BreakThroughs

Duke Cancer Institute

Winter 2022

WHEN PREVENTION PAYS OFF

Cancer Prevention Is the Ultimate Therapy

LES TODD

MICHAEL B. KASTAN

IN THE LAST HALF CENTURY, DUKE CANCER INSTITUTE has garnered national and international recognition for outstanding research, breakthrough treatments, exceptional cancer care, and support services that focus on the whole person.

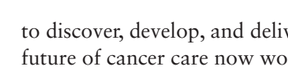
As we embark on our next 50 years, we are daring to ask a bold question: What if fewer people developed cancer? After all, cancer prevention is the ultimate therapy. That's the vision that we are working toward with our new Cancer Risk, Detection, and Interception Research Program. In this issue you'll read about this multidisciplinary group of doctors and scientists who are working together to make that vision a reality.

You will also read about an example of how the collaborative environment and wide-ranging expertise at Duke makes it the perfect place to translate findings from the laboratory to the clinic. In this case it is a test that shows promise for diagnosing pancreatic cancer in its early stages, when it is much more treatable.

As always, you will see the faces of just a few of our remarkable donors and friends who are partnering with us every day to raise awareness of and support for people with cancer and cancer research.

Thank you for all you do for Duke Cancer Institute. None of our efforts to discover, develop, and deliver the future of cancer care now would be possible without you.

"AS WE EMBARK ON OUR NEXT 50 YEARS, WE ARE DARING TO ASK A BOLD QUESTION: WHAT IF FEWER PEOPLE DEVELOPED CANCER? AFTER ALL, CANCER PREVENTION IS THE ULTIMATE THERAPY. THAT'S THE VISION THAT WE ARE WORKING TOWARD WITH OUR NEW CANCER RISK, DETECTION, AND INTERCEPTION RESEARCH PROGRAM."



Michael B. Kastan, MD, PhD
Executive Director, Duke Cancer Institute
William and Jane Shingleton Professor,
Pharmacology and Cancer Biology
Professor of Pediatrics

ON THE COVER:
When Prevention Pays Off. After taking steps to stop a pre-cancer, Therese has written two books and exercises an hour and a half every day. Read the story on page 11. Cover photo by Aurora Rose De Crosta.

Breakthroughs is produced two times a year by Duke Cancer Institute Office of Development
300 West Morgan Street, Suite 1000
Durham NC, 27701 • Phone: 919-385-3120

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Prestigious Grant Helps Explore the Origins of Cancer

A Duke Cancer Institute researcher is a member of a group receiving the prestigious Cancer Grand Challenges Grant, providing $25 million over five years to investigate the origins of cancer.

The nine-member, international research team includes Christopher Counter, PhD, a professor in the Department of Pharmacology & Cancer Biology and associate director of Basic Research in the Duke Cancer Institute. The research collaboration, called PROMINENT, focuses on how normal cells harbor mutations, and what triggers these mutations to become malignant or remain benign.

Counter's role in the research group will build on his current work in mice and other laboratory models to determine the effects of environmental, metabolic, inflammatory, and genetic stresses that cause dormant mutations to become cancerous.

"There have been major advances in treatments for cancer patients over the last few decades, many of which Duke and the Duke Cancer Institute have been at the forefront of," Counter said. "What this grant will allow us to do is to now determine how cancer first originates, with the ultimate goal of identifying ways of preventing this terrible disease before it even gets out of the starting gate."

Cancer Grand Challenges grants are awarded by Cancer Research UK and the National Cancer Institute in the US. The joint effort supports a global community of diverse, world-class research teams that work together, think differently, and take on cancer's toughest challenges.

— Alexis Porter

KEN HUTH

CHRISTOPHER COUNTER

Homegrown 'Just Ask' Program Rolls Out Nationally

LES TODD

NADINE BARRETT

The official adaptation of "Just ASK: Increasing Diversity in Clinical Research Participation" — a course developed and piloted at Duke Cancer Institute (DCI) five years ago by Nadine Barrett, PhD — has rolled out nationally.

Now trademarked by the American Society of Clinical Oncology (ASCO) and the Association of Community Cancer Centers (ACCC), the Just ASK™ Increasing Diversity in Cancer Clinical Research: An ACCC-ASCO Training Program is being offered as "an online implicit bias training program intended for all members of the research team." The training, which provides a health equity framing and lens, consists of five interactive modules that can be completed independently in about 60-90 minutes, and focuses on the broader context of structural and systemic racism.

"Structural and systemic racism manifests in many ways, one being implicit biases that limit access to quality care and research for historically marginalized populations," said Barrett, director of Equity, Community and Stakeholder Strategy within DCI's Community Outreach, Engagement, and Equity program, as well as director of the Center for Equity and Research at the Duke Clinical and Translational Science Institute. "This training is one resource that helps chip away at these pervasive and longstanding inequities, locally and nationally."

Just Ask
engaging patients, community and research teams

Created in 2017 and expanded in 2020, the Just Ask training was adapted and tested by ASCO-ACCC as a result of Barrett's work and collaborations with DCI, Duke CTSI, the Center for Equity in Research, and the Duke Office of Clinical Research (DOCR). The DOCR, under the leadership of Associate Dean for Clinical Research Denise Snyder, MS, RD, first rolled out Just Ask with the DCI clinical research teams, then expanded access to all clinical research teams across Duke through the Duke Engagement, Recruitment, and Retention Certification Program (manuscript in press). The training has also been used by other national research institutions and organizations.

— Julie Poucher Harbin

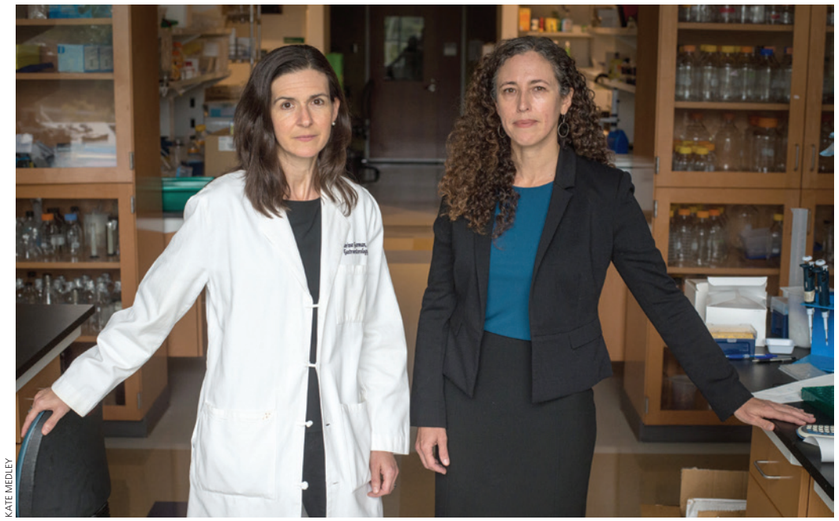
JOEY GUIDONE

MISSION: INTERCEPTION

Creating Better Ways to Stop Cancer In Its Tracks

BY **ANGELA SPIVEY**

As Duke celebrates more than 50 years of cancer breakthroughs, a new research program works toward a future when no one ever develops cancer.



KATE MEDLEY

KATHERINE GARMAN (left) and **MEIRA EPPLEIN** co-lead the Cancer Risk, Detection, and Interception Research Program.

In 2018, Meira Epplein, PhD, associate professor in population health sciences and medicine, applied an intervention to stop cancer in a setting that most might not expect: a church.

Epplein is an expert in Helicobacter pylori (H. pylori), a stomach bacterium that causes pain, nausea, or ulcers in some people, and no symptoms in others. The bug is also linked to increased risk of stomach cancer. Stomach cancer is rare, but some groups, including African Americans, Asian Americans, Hispanic Americans, American Indians, and those with Ashkenazi Jewish heritage, are more likely to develop it.

KATE MEDLEY

KATHERINE GARMAN studies these pathology slides from endoscopic biopsies to understand how to prevent stomach cancer.

In those infected with H. pylori, a two-week course of antibiotics can eradicate the bacterium and reduces risk of stomach cancer by 50%, said Epplein, whose great-grandmother died of the disease.

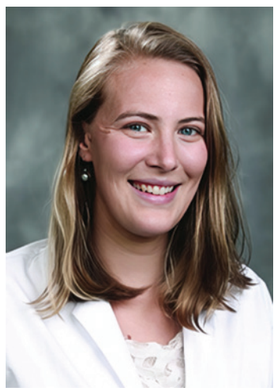
To reach people at higher risk who might not otherwise get tested and treated, Epplein partnered with Bishop Ronald Godbee of The River, one of the largest African American churches in Durham, North Carolina. Godbee introduced Epplein to the congregation, she spoke about the importance of getting tested, then they hosted a testing event at the church.

Using a breath test, the researchers tested 92 people, 23 of whom tested positive. They received letters about their results and were encouraged to share this information with their primary care doctors and ask to be treated if appropriate.

> "We want to think about stopping cancer before someone ever gets to an oncologist. We want to help clinicians think about what's on that cancer pathway and what you can do, not just to treat the symptoms and what's going on right now with your patient, but to reduce the risk of developing cancer."
>
> Meira Epplein

This pilot project is an example of a non-traditional cancer intervention that Epplein and others would like to see happen more often. She and gastroenterologist Katherine Garman, MD, MHS, associate professor of medicine, co-lead the Cancer Risk, Detection, and Interception (CRDI) Research Program at Duke Cancer Institute (DCI). The program brings together gastroenterologists, Ob/Gyns, surgeons, and other clinicians with cancer biologists, epidemiologists, biostatisticians, and others to develop new ways to identify people most at risk for cancer.

PETER ALLEN



AUSTIN ECKHOFF

FAST FACTS

THE CANCER RISK, DETECTION, AND INTERCEPTION RESEARCH PROGRAM

- Created in 2021 to focus on research that falls somewhere between cancer prevention and treatment
- Brings together gastroenterologists, Ob/Gyns, surgeons, and other clinicians with cancer biologists, epidemiologists, biostatisticians, and others to develop new ways to identify people most at risk for cancer
- Co-leaders: **Meira Epplein, PhD** and **Katherine Garman, MD**
- Steering Committee members: **Shelley Hwang, MD; Heather Stapleton, PhD; Evan Myers, MD, MPH**
- Members pursues collaborative research as well as community outreach.

The goal is to stop the disease process in the early stages, ideally even before it is considered cancer.

"We want to think about stopping cancer before someone ever gets to an oncologist," Epplein said. "We want to help clinicians think about what's on that cancer pathway and what you can do, not just to treat the symptoms and what's going on right now with your patient, but to reduce the risk of developing cancer."

As a comprehensive cancer center designated by the National Cancer Institute (NCI), Duke Cancer Institute must obtain NCI approval for new research programs, and the CRDI program was officially approved in 2021 to focus on research that falls somewhere between cancer prevention and treatment.

"Quitting smoking is an example of primary prevention, right? But interception means intervening once someone has started down the cascade of events leading to cancer," Epplein said. She credits DCI Deputy Director Steve Patierno, PhD, with the inspiration for this new niche at Duke, as well as the work of Shelley Hwang, MD, vice-chair of research in the Duke Department of Surgery, who leads a large national study to determine the benefits of treatment versus watchful waiting for so-called stage 0 breast cancer (also called ductal carcinoma in situ). Hwang is a member of the CRDI program's steering committee.

Duke Cancer Institute
50th Anniversary

Other steering committee members are Heather Stapleton, PhD, the Ronie-Richele Garcia-Johnson Distinguished Professor of Environmental Sciences and Policy in the Nicholas School of the Environment, who explores new biomarkers for interception and early disease risk in people exposed to cancer-causing chemicals, and Evan Meyers, MD, MPH, the Walter L. Thomas Distinguished Professor of Obstetrics and Gynecology, who specializes in mathematical modeling and decision analysis.

Program members work in their own labs but meet regularly as a "think tank" to present findings and share ideas for common themes to explore. In addition, members are encouraged to pursue community outreach to share what they learn with the public.

NEW TECH TO UNDERSTAND PRE-CANCER

Several scientists in the CRDI program study abnormal tissue that can be a precursor to invasive cancer. Some of these lesions can be easily removed before they turn into cancer, such as colon polyps removed during a screening colonoscopy. But for many cancers, removal of pre-cursor lesions is more invasive, and knowing which are most likely to turn into cancer isn't an exact science.

For instance, for both pancreatic cancer and esophageal cancer, pathologists grade the precursor lesions by looking at their size and physical appearance. Peter Allen, MD, professor of surgery and chief of the division of surgical oncology, said that for intraductal papillary mucinous neoplasms (IPMNs), which are pancreatic cysts that can sometimes develop into pancreatic cancer, this grading is imprecise.

"Our problem right now is it is very difficult for us to accurately identify the grade of dysplasia in a patient's cyst without an operation," Allen said. "We're trying to identify RNA or DNA markers in the surrounding fluid that help us more accurately determine the grade."

Even though only 20% of these pancreatic lesions develop into cancer, a better grading system could save lives, Allen said, because pancreatic cancer is so hard to diagnose in the early stages, when it's most treatable.

YOU CAN HELP

Please join us in creating a future when fewer people get cancer. To give, please use the enclosed envelope, or visit **bit.ly/dciwinter22.**

MEIRA EPPLEIN and **KATHERINE GARMAN** work together to understand disparities in stomach cancer and to find a way to identify stomach cancer early.

General surgery resident Austin Eckhoff, MD, spent two years performing research in Allen's laboratory to study these lesions using a technology that was named the "Method of the Year" by the journal Nature Methods in 2020.

"Spatial transcriptomic profiling gives us two technologies together that we've been using in science for years," Eckhoff said. "It gives us both histology, so you can see cells and the overall tissue structure at a magnified level, but then for regions that you select, it lets you know about gene expression." It's more precise than bulk RNA sequencing, which shows only the average gene expression from RNAs across a sample of cells, Allen said.

Eckhoff's studies show that in pancreatic lesions from a single patient, high-grade and low-grade cells grow side by side, just 1.5 millimeters apart. So relying on images alone could cause some high-grade lesions to be missed. "We usually use CT scans to decide if a lesion needs to be resected [removed]," she said. "The sensitivity and specificity of that is only about 60%," she said.

Early results from this work, published July 2022 in the Annals of Surgical Oncology, using samples from 12 patients, suggest that high-grade lesions have a larger population of immune system cells called macrophages, compared to T cells, which can help fight cancer. The team is exploring further in hopes of finding a RNA or DNA signature for high-grade dysplasia that could be used in the clinic, and to better understand the role that inflammation plays. "We have found that as these lesions progress to cancer, they develop inflammation," Allen said. "Whether the inflammation is a driver of that progression, or it's a response to that progression — the chicken or egg question — we don't know."

PERSONALIZED SCREENING?

Treating H. pylori is a cancer-prevention tactic that doesn't happen as often as it should, Epplein said. About half of the world's population, and a third of the United States population, is infected with H. pylori, she said. But because only about 3% of those people will go on to develop cancer, many doctors don't test and treat for the bacterium.

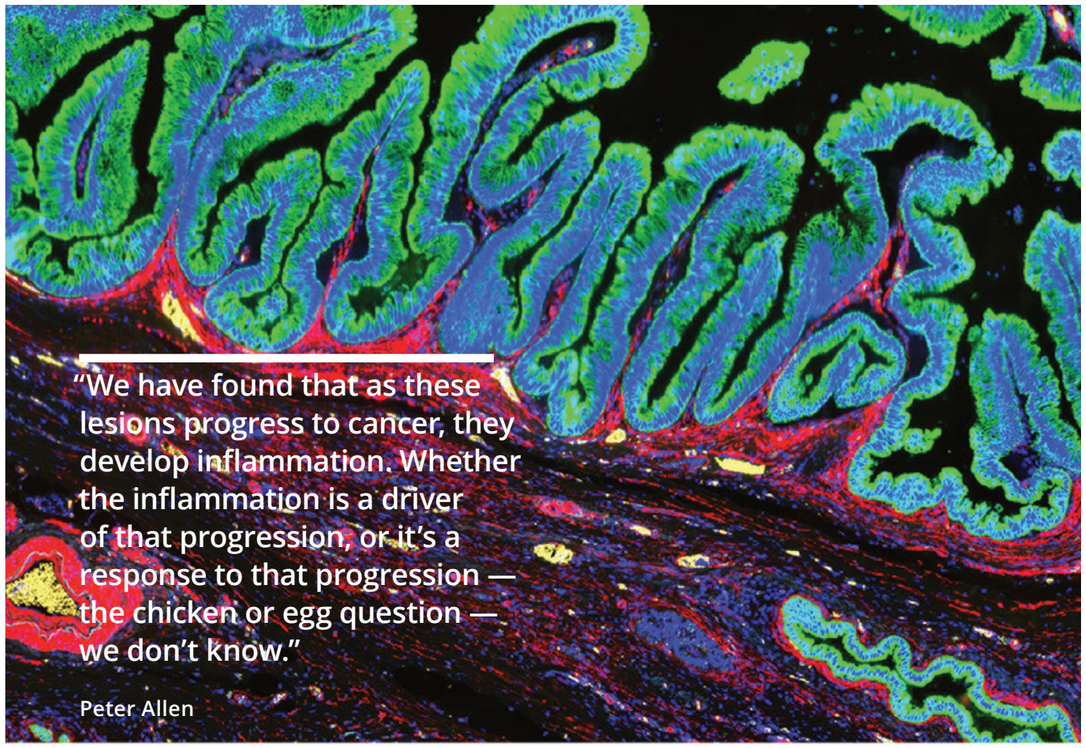
Epplein encourages doctors to talk to patients about testing, especially if they are in a high-risk group, have unexplained gastric distress, or have recently immigrated from a high-risk country.

In addition to co-leading the CRDI program, Epplein and Garman work together to understand disparities in stomach cancer and to find a way to identify the cases of H. pylori that are most likely to turn into cancer. Funded with a National Cancer Institute Exploratory Grant (P20), they study banked tissue samples and surveys from people who have been treated for H. pylori to understand the role of family history, diet, exposure to stress, and the strain of the bacterium in people who develop cancer.

In a separate project, Garman uses cells from patients who donate tissue samples after an endoscopy (tissue biopsy of the stomach) to grow "organoids" — masses of cells that resemble a simplified organ. She is fascinated by the unusual patterns she has seen in organoids from patients who have inherited or acquired certain molecular mutations. Rather than growing in the usual uniform circle, these cells have arms or buds extending this way and that. "The message from these pictures is these molecular mutations are probably really important," she said. She noted that this is an ongoing area of research.

> "At times people who have access to these more advanced tests and screening are those with money and resources. We will need to understand how to make sure certain people aren't excluded."
>
> Meira Epplein

For instance, studies in the last few years have shown that the BRCA1 and BRCA2 mutations, long linked to



A microscopy image showing inflammation in an intraductal papillary mucinous neoplasm (a lesion that can sometimes develop into pancreatic cancer).

> "With some of these molecular approaches, we will have better luck narrowing down the people who will really benefit from invasive screening tests, like an endoscopy where you have to miss a day of work and get sedation."
>
> Katherine Garman

increased breast and ovarian cancer risk, are also linked to increased stomach cancer risk, but that isn't yet taken into account clinically, Garman said. "With some of these molecular approaches, we will have better luck narrowing down the people who will really benefit from invasive screening tests, like an endoscopy where you have to miss a day of work and get sedation," she said.

The research in the CRDI program is heavy on new technology, but figuring out how to apply it to those who need it most is a priority, Epplein said. "We don't want everyone going through a mass of invasive screening tests," she said. "And, at times people who have access to these more advanced tests and screening are those with money and resources. We will need to understand how to make sure certain people aren't excluded."

Bringing together these researchers and clinicians from different disciplines has reminded them of the similarities across different cancer types. "We're looking at very similar aspects of the disease, even though they're in different organs," Allen said.

Epplein gives the example of a mutation in the P53 gene, which is common across many cancers. She said the group envisions a future when doctors could better measure each individual's overall cancer risk. "As we are getting better at developing biomarkers, especially non-invasive ones, we can think more broadly," she said.

WHEN PREVENTION PAYS OFF

AURORA ROSE DE CROSTA

At age 65, Therese, a psychologist, runs two psychotherapy practices and finds time to exercise an hour and a half nearly every day, whether that means strength training, Peloton sessions, or long walks around the city of Manhattan. "My trainer says that I'm in the shape of an amateur athlete," she said.

She is grateful that she is so healthy, considering that 15 years ago she underwent a major procedure to remove a pre-cancerous lesion from her pancreas.

In 2007, her gynecologist encouraged her to have frequent ovarian cancer screenings because of a history of breast and other cancers in her family. She decided to have an ultrasound of her ovaries and her abdomen.

"My radiologist had the wand on my abdomen, and he said, 'There's a little tumor on your pancreas. I don't think it's malignant, but you're going to need to go for an MRI right away,'" Therese said. She was diagnosed with an intraductal papillary mucinous neoplasm (IPMN). These lesions are most often found only when screening for other issues, and they are often benign. But in 20 to 30% of cases, they can develop into cancer.

Therese's lesion was determined to be high risk, with many inflammatory cells, and it needed to be removed. She was consulting with several doctors, but then her good friend, a surgeon at Memorial Sloan Kettering Cancer Center, said, "Please, before you do anything, you must see Dr. Allen." He was talking about **Peter Allen, MD,** who at the time was a surgical oncologist at Memorial Sloan-Kettering.

Therese was scheduled for an endoscopic biopsy at a different hospital. "But Dr. Allen said, 'Don't. It can cause complications, and we have to open you up anyway.' Thank goodness I found him," she said.

Allen performed the complex surgery, called a Whipple procedure, as his first case after the 2007 Labor Day holiday. "It really does a number on your digestive system," Therese said. "I lost 10% of my body weight."

Today, Therese is happy to say she has to work at not gaining weight just like any other woman her age. "A Whipple redesigns your digestive system, so it gets a little fussy sometimes. But it's a very tiny price to pay for saving my life," she said. Since the procedure, she has written and published two books, including a 2021 book about practicing during the pandemic ("How Are You? Connection in a Virtual Age.")

In 2018, Allen moved to North Carolina to become chief of surgery at Duke Cancer Institute. Therese takes time away from her writing and her practices to travel to Duke to see him once a year, to ensure her remaining pancreas stays healthy.

She also supports his research that aims to improve classification of IPMNs and find more reliable ways to diagnose pancreatic cancer in the early stages.

"I wanted to stay with Dr. Allen. That's how much trust I have in him," Therese said. "He is highly professional. He's really on top of the situation. And then he's just a really decent human being. He's a mensch. It's hard to describe, but that means he's a person of true integrity."

— Angela Spivey

In Search Of:
Early Diagnosis of Pancreatic Cancer

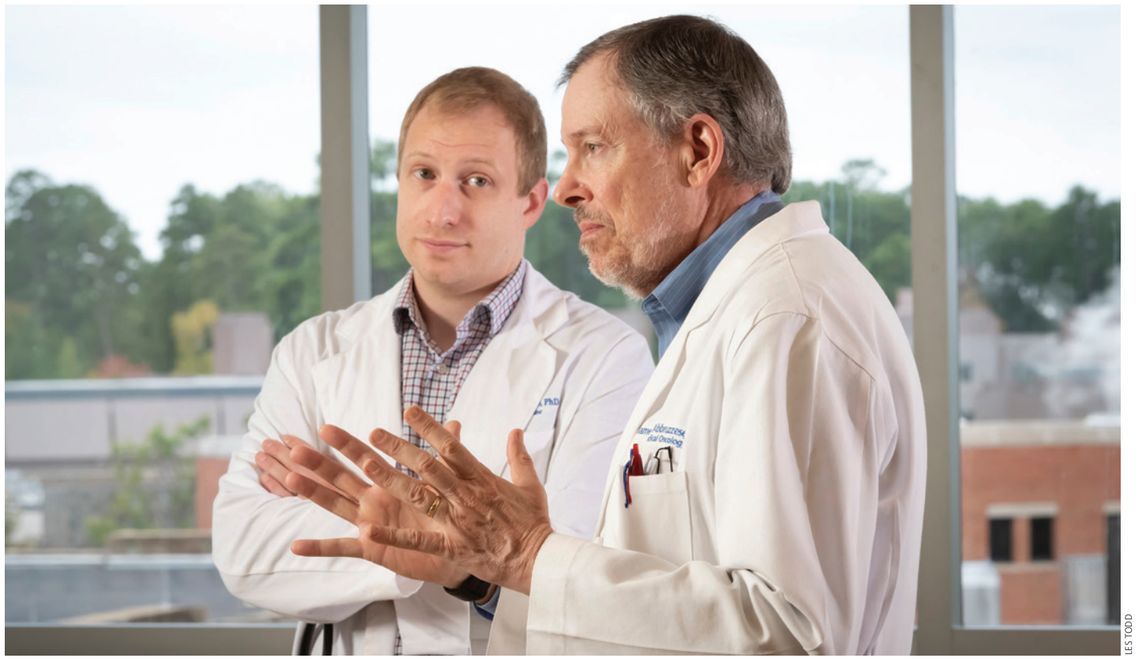
BY ANGELA SPIVEY

Pancreatic cancer is one of the most challenging types because it is most often diagnosed in the late stages, when surgery isn't possible. In 2022, the five-year survival rate for the disease is 11%, a slight increase from last year, according to the American Cancer Society.

TO MAKE OUTCOMES BETTER, researchers around the world are trying to find a marker from blood or some other bodily fluid that would reliably diagnose pancreatic cancer in its early stages, said Jim Abbruzzese, MD, Duke Cancer Institute Distinguished Professor of Medical Oncology. Abbruzzese sees promise in a test that has been studied in the lab of Chris Counter, PhD, George Barth Geller Distinguished Professor of Pharmacology. Abbruzzese and hematology/oncology fellow Ryne Ramaker, MD, PhD, are beginning work to translate it to patients.

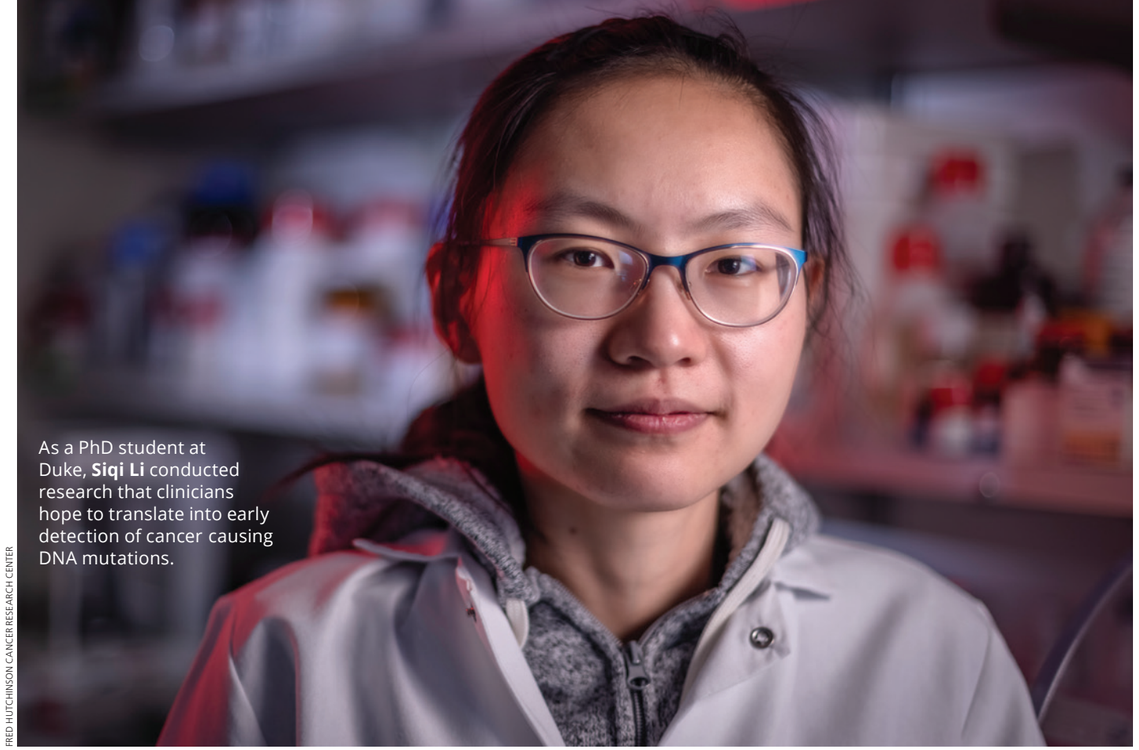
Counter's lab tries to capture the moment when a normal cell progresses to a tumor, then study it. Even in a cancer with lots of successful treatment options, like melanoma, the best bet is still finding the disease early, said Counter, whose mother-in-law Linda Woolfenden died of melanoma. It's even more important in a challenging disease like pancreatic cancer.

Siqi Li, PhD, now a Damon Runyan fellow at Fred Hutchinson Cancer Research Center, was a PhD student in Counter's lab when she became intrigued by a method



LES TODD

Hematology/oncology fellow **Ryne Ramaker** (left), and clinician **Jim Abbruzzese** aim to translate a potential early diagnostic test for pancreatic cancer from the lab to the clinic.



FRED HUTCHINSON CANCER RESEARCH CENTER

As a PhD student at Duke, **Siqi Li** conducted research that clinicians hope to translate into early detection of cancer causing DNA mutations.

called maximum-depth sequencing, which was developed by researchers in the lab of Evgeny Nudler, PhD, at New York University to detect mutations that lead to antibiotic resistance in bacteria.

"Siqi saw the parallels between bacteria and cancer, and she was very interested in using this assay in mammals," Counter said. "So she adapted this assay with the help of the lab of Dr. David McAlpine here at Duke for the mammalian genome to capture mutations causing cancer."

> "EARLIER DIAGNOSIS AND EARLIER UNDERSTANDING OF THE GENETIC PROFILE WILL OPEN UP THE DOOR TO THINK ABOUT THE DISEASE IN A MORE NUANCED WAY."
>
> Ryne Ramaker

Counter's team found that this technology captures mutations that are too few and far between to be detected by traditional next-generation gene sequencing. "The assay was so sensitive, that Siqi was able to detect a cancer-causing mutation a week after mice were exposed to an environmental carcinogen," Counter said. The team published results of this work in 2020 in the journal Nature Communications and in 2022 in the journal eLife. The studies were supported in part by a Duke Cancer Institute pilot grant, a program sustained by donor funds.

The test holds promise not only because of its sensitivity, but also because it's specific to KRAS, a gene commonly mutated in pancreatic cancer, Abruzzese said.

The translational studies, which were just funded by the National Cancer Institute, will try to find out whether the method can identify KRAS mutations in blood from a small number of patients already diagnosed with pancreatic cancer. Then the team will compare those results with those from traditional next-generation sequencing. Ramaker, the fellow, will work with Counter to evaluate and enhance the test and will talk to patients about joining the study. "My hope is to be involved in both ends and bridge the lab and the clinic," he said.

"Because pancreas cancer is diagnosed usually at a later stage, we don't have the opportunity to conduct many careful studies with patients who have earlier disease," Ramaker said. "Earlier diagnosis and earlier understanding of the genetic profile will open up the door to think about the disease in a more nuanced way."

YOU CAN HELP

Your support makes it possible to translate findings like this from the lab to the clinic. To give, please use the enclosed envelope, or visit **bit.ly/dciwinter22.**

AURORA ROSE DE CROSTA

Helping Duke
Give Back to the World

Duke alum Leslie Graves has known about Duke's mission to provide life-changing cancer care since she was a teenager. Her father was a childhood friend of legendary cancer surgeon William Shingleton, MD, when the two were growing up in eastern North Carolina.

IN 1973, WHEN SHINGLETON BECAME THE FOUNDING DIRECTOR OF DUKE COMPREHENSIVE CANCER CENTER, (now known as Duke Cancer Institute), Graves' father, John Graves, a Duke alum, began supporting the effort. "He felt like that it was such an incredible organization, and he talked to me about it," Graves said. "He was super proud of his childhood friend."

She witnessed firsthand the compassionate care Duke provides when her father was treated for bladder cancer. "He felt they took really great care of him, extended his life, and honored his wishes about his treatment," Graves said. He sadly lost his battle with the disease in 2009.

Graves serves as treasurer of the Fibromalellar Cancer Foundation, and in 2017 she joined the Duke Cancer Institute Board of Advisors. She served as vice-chair for four years, and in 2022 she began serving as chair. In October 2022, Graves received the William W. Shingleton Award, the highest honor given to friends of Duke Cancer Institute.

"I come from a long line of Blue Devils," Graves said. "Duke Cancer Institute allows you to help Duke give back to the rest of the world. I can't do what Dr. Michael Kastan and his fabulous team can do, but I can help them do it," she said.

While her daughter, Elizabeth, attended Duke and played lacrosse, Graves organized an annual game benefiting Duke Cancer Institute. She has also supported the Duke Center for Brain and Spine Metastasis. Most recently, she made a planned gift and a special gift honoring Duke cancer's 50th anniversary.

"You don't have to give at a high level," she said. "Whatever anyone can do will help."

> "I COME FROM A LONG LINE OF BLUE DEVILS. DUKE CANCER INSTITUTE ALLOWS YOU TO HELP DUKE GIVE BACK TO THE REST OF THE WORLD. I CAN'T DO WHAT DR. MICHAEL KASTAN AND HIS FABULOUS TEAM CAN DO, BUT I CAN HELP THEM DO IT."
>
> Duke alum Leslie Graves

YOU CAN HELP

To learn how you can find a way to help support Duke's next 50 years of life-changing care, please contact DCI Development at **919-385-3120** or **dcidevelopment@duke.edu.**

A Sense of Peace

BY ANGELA SPIVEY

IN 2016, WHEN PAT SMITH FIRST FELT A LUMP ON HER THIGH, SHE DIDN'T THINK MUCH ABOUT IT. But a "just-in-case" MRI led to a biopsy, and then her doctor told her it was a leiomyosarcoma — an aggressive, cancerous tumor.

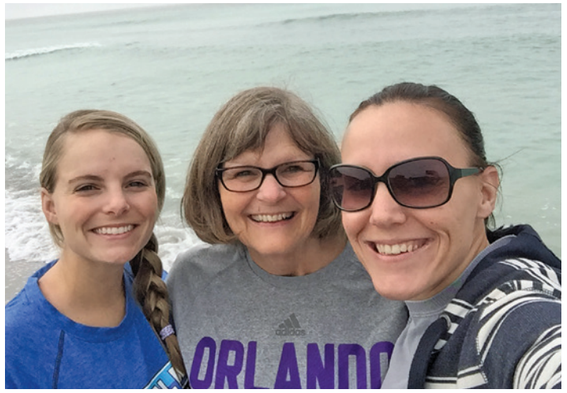
Smith, who lives in Florida, had never heard of a leiomyosarcoma, and for good reason. They are rare, as are all sarcomas (soft tissue cancers). Leiomyosarcomas grow in the smooth muscles, which are in the hollow organs of the body, such as the intestines, stomach, bladder, and blood vessels.

Smith had gone to the appointment alone because she wasn't expecting her biopsy results so soon. Stunned, she went home to tell her husband, Randy, and to call her three adult children.

Her son impressed upon her that because leiomyosarcomas are so rare, she should get treatment at a center that sees a lot of these types of tumors. Then she remembered that her good friend Andrea Erwin is retired from Duke University and volunteers at Duke Cancer Center. Erwin arranged for someone from Duke to call her that same afternoon.

As it turned out, Duke has a team of 25 specialists focused on sarcomas. Smith had an appointment scheduled in two weeks with David Kirsch, MD, Barbara Levine University Distinguished Professor, and Brian Brigman, MD, professor of orthopaedic surgery, and other providers.

"The greatest thing is that when I met each one of them, no one rushed me," Smith said. "And they all said, 'What do you know about your particular type of tumor?' And they all explained it, and it was like they had all the time in the world," Smith said.



Pat Smith, center, with her daughters Claibourne and Christine

> "I chose to come back to Duke because this is the best place to take care of me," Smith said during a visit to Duke Cancer Center. "I walk in that front door down there, and I feel this peace wash over me."
>
> Pat Smith

When she was first diagnosed, she remembers thinking "Why me?" Then she prayed about it. "I said to myself, 'Pat, God has this. You've found a great place to go, and they're going to take care of you, and you're going to have a positive attitude.'"

Smith started keeping a "blessings list," naming all the positive things about her cancer experience. "You really can meet a lot of great people," Smith said. "I'm originally from North Carolina, and I have connected with old friends."

Smith had radiation every day for several weeks, staying with her friend Andrea. A month later, she had surgery.

She is now considered cancer free, though doctors at Duke watch her closely. Every three months, she has a CT scan of her lungs, because that's where this tumor tends to spread. She also has a yearly MRI of her leg. Smith prefers to come to Duke for those screenings. "I chose to come back to Duke because this is the best place to take care of me," she said during a visit to Duke Cancer Center. "I walk in that front door down there, and I feel this peace wash over me."

Since her diagnosis, Smith has welcomed two grandchildren, and she enjoys taking them to the beach. In November 2022, she and her husband, Randy, will celebrate 40 years of marriage.

FAST FACTS
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LEUKEMIA DRUG SHOWS PROMISE AGAINST METASTATIC BREAST CANCER

In animal studies led by researchers at Duke Cancer Institute, a drug approved to treat leukemia disrupted the ability of HER2-positive breast cancer tumors to colonize the brain.

The finding, published in August 2022 in the journal Cell Reports, provides evidence for human trials and suggests a potential new approach to derail one of the main ways that breast cancer turns deadly.

"We have made huge strides in treating HER2-positive breast cancers, but when tumors escape the therapies, they often metastasize to the brain," said senior author Ann Marie Pendergast, PhD, professor and vice chair of the Department of Pharmacology and Cancer Biology at Duke University School of Medicine.

"When brain metastasis occurs, treatments are unsuccessful either because the tumors have developed resistance, or the therapies cannot penetrate the blood-brain barrier," Pendergast said. "This remains a devastating diagnosis for patients."

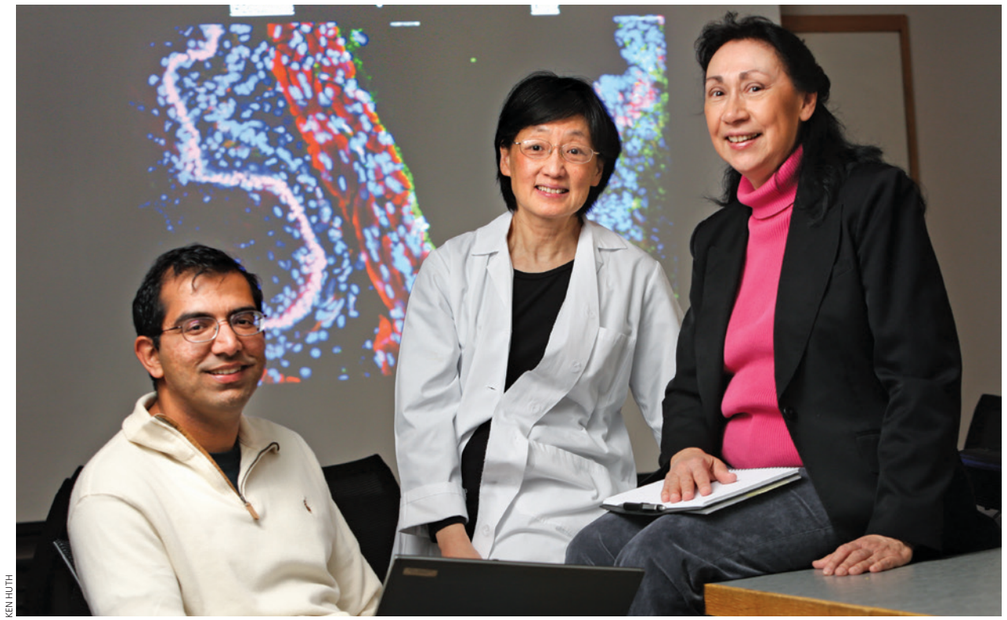
Pendergast and colleagues looked at how HER2 promotes breast cancer growth, particularly after becoming resistant to targeted treatments that have been highly successful in prolonging lives. The HER2 protein is a driving force in 30% of breast cancers, with approximately 45% of these leading to brain metastases.

The researchers focused on a pair of enzymes called ABL1 and ABL2 kinases that regulate the expression of HER2. The researchers found that these kinases play a critical role in creating the conditions that allow HER2 to accumulate on the surface of breast cancer cells, fueling breast cancer tumor metastasis.

Experimenting in mice, Pendergast and her team were able to disrupt the ABL kinases using a leukemia drug called asciminib. A kinase inhibitor, the drug is not impeded by the blood-brain barrier in tumor-bearing mice and interferes with the ABL kinases' signaling mechanism.

In addition to Pendergast, study authors include Courtney M. McKernan, Aaditya Khatri, Molly Hannigan, Jessica Child, Qiang Chen, Benjamin Mayro, David Snyder, and Christopher V. Nicchitta.

— Sarah Avery



KEN HUTH

Resident **AADITYA KHATRI, MD,** staff scientist **JING JIN GU, PHD,** and **ANN MARIE PENDERGAST, PHD**

FEED YOUR FACE. In September 2022, Michael Mackey joined family, friends, and the Duke cancer clinicians who had cared for his late wife, including **Susan Blackwell, PA-C,** and **Jeffrey Crawford, MD,** at an annual fundraiser dinner that he and his wife, Trish, co-founded to raise money for lung cancer research at Duke. The couple started the **Feed Your Face** dinner in 2017 after Trish, a nurse at Duke for 30 years, was diagnosed with stage 4 lung adenocarcinoma. She passed away in October 2019. This year's dinner raised nearly $9,000 to support Duke lung cancer research. "It was just the way Trish would want it. It was nothing but a love fest," Mackey said. "Duke gave Trish approximately 18 months of quality of life when we were able to go out and enjoy things. As one of my sons said, we need to continue the dinner to hopefully find a cure so other families don't have to go through what we went through."

Tim Malloy (center) with co-organizers **Mark Babashanian** and **Randy Rowan**

TIM MALLOY describes his late daughter, Molly Malloy Smith, as "Full of Irish moxie, infectious loud laughter, quick, sharp wit." That's the attitude he and family and friends bring each year to the **Molly Malloy Smith Memorial Golf Tournament** in Chesapeake, Virginia. Smith died from skin cancer in 2015, and the event has honored her every year since 2016 (except for a pandemic-imposed break in 2020). Including the 6th annual tournament held in October 2022, the event has raised more than $290,000 for Duke cancer research.

"Although Molly's cancer was too far along for the Duke Cancer Institute to save her, we were so impressed with the expertise of their doctors, nurses and other clinical staff, and the loving care they all gave her. We are committed to do all we can to support Duke Cancer Institute and to ensure better outcomes for those who come after Molly," Malloy said.

SHINGLETON AWARDEES. In October 2022, members of the Shingleton Society met to hear from Duke Cancer Institute researchers and honor this year's Shingleton awardees:

- The William W. Shingleton Award: **Leslie Ann Graves**
- The Shingleton Award for Distinguished Service: **The Menges Family and the I'm Not Done Yet Foundation**
- The Shingleton Award for Community Partnership: **Clayton Homes of Oxford**
- The Shingleton Award for Caregiver Partnership: **Dan George, MD**

The Shingleton Society honors those who, during a fiscal year (July 1 through June 30), have made a gift of $1,000 or more to Duke Cancer Institute. For more information or to apply for membership, please contact Sharon White, Senior Director of Leadership Annual Giving, at 984-227-1410.

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RINGING THE BELL

Several Duke Cancer Institute representatives were thrilled to join the founders of the **I'm Not Done Yet Foundation,** an important partner with the Duke Cancer Teen and Young Adult Oncology Program, to ring the opening bell at Nasdaq on Friday, Oct. 7.

The foundation was invited to ring the bell to celebrate their incredible work to bring awareness to the need for support for young adult cancer patients and survivors. The I'm Not Done Yet Foundation was started by Peter and Liz Menges, the parents of Bobby Menges, a Duke student who succumbed to cancer at 19 years old.

YOUR GIFT CAN HELP MORE FAMILIES.
Please use the enclosed envelope, or visit **bit.ly/dciwinter22**

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