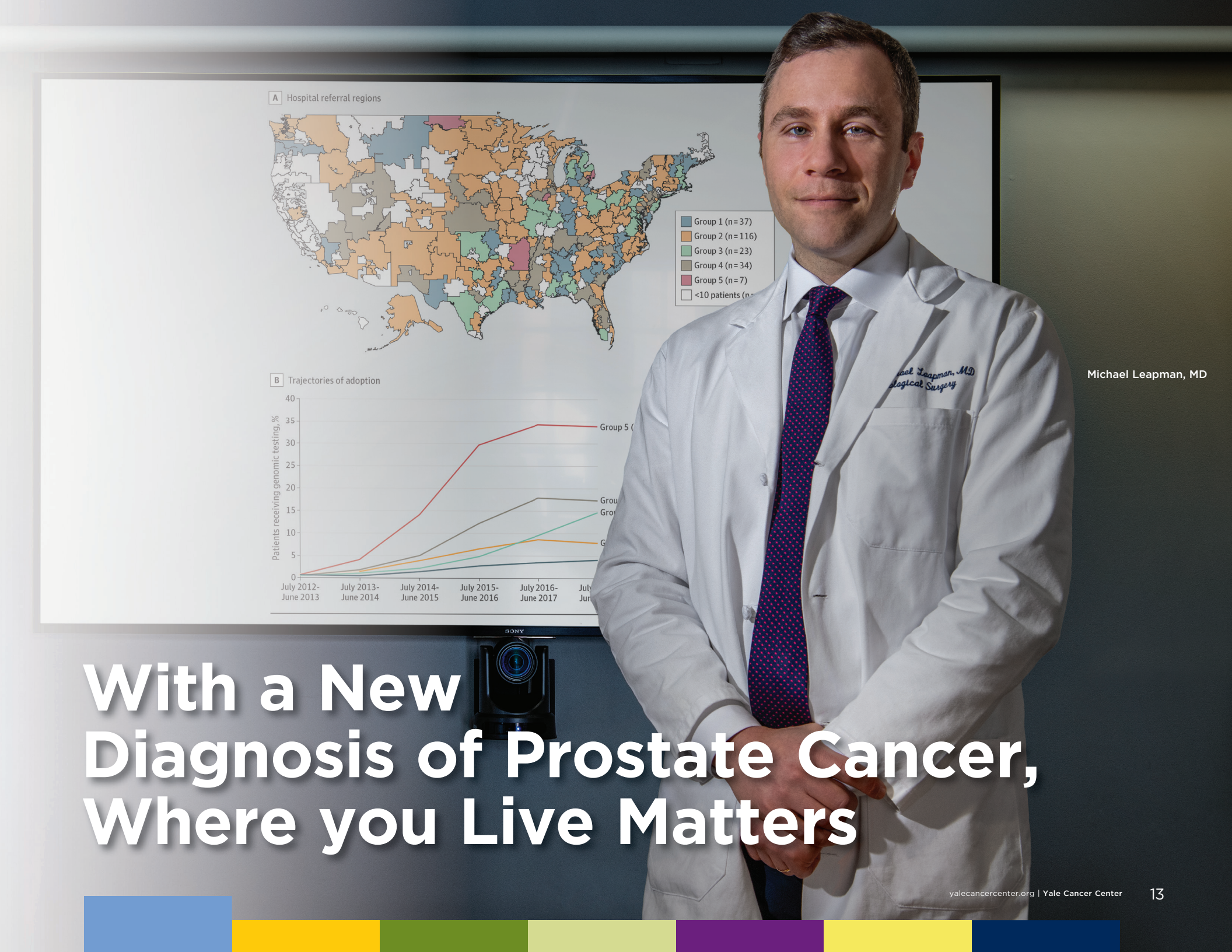
Study findings also cast light on a reluctance to accept new technologies in cancer care. In the first year of claim data (July 2012 through June 2013), researchers found minimal baseline use of genomic testing—0.8%, but adoption of this testing increased to 11.3% by the end of the five-year study period (July 2017 through June 2018).

The researchers hypothesized that use of gene expression testing could be driven by multiple factors such as stronger preferences for emerging technologies by some providers and regions, greater patient interest, or industry involvement and marketing.

It remains to be seen whether utilizing gene expression testing has an impact on a patient's health outcome, an angle not explored in this first review of claim data. Correlating evidence in their findings also showed that the high usage of testing was found in regions of advanced education and high income, leading to speculation of an emerging economic barrier, another subset of data that warrants further investigation.

"Ultimately, these findings can sharpen our broader clinical focus on ensuring that prognostic testing is used in patients who stand to benefit from their results," Dr. Leapman added.

"Some regions had minimal or no use of genomic testing, while others had high levels of use, implying that decisions to test are highly discretionary," said Dr. Leapman. "In addition, there were groups of geographically unrelated regions that shared a similar pace of growth over time. These findings raise questions about shared factors that might promote rapid uptake of new cancer technologies."



Michael Leapman, MD

With a New Diagnosis of Prostate Cancer, Where you Live Matters

Tamar Taddei, MD

Adapting to the Changing Liver Cancer Landscape

In the United States, hepatitis C has long been the number one driver of hepatocellular carcinoma (HCC), the most common liver cancer and the fourth-leading cause of cancer-related deaths worldwide. Between three to five million Americans are living with chronic hepatitis C, but 4 in 10 do not realize they have it. More than 75 percent of patients are baby boomers, whose many years of undetected liver damage from hepatitis C make them particularly vulnerable to HCC.

In recent years, the liver cancer landscape has been rapidly changing in the United States. Skyrocketing hepatitis C cases, the emergence of a worrying new at-risk group for hepatitis C, and a surge in non-viral etiologies of HCC are presenting Yale Cancer Center researchers and clinicians with new challenges and opportunities in their approach to patient outreach and treatment.

In April 2020 the CDC announced that new hepatitis C cases in the U.S. are four times higher than they were a decade ago. In addition, adults 20 to 39 years old now have the highest rates of new cases. In response, the CDC changed its testing recommendations, advising all adults to be tested for hepatitis C at least once.

"The opioid epidemic is causing this very high prevalence among millennials," explained Tamar Taddei, MD, Associate Professor of Medicine (Digestive Diseases) and Director of the Liver Cancer Program at VA Connecticut Healthcare System. Hepatitis C is usually spread through blood, often from injection drug use. Opioid users commonly progress from prescription oral medications to injection drugs. "These younger people need to get tested and treated for hepatitis C immediately," Dr. Taddei said. "There's now a very effective cure for hepatitis C; we don't want them to develop cirrhosis or liver cancer."

Since 2014, direct-acting antivirals (DAAs) have become the standard of care for hepatitis C. "You can't underestimate the historical importance of the rise of oral DAA therapy and its impact on clinical management and overall epidemiology of hepatitis C," said Joseph Lim, MD, Director of the Yale Viral Hepatitis Program. "We're able to cure over 90 percent of patients with hepatitis C with these two- to three-month oral regimens and substantially reduce the risk of liver cancer and need for liver transplantation."

However, patients who already have cirrhosis are still at risk for liver cancer even after they are cured of hepatitis C. Using national VA electronic medical record data, Dr. Taddei and colleagues analyzed records of more than 48,000 VA patients who were cured of hepatitis C with antiviral treatment. Patients with stage 3 or 4 liver fibrosis at the time of treatment continued to have a high -risk of HCC for up to 10 years. The duration was startling. "These patients should still receive liver cancer screening with an ultrasound every six months. It's vital they continue, because if HCC is diagnosed at an early stage it is curable," she explained.

In a separate study, Dr. Taddei found that patients with cirrhosis benefitted from the use of statins, drugs which reduce lipids in the blood but may also have a favorable effect on portal hypertension. "Portal hypertension, or high blood pressure in the liver – the consequence of cirrhosis – leads to severe complications," she said. "People in our observational study on statins lived longer. We next want to see whether statins can prevent decompensation, when the scarring becomes so severe the liver starts to fail." She has launched a four-year clinical trial in which half of the anticipated 500 patients enrolled will take simvastatin for two years, while the other half will take a placebo; both groups will be observed for two years for hepatic decompensation.

The elevated, sustained risk of HCC in patients with cirrhosis is often driven by diabetes and obesity. Those two risk factors are also behind an alarming increase in non-alcoholic fatty liver disease (NAFLD). "The sheer number of people at risk is impressive," said Mario Strazzabosco, MD, PhD, Clinical Program Leader of Smilow Cancer Hospital's Liver Cancer Program and Deputy Director of the Yale Liver Center. "Ten years ago, we thought NAFLD was a benign condition. But then we realized it can lead to cirrhosis, and in some cases, it can lead to liver cancer without cirrhosis. So it's even more important to devise screening protocols that are both clinically effective and cost effective."

In 2020, Drs. Lim and Strazzabosco contributed to screening and surveillance guidance for HCC in NAFLD patients. Their individual papers each recommended ultra-sound to screen for HCC in NAFLD patients with cirrhosis.

"This is a story that is still being written, and there's a lot of research that needs to be done," said Dr. Strazzabosco. He is compiling a database of liver cancer patients to review their individual etiologies, treatments, and outcomes to improve clinicians' decision-making for future patients. "You have to look at all the risk factors in a single patient in order to combat a successful fight against this cancer," said Dr. Strazzabosco. "That is what we do in our program."

When lung cancer and breast cancer relapse, they often metastasize in the brain. The tumors that arise in the brain develop novel characteristics, differences that often confer resistance to existing drug therapies and create opportunities for new detection and treatment approaches for Yale Cancer Center researchers.

"We often think of metastasis as this orderly progression of events," said Don Nguyen, PhD, Associate Professor of Pathology and Medicine (Medical Oncology), "whereby malignant cells first spread from a primary tumor to eventually colonize a distant organ. But it's actually quite dynamic and context-dependent. It's driven both by molecular underpinnings of the tumor and by how the tumor cells interact with their overall environment."

Dr. Nguyen focuses his research efforts on the progression and metastasis of lung cancer. "The incidence of brain metastasis in patients who have other types of cancer is on the rise," he explained. "One of the central questions we have is, are the mechanisms that drive a lung cancer to metastasize to the brain similar, or different, than in other disease types? And how can we leverage different molecular profiling techniques to compare and contrast these metastases so we can analyze what is going on in the tumors as well as in the tumor microenvironment?"

In their recent research, Dr. Nguyen and his team have made several significant discoveries on both fronts. Their experiments began in mice with a human lung cancer cell line that quickly metastasizes to the brain. They found changes in thousands of genes in the tumor cells and stromal cells, induced by the tumor microenvironment (TME). "The extent of those changes surprised us," he said.

They validated some of their findings by examining human tissue samples. They then expanded their scope by testing xenograft models of breast cancer and melanoma metastases in the brain. They found the same surprising scale of epigenetic change.

"Regardless of where the cancer originated, once it spread to the brain the tumors exhibited molecular changes that made them act more like neurons," Dr. Nguyen said. "They started to express molecules that are involved in cell communication. Neurons are known to do this because cell-to-cell interactions are essential for propagating more signals in the brain. One of the fascinating questions we're trying to answer is whether the tumor cells are able to engage in similar interactions for them to survive in this unique environment. And if we were to disrupt that signaling, would we be able to reduce tumors that are already in the brain?"

These cells exhibited remarkable plasticity; when removed from the TME, they stopped acting like neurons. "These traits were reversible," he added. "That tells us these changes are epigenetic in nature, occurring in response to input from the tumor microenvironment. That makes them a promising target."

Dr. Nguyen's team was also surprised to find two anti-inflammatory biomarkers, Lag-3 and Tim-3, were significantly upregulated in the TME compared to healthy brains. "These proteins are typically found as immune checkpoint regulators on T cells," Dr. Nguyen explained. "We found they were expressed on resident microglia, an immune cell that's very specific for the central nervous system. These proteins hadn't been considered a therapeutic target in brain metastases before, but now they offer potential opportunities for treatments."

This research provided preliminary data for a five-year, nearly $4 million grant that the National Cancer Institute (NCI) awarded to Dr. Nguyen and Katerina Politi, PhD, Associate Professor of Pathology, to generate and evaluate patient-derived models to study resistance to targeted therapies in EGFR mutated lung cancer.

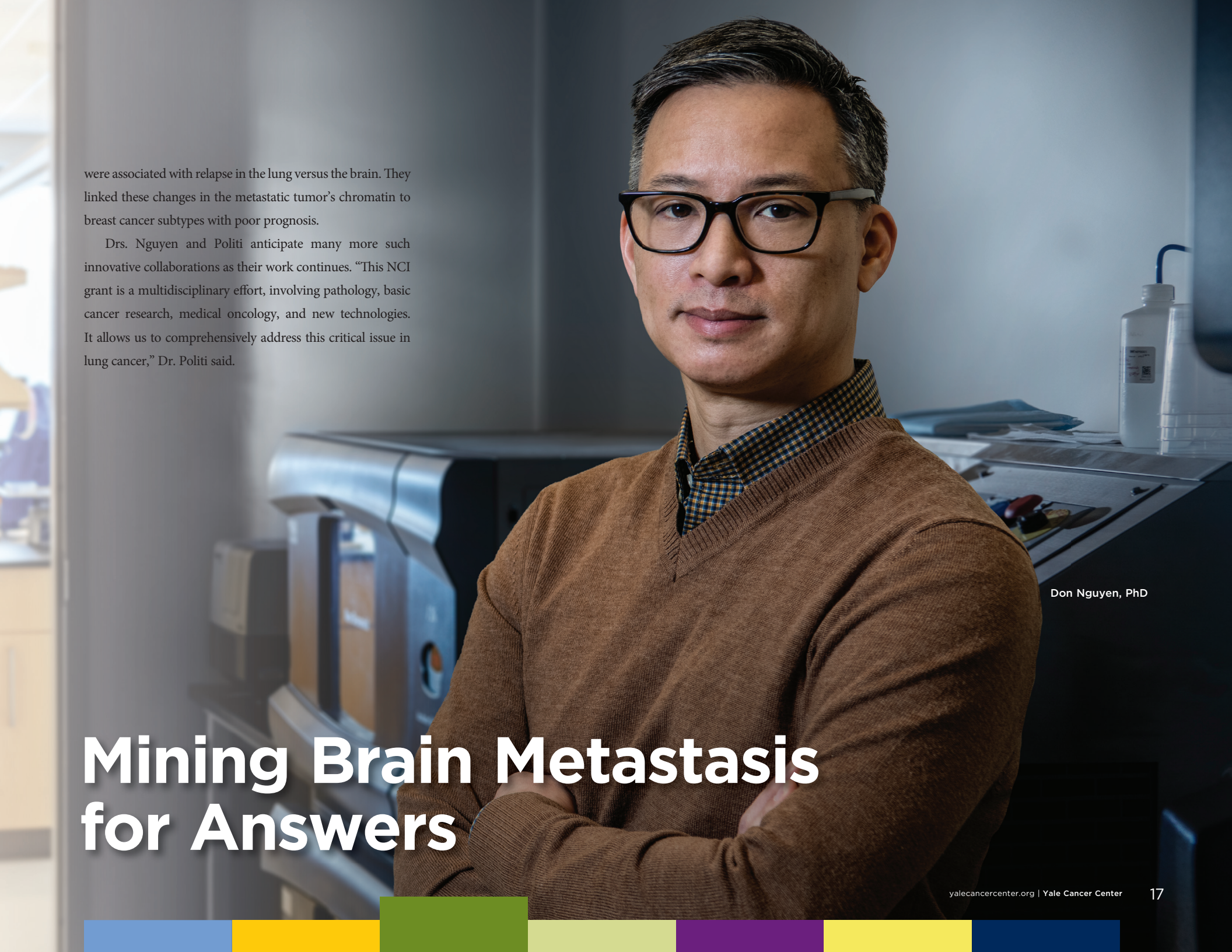
"Tyrosine kinase inhibitors are targeted therapies that are used as the first line of treatment for this disease. However, drug resistance inevitably emerges, limiting their curative potential," Dr. Politi explained. "Through this research, we are focused on understanding how resistance is linked to metastasis, and whether resistance is different at different metastatic sites in the body. By studying patient-derived models, we can learn from the complexity of human tumors directly to understand how they change through treatment, which is very exciting."

The grant is part of the NCI's Patient-Derived Models Consortium. At Yale Cancer Center, the grant is increasing cross-disciplinary collaboration, not just among Drs. Nguyen and Politi's teams, but also with experts from the lung and melanoma programs as well as the Genetics, Genomics, and Epigenetics Program.

For example, Dr. Nguyen partnered on a 2020 study with Qin Yan, PhD, Associate Professor of Pathology to identify distinct and substantial epigenomic changes in breast cancer cells that metastasize to the lung and brain. Furthermore, they could distinguish the pathways—which transcription factors

were associated with relapse in the lung versus the brain. They linked these changes in the metastatic tumor's chromatin to breast cancer subtypes with poor prognosis.

Drs. Nguyen and Politi anticipate many more such innovative collaborations as their work continues. "This NCI grant is a multidisciplinary effort, involving pathology, basic cancer research, medical oncology, and new technologies. It allows us to comprehensively address this critical issue in lung cancer," Dr. Politi said.



Don Nguyen, PhD

Mining Brain Metastasis for Answers

Rallying Resources Around DNA Repair Research

When it comes to unlocking the secrets of DNA repair, Ranjit Bindra, MD, PhD, doesn't think in terms of just resources. The Professor of Therapeutic Radiology and Pathology favors a far mightier word: armamentarium. Based on the Latin word for "armory," it describes the collection of medicines, equipment, and techniques.

Yale Cancer Center has an especially impressive armamentarium in the study of BRCA1 and BRCA2, proteins involved with DNA repair that, when mutated, can cause breast, ovarian, prostate, and pancreatic cancers. So, when a $1 million grant became available for BRCA research from the Gray Foundation in 2018, a team of Yale experts combined their collective skills to secure the gift.

In the two years since, Yale's team has made significant advances in targeting the BRCA-dependent DNA repair axis for cancer therapy. "Both the BRCA1 and BRCA2 protein are involved in DNA repair," said Megan King, PhD, Associate Professor of Cell Biology and of Molecular, Cellular and Development Biology and co-leader of the Radiobiology and Radiotherapy Research Program at Yale Cancer Center. "However, the work we've done has shown us that they have fundamentally different mechanisms. That's important, because typically in clinical trials we lump together patients with BRCA1 and BRCA2 mutations. We need to think about these patient populations differently."

Those mechanisms affect which kind of therapies might work once cancer patients relapse on PARP inhibitors. For example, Dr. King has identified that if BRCA1 tumors stop expressing the 53BP1 or REV7 protein, they become resistant to PARP inhibitors. That's because the absence of those proteins allows a third enzyme, called the Bloom syndrome protein (BLM), to resume the resection of DNA double-strand breaks and go into repair overdrive called "hyper-resection."

Dr. King's research identified BLM as a novel therapeutic target. She already has a candidate in mind for the job: a new class of drugs called ATR kinase inhibitors. "BLM's hyper-resection is a vulnerability that makes it sensitive to ATR inhibitors," Dr. King explained. She is working to design a clinical trial for ATR inhibitors in BRCA1 patients with fellow Gray Foundation team member Patricia LoRusso, DO, Professor of Medicine and Associate Cancer Center Director of Experimental Therapeutics.

The team's expert on BRCA2 is Ryan Jensen, PhD, Associate Professor of Therapeutic Radiology and Pathology. He was the first scientist to purify and study the properties of the full-length BRCA2 protein. In collaboration with AstraZeneca, Dr. Jensen has focused on three BRCA2 reversion alleles that reactivate DNA repair functions in tumor cell DNA from ovarian cancer patients who relapsed on a PARP inhibitor. He's currently researching whether these alleles alone cause resistance to PARP inhibitors. Dr. Jensen's team hopes this "reverse translation" approach will accelerate our understanding of why BRCA2 plays such a crucial role in responding to PARP inhibitors.

Enter Dr. Bindra, whose expertise in drug development drives the translation of these laboratory targets into patient therapies. His high-throughput testing capabilities enable him to conduct 96- and 384-well plate-based screening assays in PARP-naïve and resistant cell lines. Dr. Bindra can look at 384 tiny wells overnight and analyze the images and discover patterns automatically.

Using Dr. Bindra's library of DNA repair inhibitor and damaging agents, he mixes them to create new therapeutic combinations to replace current PARP inhibitors. "When we do this testing in an academic setting instead of a pharmaceutical one, we're able to profile all drug candidates out there," Dr. Bindra said.

These cell lines have proven invaluable in Yale's DNA repair research. Faye Rogers, PhD, Associate Professor of Therapeutic Radiology, tapped the library for a cell line in her research on the use of endophytes to develop novel cancer-fighting compounds. Endophytes are fungus or bacteria known as an untapped source for finding novel bioactive natural products.

An undergraduate student in Dr. Rogers' lab collected endophytes while in Ecuador with Yale's Rainforest Expedition and Laboratory course. Dr. Rogers identified one that produces a compound that inhibits DNA double-strand break repair in cancers with repair deficiencies. "We're now moving forward to come up with a synthetic version of this compound and conducting some medicinal chemistry to improve its efficacy," she said.

Dr. Rogers has returned the favor to the Bindra library. She has advised Dr. Binda's students in how to synthesize new classes of DNA repair inhibitors that will further expand their testing capabilities of new compounds. "When you bring together people with different skills and perspectives," Dr. Bindra said, "it adds so much more value to the conversation." And adds yet more invaluable tools to Yale's DNA repair armamentarium.

Obesity has long been identified as a risk factor for pancreatic cancer, but how to leverage that knowledge for prevention and treatment has been elusive. Mandar Deepak Muzumdar, MD, is in the process of changing that.

Dr. Muzumdar has uncovered hormonal activity associated with obesity that creates targets for drug development. He was lead author of a paper published in the journal *Cell* in May 2020 that revealed the role of the peptide hormone cholecystokinin (CCK)–made within the pancreas itself–in accelerating tumor progression in pancreatic ductal adenocarcinoma in mice. Dr. Muzumdar's discovery raises the possibility of more effective drugs in the battle against pancreatic cancer–as well as a new promising strategy of employing endocrinology and genetics in concert to explore the mechanisms driving obesity-related cancers.

The paper is the result of intensive work since his arrival at Yale Cancer Center three years ago. But its genesis stretches back more than a decade to when Dr. Muzumdar was a medical student at Stanford. "On my clinical oncology rotation, one of the things that was impressed upon me was to learn the risk factors of different cancer types," he said. "It never quite made sense why it would matter, because at that point the patient had already been diagnosed with cancer. It was not clear that knowing the risk factors would really change their treatment."

As his studies continued, obesity was getting increasing attention as a risk factor in pancreatic and other cancers. But there was scant knowledge about exactly how obesity was contributing to malignancies. "I conceived this project to study this in more tractable animal models that would allow us to understand causal relationships between obesity and cancer, and then hopefully understand mechanisms. In the last few years of my research fellowship before coming to Yale, I developed a mouse model to study this phenomenon. I was fortunate to go where the science led us and to find collaborators to help us here at Yale to really dive deep."

"We also had a very diverse array of trainees who were involved in the project. I think training the next generation of scientists in cancer biology is really important. I take pride in the fact that we were able to involve so many trainees to make important discoveries," he said.

His work showed that tumor progression could be slowed or stopped in mice with precancerous tumors if they lost weight. Unfortunately, since pancreatic cancer is typically diagnosed in advanced stages in humans, that finding does not point to a treatment option. But Dr. Muzumdar said that the information will be important for doctors to use in counseling weight loss for patients who may be at high-risk for pancreatic cancer.

Late diagnosis is one of the reasons that pancreatic cancer has a higher mortality rate than most. "I think I was drawn to this primarily because it remains a challenging disease," Dr. Muzumdar said. "I was also drawn because I was personally impacted by gastrointestinal cancer, with my father who passed away from duodenal cancer."

Dr. Muzumdar is an Assistant Professor of Medicine (Medical Oncology) and Genetics. He expected the KRAS gene, which has mutations in more than 90 percent of pancreatic cancer patients, to loom large in his investigations. "A few years ago, we tried to test whether KRAS was a good target in pancreatic cancer. Instead of drugs, which weren't available, we used genetic tools to eliminate KRAS in pancreatic cancer cells, and through these studies we found that over half of the pancreatic cancer cell lines that we eliminated KRAS in could survive nevertheless."

This led him to think about looking "beyond the gene" to other activity within the pancreas and ultimately to CCK. The investigation reinforced Dr. Muzumdar's belief in "team science" as endocrinology became important in his own work. He is the leader of the Yale Pancreatic Cancer Collaborative (see feature article), which aims to help scientists from various disciplines work together to accelerate discovery around better prevention and treatment.

"There is no single lab that can do everything. Every lab has its expertise, and there's relationships that are required between basic scientists, translational researchers, and clinicians to effectively take advantage of the basic science and bring it to the clinic," he said. Collaboration also helped him validate critical findings in this investigation. "We were able to validate findings, for example, from our animal models in human biospecimens. We were able to profile for these hormonal factors in human specimens and validate that they were present where we thought they would be." Based on these findings, Dr. Muzumdar believes that targeting CCK or other hormones made within the pancreas may become an important strategy in pancreatic cancer prevention or even treatment. He was recently awarded a 2021 Damon Runyon-Rachleff Innovation Award from the Damon Runyon Cancer Research Foundation and will continue to "understand that fundamental biology of pancreatic cancer in hopes of informing better ways of preventing and treating the disease."

Mandar Deepak Muzumdar, MD

Curiosity and Collaboration Work Together to Solve a Cancer Mystery

Taking a Dumbbell to Drug-Resistant Cancers

The partnership of Daniel Petrylak, MD, and Craig Crews, PhD, didn't quite form by accident, but it was spurred by a bit of luck.

Dr. Crews is the John C. Malone Professor of Molecular, Cellular, and Developmental Biology and a Professor of Chemistry, of Pharmacology and of Management, plus the Executive Director of the Yale Center for Molecular Discovery.

Dr. Petrylak is a Professor of Medicine (Medical Oncology) and Urology at Yale Cancer Center and Smilow Cancer Hospital and a pioneer in treatments for prostate, bladder, kidney and testicular cancer.

The pair met at an informal get together hosted by the chemistry department to show their researchers' work. In addition to his roles at Yale, Dr. Crews is also a biotech entrepreneur. He and Dr. Petrylak realized that they might be able to collaborate on a new kind of drug to treat prostate cancer.

The CEO of Proteolix, Dr. Crews' first company, died of the disease, and he "wanted to make sure that if I had the opportunity to develop another oncology company, the first cancer I'd target would be prostate," Dr. Crews said.

When he was talking with potential investors for his new company, Dr. Crews said he "dragged them down to Dan's office, and Dan was kind enough to entertain the two of us and convince the investor that a new class of cancer treating drugs was possible, and needed."

Together, they have done exactly that with ARV-110, a proteolysis-targeting chimaera, or PROTAC, now in clinical trials at Smilow Cancer Hospital. It is designed to get around the "drug resistant" part of drug resistant prostate cancer, with the promise that the same concept can work in other cancers that are currently considered untreatable.

PROTACs work by using elements of the body's natural protein recycling system, and recruiting them towards cancerous proteins. "We're using this biological function and hijacking it to get rid of other proteins," explained Dr. Crews, who is developing this drug through Arvinas, the company he founded in part by introducing those investors to Dr. Petrylak. "It's co-opting a natural process and is a completely different approach from how other cancer drugs work today."

PROTACs do this in dumbbell form. One side binds to a cancer protein with the other latching onto a ubiquitin ligase, which adds a "flag" to mark proteins as ready for recycling. Proteasomes roam around cells looking for those flags so they know what to pick up and shred. Once PROTACs mark a cancer protein with a flag, proteasomes pick it up and recycle it just like any other protein.

Dr. Crews first came at the problem from the opposite direction. Instead allowing the ubiquitin system to break cancer proteins down, he worked on a drug that gummed up the works. As a result, levels of toxic proteins that should have been recycled kept building up until they killed the cell. It worked and became carfilzomib, a treatment for multiple myeloma.

But using the body's own recycling system to eliminate problem proteins made more sense. It's also more efficient. "It only takes one PROTAC to take out about 400 proteins," said Dr. Petrylak. One PROTAC can keep flagging cancer proteins over and over and over again.

ARV-110 specifically targets metastatic castration-resistant prostate cancer (mCRPC), which accounts for most of the 28,000 prostate cancer deaths in the U.S. each year. Hormone sensitive prostate cancer is typically treated with androgen deprivation treatments, which block the natural production of cancer-spurring androgens. While initially effective, most patients become resistant to it, after which the cancer can metastasize.

In a preliminary Phase I clinical trial of 22 patients who had already undergone at least two different unsuccessful treatments, seven were treated with the level of ARV-110 that pre-clinical trials showed should be effective. Of those seven, two patients had a more than 50 percent reduction in prostate-specific antigen (PSA). One patient's tumor shrunk more than 50 percent. "In some patients, the response lasted for more than seven months," said Dr. Petrylak.

The hope is that PROTACs can treat other "undruggable" cancers that don't respond to current treatments, including types of lung, breast, and colorectal cancers that may not have an active site on which a small-molecule drug or monoclonal antibody could bind. PROTACs don't need that specific of a site. "This is not an approach that is prostate-specific. It's not even target-specific. You can have multiple targets that you want to down regulate," said Dr. Petrylak.

The research has been invigorating, and exciting, he added. "I've had so much fun working on this from the standpoint that it's incredibly justifying to see something that Craig has done in the laboratory and then take that into patients and learn a lot about not just this drug but also the biology of diseases."

Our bodies have two immune systems: the innate one we are born with that is capable of inducing a rapid immune response; and the adaptive one, which is prompted into action by the innate immune system. The innate immune system detects an intruder and sends out a first line of defense, and directs the adaptive immune system to create a more specific and nimble response.

Cancer can proliferate when the immune system fails to destroy cancerous cells. Tumors can, for example, neutralize pathways that lead to the production of T-cells, a type of white blood cell the body creates that forms part of the adaptive immune system and can attack cancer.

And while checkpoint inhibitor drugs, a newer class of cancer treatments, can block this type of cancer defensive move, they don't always work. In fact, only 15 to 20 percent of patients respond to the drugs, and they are not effective on some cancers at all, including types of brain, breast, ovarian, pancreatic, and colon cancers.

Instead of relying solely on the adaptive immune system to sustain an on the ground defense, two Yale Cancer Center scientists have gone upstream. Their research focuses on Tyro3, Axl, and MerTK, a group of receptor tyrosine kinases collectively known as TAM, which together play a key role in regulating the innate immune system.

Together, they are testing small molecule drugs to "release the brakes," explained Sourav Ghosh, PhD, Associate Professor of Neurology and Pharmacology, which allows the innate immune system to direct T-cells themselves and boost the effectiveness of checkpoint inhibitor drugs.

"If you inhibit the TAMs, you release the brake on the innate immune system response, and mount a much stronger response to the cancer," added Carla Rothlin, PhD, Dorys McConnell Duberg Professor of Immunobiology and Pharmacology and Howard Hughes Medical Institute Faculty Scholar. Going straight to the innate immune system skips the war between cancer's defenses and adaptive immune system responses.

When the innate immune system detects an invader, like a virus, it creates a range of responses, including natural killer (NK) cells, which are a blunt force, front line attack, and dendritic cells, which direct the adaptive immune system to spring into action and create specific responses. One of those responses are T-cells to go after that specific intruder and also establish an immunological memory to respond to a recurrence.

"The adaptive immune system is more precise and focused," said Dr. Ghosh.

Normally, TAMs inhibit some inflammation of an immune system response. While that is good if you don't want a papercut on your finger to flare out of control while the body repairs the wound, it's not always good when it comes to attacking cancers.

Small molecule inhibitors or biologics to inhibit the inhibitors could break the brakes and allow the innate immune system to get T-cells where they need to go. "Our hope is that by targeting the innate immune system, you can get T-cells to come to the tumor and engage them," said Dr. Ghosh. "We are trying to make the immune system trainers better."

That means tumors that are now considered "cold" or T-cell excluded "may be where we see the most effect of this immune system blockade if the immune system is a little bit on hyperdrive and then engage the T-cells to go to tumors unphased by checkpoint blockers," he added.

The pair is currently working with Sarah Goldberg, MD, MPH, Associate Professor of Medicine (Medical Oncology), on launching a clinical trial for the TAM inhibitor sitravatinib, to determine if, when combined with the checkpoint inhibitor immunotherapy drug pembrolizumab, it can provoke a better immune system response. They plan to enroll 70 patients from Smilow Cancer Hospital and one other hospital site in the trial.

"Pembrolizumab is one of the standard treatment options for patients with advanced non-small cell lung cancer with PD-L1 expression of at least one percent, but unfortunately many patients will not benefit from this treatment," said Dr. Goldberg. It's only about 15 percent effective in treating advanced non-small cell lung cancer. Based on Drs. Rothlin and Ghosh's findings, Dr. Goldberg and oncology fellow Emily Collier, MD, believe that "targeting certain characteristics in the tumor microenvironment with sitravatinib might make the immunotherapy work even better."

Dr. Rothlin said that even though this discovery could lead to cancer treatments, that's not the primary focus of their work. "We study how you regulate how much your immune system responds, and how long your immune system responds," Dr. Rothlin said, which leads to a better understanding of how our bodies work and yes, potentially, help cancer patients for whom current treatments have failed. "That's the beauty of basic science," she said.

Releasing the Brakes on an Innate Immune System Response

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Patricia LoRusso
David Madoff
Scott Miller
Jennifer Moliterno Gunel
Bryce Nelson
Natalia Neparidze
Antonio Omuro
Terri Parker
Farzana Pashankar
Pasquale Patrizio
Peter Peduzzi
Nikolai Podoltsev
Thomas Prebet
John Roberts
Michal Rose
William Mark Saltzman
Alessandro Santin
William Sessa
David Spiegel
Preston Sprenkle
Stacey Stein
Mario Strazzabosco
Seyedtaghi Takyar
Vasilis Vasiliou
Sarah Weiss
Amer Zeidan
Daniel Zelterman
Jianbing Zhou

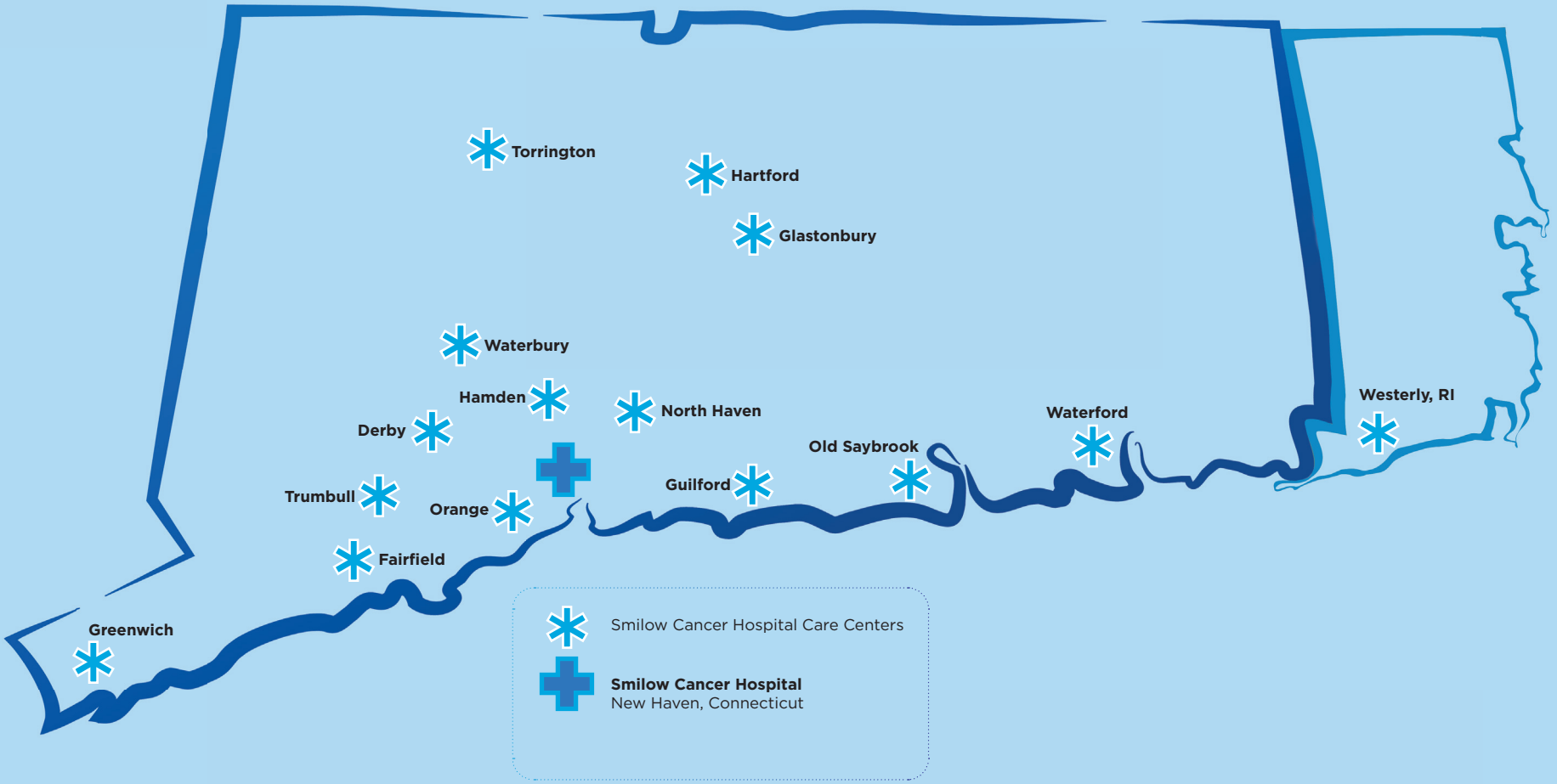
Genomics, Genetics, and Epigenetics

Nita Ahuja
Claudio Alarcon
Allen Bale
Linda Bartoshuk
Susan Baserga
Jean Bolognia
Marcus Bosenberg
Demetrios Braddock
Sidi Chen
Keith Choate
James Clune
Lynn Cooley
Jose Costa
Andrew Dewan
Nadya Dimitrova
Mark Gerstein
Antonio Giraldez
Murat Gunel
Shangqin Guo
Ruth Halaban
Stephanie Halene
Erin Hofstatter
Gloria Huang
Farren Issacs
Dhanpat Jain
Lucia Jilaveanu
Samuel Katz
Sajid Khan
Kenneth Kidd
Yuval Kluger
Christine Ko
William Konigsberg
Diane Krause
David Leffel
Bluma Lesch
Morgan Levine
Peining Li
Haifan Lin
Xavier Llor
Jun Lu
Charles Lusk
Shrikant Mane
Mandar Muzumdar
Sigrid Nachtergaele
Karla Neugebauer
James Noonan
Manoj Pillai
Manju Prasad
Lajos Pusztai
Peter Schwartz
Emre Seli
Jeffrey Sklar
Hugh Taylor
Toma Tebaldi
Jeffrey Townsend
Zuoheng Wang
Sherman Weissman
Frederick Wilson
Andrew Xiao
Mina Xu
Tian Xu
Qin Yan
Hongyu Zhao
Minghao Zhong

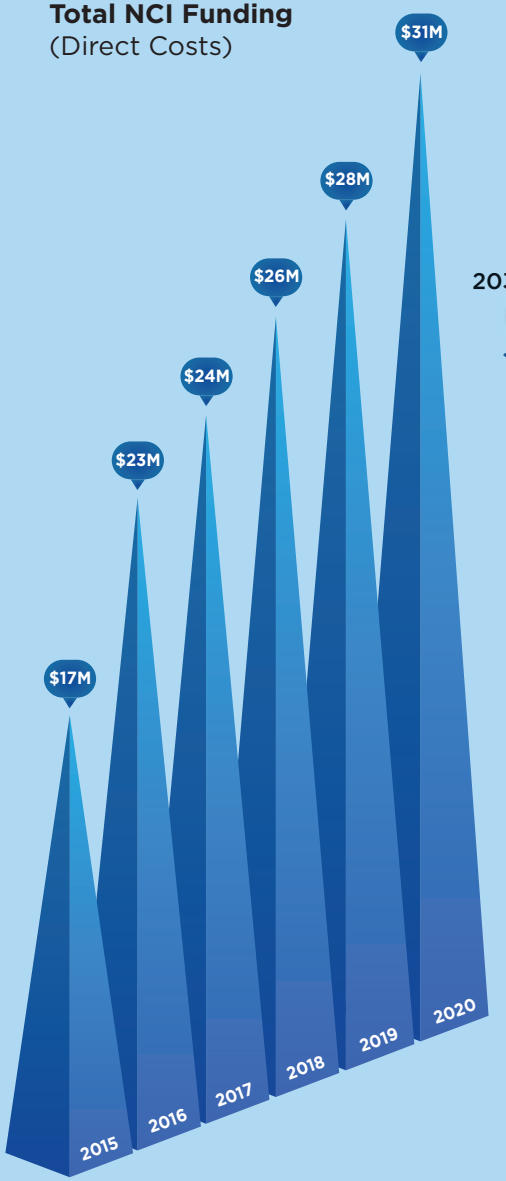
Radiobiology and Radiotherapy

Sanjay Aneja
Ranjit Bindra
Justin Blasberg
Franziska Bleichert
Daniel Boffa
Douglas Brash
Zhengxin Cai
Richard Carson
Sandy Chang
Zhe Chen
Veronica Chiang
John Colberg
Daniel Coman
Joseph Contessa
Francesco D'Errico
Shari Damast
Roy Decker
Jun Deng
Frank Detterbeck
James Duncan
Luisa Escobar-Hoyos
Suzanne Evans
Peter Glazer
Fanqing Guo
James Hansen
Susan Higgins
D.S. Fahmeed Hyder
Ryan Jensen
Lilian Kabeche
Megan King
Bernadette Marquez-Nostra
Meena Moran
Evan Morris
Rosa Munoz Xicola
Ravinder Nath
Henry Park
Abhijit Patel
KennethRoberts
Faye Rogers
David Stitelman
Christopher Tien
Lynn Wilson
James Yu

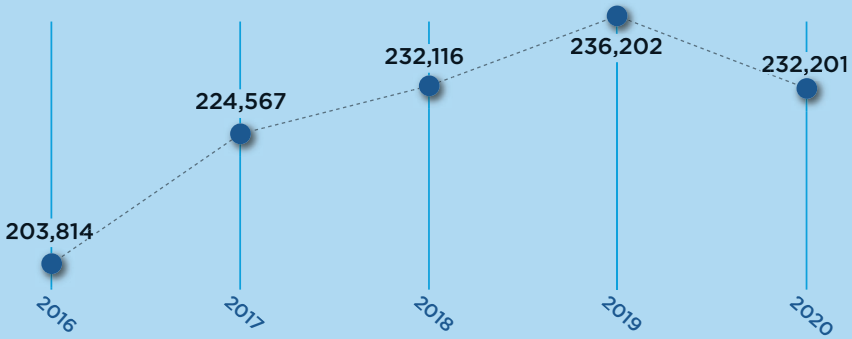
Yale Cancer Center and Smilow Cancer Hospital Data



Total NCI Funding
(Direct Costs)



Clinical Volume



Office Visits by Year

2019 Top Ten Cancer Sites
at Smilow Cancer Hospital

MALE			FEMALE		
PROSTATE	16.8%	552	1220	32.5%	BREAST
LUNG & BRONCHUS	12.3%	405	421	11.2%	LUNG & BRONCHUS
MELANOMA	7.9%	260	209	5.6%	MELANOMA
NON HODGKIN'S LYMPHOMA	6.0%	196	209	5.6%	THYROID
COLORECTAL	5.6%	185	203	5.4%	BRAIN & CNS
ORAL CAVITY & PHARYNX	5.3%	176	201	5.4%	CORPUS & UTERUS
LEUKEMIA	5.2%	171	173	4.6%	COLORECTAL
BRAIN & CNS	4.9%	160	151	4.0%	NON HODGKIN'S LYMPHOMA
URINARY BLADDER	4.5%	149	101	2.7%	PANCREAS
KIDNEY & RENAL PELVIS	3.7%	122	95	2.5%	LEUKEMIA
OTHER	27.8%	916	774	20.6%	OTHER
		TOTAL: 3,292			3,757: TOTAL

Publications
from Yale Cancer Center Members

June 30, 2019 – July 1, 2020

826 PUBLICATIONS

173 High Impact Publications
IF > 10, including:

- 54 – Nature/Nature Specialty
- 24 – Journal of Clinical Oncology
- 11 – Cell/Cell Specialty
- 11 – Science/Science Specialty
- 9 – JAMA/JAMA Oncology
- 7 – Lancet/Lancet Oncology
- 6 – Blood
- 6 – New England Journal of Medicine
- 4 – Annals of Oncology
- 4 – Hepatology
- 4 – Journal of Clinical Investigation
- 4 – Journal of the National Cancer Institute
- 4 – Molecular Cell
- 3 – Gastroenterology

“2020 HAS BEEN AN AMAZING JOURNEY AND WE’RE GRATEFUL THAT WE ENDURED TOGETHER.”


Yale
NewHaven
Health

YaleNewHavenHealth
Smilow Cancer Hospital

Yale CANCER CENTER
A Comprehensive Cancer Center Designated by the National Cancer Institute

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