

The James



THE OHIO STATE UNIVERSITY
COMPREHENSIVE CANCER CENTER

2018 Pelotonia Investment Report

10 YEARS
OF PELOTONIA
DECADES OF
IMPACT



On Nov. 15 we'll all find out how much money Pelotonia 18 raised for cancer research at Ohio State as we put a lid on the 10th anniversary installment of this annual grassroots cycling event.

Projections indicate that this year's event, held Aug. 3-5 on 10 riding routes between the Columbus area and Gambier, Ohio, may yield another record yearly fundraising amount thanks to the combined efforts of the thousands of people who rode in, donated to or volunteered for this monumental undertaking.

Shortly before the official Oct. 5 fundraising deadline, the Pelotonia website indicated that the 2018 event had raised more than \$20 million—boosting the overall 10-year total to more than \$176 million—but the money was still being counted. A final total will be revealed at the Nov. 15 check celebration.

Whatever the total, we can all be assured that, because of Pelotonia's major funding partners—including Huntington, L Brands Foundation, Peggy and Richard Santulli, and the AEP Foundation—every dollar raised by riders, virtual riders and donors will go directly to cancer research at The Ohio State University Comprehensive Cancer Center – James Cancer Hospital and Solove Research Institute (OSUCCC – James).

So in a wider sense, although the tallying is done, we are not really putting a lid on Pelotonia 18. Yet to come from this year's outing are all of the funding allocations and the exciting discoveries they will surely yield in our continuing quest to conquer cancer.

This investment report summarizes how Pelotonia funds have been distributed over the event's first nine years to benefit such key areas as an Intramural Research Program for teams of faculty scientists, a Fellowship Program for students conducting cancer research with faculty mentors, purchases of sophisticated equipment, large-scale strategic investments, major statewide initiatives to improve cancer prevention and care around Ohio, and support for newly recruited cancer scientists.

Pelotonia represents our collective retaliation against cancer, a formidable foe that in some way touches the lives of everyone. Pelotonia 18 was fueled by 8,470 riders, more than 3,000 virtual riders, over 3,000 volunteers, and countless donors and planners. To each of you we extend our deepest gratitude for helping us pursue our shared vision of creating a cancer-free world.

Raphael Pollock, MD, PhD
Director, The Ohio State University
Comprehensive Cancer Center

William Farrar, MD
Interim CEO, James Cancer Hospital and
Solove Research Institute

COMMUNITY COMES TOGETHER FOR HISTORIC 10TH PELOTONIA



“Never underestimate the determination of the human spirit.”

So said Sherry Wang, a 24-year-old ovarian cancer survivor whose simple imperative sentence captured the essence of Pelotonia 18, the 10th anniversary installment of a grassroots cycling event that over the years has raised more than \$176 million for cancer research at the OSUCCC – James.

Wang was one of three cancer survivors who addressed the thousands of people in attendance at the Aug. 3, Opening Ceremony for Pelotonia 18, which drew a record 8,470 riders and, as of Oct. 2, had raised more than \$20 million. Fundraising for Pelotonia 18 ended on Oct. 5.

The three were summoned to the stage, along with a physician or scientist who was integral to each one's treatment at the OSUCCC – James, by Pelotonia CEO and President Doug Ulman after he reiterated the evening ceremony's prevailing theme.

“Tonight is all about you, the community and the impact that you're creating,” Ulman said. “You are the rock stars and the celebrities of this movement.”

“But there's one other group of heroes that we want to recognize tonight, and those are the survivors and patients we ride in honor of every year,” Ulman added. “Please welcome three remarkable individuals: Rhonda Ball, Jay McDaniel and Sherry Wang.”

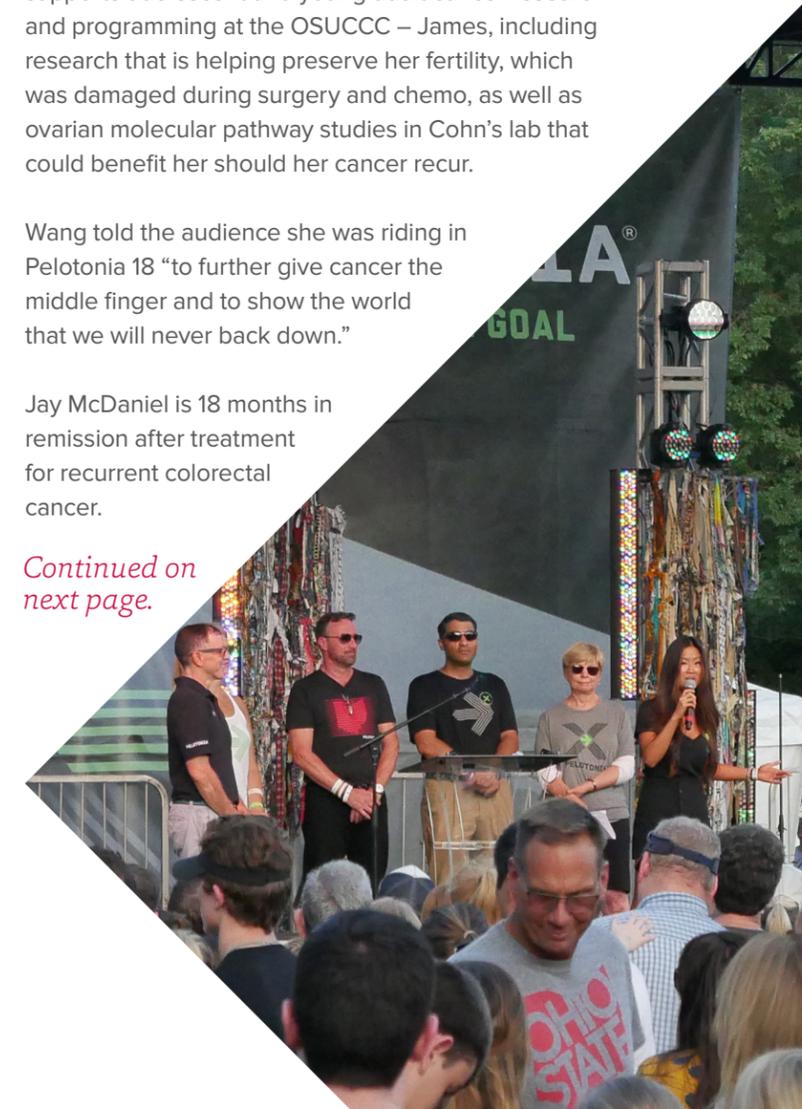
Wang, who was diagnosed in February 2017 while living in Chicago and later underwent 17 rounds of chemotherapy at the OSUCCC – James, managed to ride in Pelotonia 17 just two weeks after her final chemo treatment. Two weeks after her ride, she learned from her oncologist, David Cohn, MD, that her post-chemo scans were clear. In July 2018 she celebrated one year of being cancer-free.

“It is because of you that I get to celebrate such an incredible milestone and live my life to the fullest every day,” Wang said. She noted that Pelotonia funding supports adolescent and young adult cancer research and programming at the OSUCCC – James, including research that is helping preserve her fertility, which was damaged during surgery and chemo, as well as ovarian molecular pathway studies in Cohn's lab that could benefit her should her cancer recur.

Wang told the audience she was riding in Pelotonia 18 “to further give cancer the middle finger and to show the world that we will never back down.”

Jay McDaniel is 18 months in remission after treatment for recurrent colorectal cancer.

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COMMUNITY COMES TOGETHER FOR HISTORIC 10TH PELOTONIA

During his treatment, he took part in the Pelotonia-funded Ohio Colorectal Cancer Prevention Initiative (OCCPI), a statewide screening project led by Heather Hampel, MS, LGC.

After McDaniel tested positive for Lynch syndrome (LS), an inherited genetic disorder that predisposes to colorectal and other cancers, his children and 38 other relatives were screened by Hampel for LS. His oldest daughter and a cousin also tested positive and will undergo frequent surveillance measures to help prevent cancer.

When McDaniel's cancer recurred, he underwent surgery and joined a clinical trial that led to his remission. Pelotonia funds helped support the OCCPI's work, which is estimated to save nearly 1,000 years of life for Ohioans. "Without the clinical trials that you help sponsor, I may not be alive today," McDaniel said. "You've helped stop cancer in my family at this generation."

In Rhonda Ball's presentation, she said she and her husband were frightened in 2014 when they learned that she had a metastatic cancerous tumor of unknown origin in her abdomen. "It was a terrible prognosis.

We knew we were in for a fight, and that realistically it was a fight we were probably not going to win."

But when an OSUCCC – James Precision Cancer Medicine team led by Sameek Roychowdhury, MD, PhD, analyzed her tumor DNA through a test supported by Pelotonia, they found a biomarker for a genetic mutation called microsatellite instability that enabled them to enroll her on a clinical trial involving an immunotherapy drug that targets this biomarker. Within months, her tumor was gone.

"On July 24, I finished my 52nd and final treatment as part of that two-year study at The James," Ball told the crowd. "When I asked my doctor what I should say if somebody asks whether I still have cancer, he said, 'Not anymore.' Three and a half years ago, not in my wildest dreams could I have dared to hope for that kind of an answer. Thanks for all you do to raise these all-important research dollars. You are saving lives ... you saved mine, and for that I am forever grateful."

Ulman also called to the stage a number of people and groups to be acknowledged for their roles in Pelotonia: board members, researchers, 10-year riders, 10-year volunteers and OSUCCC – James leaders, including OSUCCC Director Raphael Pollock, MD, PhD, James Interim CEO William Farrar, MD, OSUCCC Deputy Director Peter Shields, MD, and OSUCCC – James Chief Medical Officer David Cohn, MD. //



PELOTONIA 18 FUNDRAISING TOTAL TO BE REVEALED NOV. 15

Key Pelotonia Funding Partners



Major Funding Partners

Huntington



L Brands Foundation



Peggy and Richard Santulli



AEP Foundation



Supporting Funding Partners

Lilly Oncology



Harold C. Schott Foundation



Notable Funding Partners

Cardinal Health



Nationwide



Diamond Hill Capital Management

2018 was Pelotonia's 10th year, and the total amount raised by riders, virtual riders and volunteers since 2009 had totaled more than \$176.43 million as of Oct. 2. Fundraising for Pelotonia 18 officially ended Oct. 5; the total amount raised for this year's event will be revealed at a Nov. 15 celebration event at Express Live.

Thanks to Pelotonia's major funding partners—including L Brands Foundation, Huntington, Peggy and Richard Santulli, and the AEP Foundation—every dollar raised by riders, virtual riders and donors goes directly to cancer research at the OSUCCC – James.

Pelotonia CEO and President Doug Ulman says some 30,000 people have ridden in the cycling event since it began in 2009, and he reports that the event over the years has benefited from 1.1 million donations from people in 65 countries and all 50 U.S. states. The 8,470 cyclists in Pelotonia 18 were from 42 states and 15 countries. This year's event also benefited from more than 3,000 volunteers and over 3,000 virtual riders. //



9-YEAR PELOTONIA FINANCIAL SUMMARY

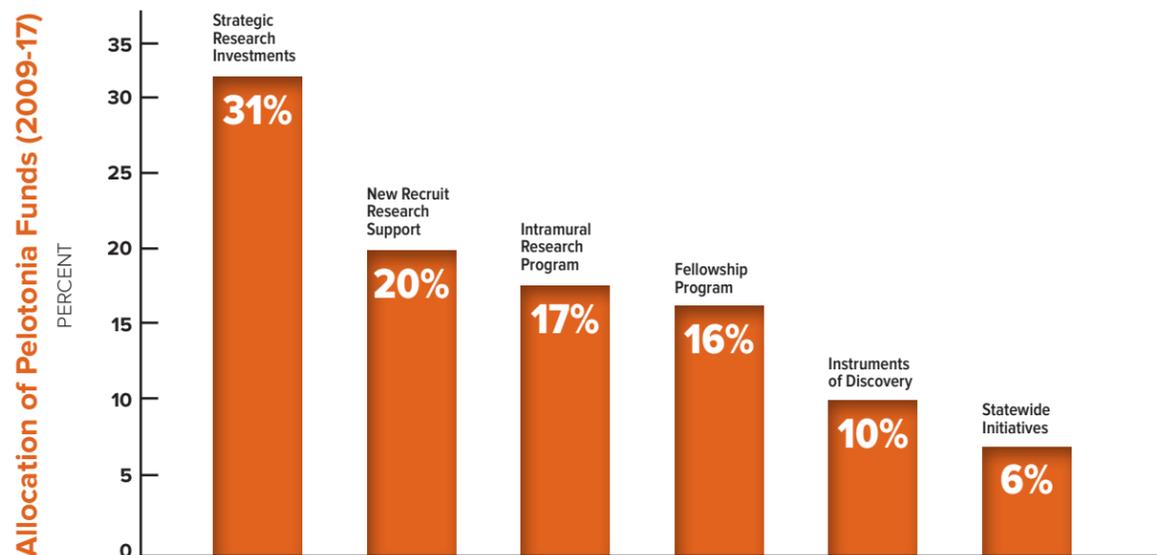
Pelotonia funding supports projects that address many aspects of cancer, including research, diagnosis, treatment, psychosocial issues, prevention, accelerated drug development and large initiatives to change the landscape of cancer care. The OSUCCC – James allocates the money to six major spending areas:

- **An Intramural Research Program** that has provided 133 faculty research teams with grants totaling \$13.7 million;
- **A Pelotonia Fellowship Program** that has awarded 479 fellowships totaling more than \$15 million to Ohio State students in any discipline who want to conduct cancer research with faculty mentors;
- **Instruments of discovery**, or the purchase of sophisticated equipment for cancer research;
- **Three statewide initiatives** that work with community hospitals to take aim at specific cancers;
- **Strategic research investments** such as a Drug Development Institute, Digital Pathology and a Total Cancer Care® protocol;
- **Support** for newly recruited cancer researchers so they can continue their work upon arrival at Ohio State.

Bringing Knowledge to Bear in the Fight Against Cancer

Pelotonia research funding has been allocated to investigators in 11 of the 15 colleges at Ohio State, as well as at Nationwide Children’s Hospital in Columbus and at Cincinnati Children’s Hospital Medical Center:

- College of Medicine
- College of Public Health
- College of Nursing
- College of Dentistry
- College of Pharmacy
- College of Veterinary Medicine
- College of Food, Agricultural and Environmental Sciences
- College of Law
- College of Education and Human Ecology
- College of Engineering
- College of Arts and Sciences



INSPIRING INNOVATION

Pelotonia Idea Grants Help Researchers Pursue Fresh Approaches

Bold, insightful ideas fuel cancer research, but those ideas will go no further than a researcher’s notebook without funding. Unfortunately, funding for innovative ideas can be difficult to acquire.

For researchers at the OSUCCC – James, Pelotonia-funded Idea Grants help to resolve that dilemma.

Idea Grants encourage teams of faculty scientists to pursue original ideas and break new ground in research-based treatment. Researchers can apply twice a year for funds to support studies that test their hypotheses and produce data needed to apply later for larger grants from such external sources as the National Cancer Institute.

To date, 133 OSUCCC – James research teams have received Pelotonia-funded Idea Grants collectively totaling \$13.7 million. These competitive grants provide support for two years and for up to \$200,000 each. The awards represent the work of researchers across eight colleges at Ohio State plus Nationwide Children’s Hospital and Cincinnati Children’s Hospital Medical Center.

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“We are able to maintain momentum in moving strong emerging research ideas forward thanks in large part to funds raised by the dedicated community of Pelotonia riders, virtual riders, volunteers and corporate sponsors,” says OSUCCC Director Raphael Pollock, MD, PhD, a medical scientist who also rides in Pelotonia.



Here are examples of Pelotonia Idea Grants awarded in a recent funding cycle. They are listed along with their principal investigators.

Biomarkers to Predict Endometrial Cancer Recurrence



Ashley Felix, PhD, MPH,
College of Public Health; OSUCCC – James Cancer Control Program

Endometrial (uterine) cancer is the most common cancer of the female reproductive tract. Following primary treatment, women are at risk of the cancer returning, most commonly in the vagina.

Clinicians need tools to predict which women will experience a vaginal recurrence so they can provide the most appropriate treatment, but no such prediction tools exist. In this study, OSUCCC – James researchers are trying to identify molecular biomarkers for disease recurrence by studying vaginal tampon blood samples from patients diagnosed with endometrial cancer.

Understanding Pathways to Treatment Resistance



Anne Strohecker, PhD,
College of Medicine, Department of Cancer Biology and Genetics; OSUCCC – James Molecular Biology and Cancer Genetics Program

Scientists know that cancer cells exploit the body's natural cellular process of breaking down and recycling cellular material—a process called autophagy—to meet their increased energy needs.

Through laboratory experiments, this study seeks to understand autophagy pathways that disrupt and undermine the effectiveness of cancer treatment regimens. These researchers will look at the impact of “turning off” a specific gene involved in autophagy in an established model of non-small cell lung cancer.

Drug Therapy to Stop Severe Muscle Loss in Patients



Christopher Coss, PhD,
College of Pharmacy; OSUCCC – James Molecular Carcinogenesis and Chemoprevention Program

The involuntary loss of skeletal muscle and fat tissue associated with many types of cancer is called cancer cachexia. This occurs in more than half of advanced cancer cases, reducing both the quality and length of a patient's life.

There are no U.S. Food and Drug Administration-approved treatments to combat cachexia, but OSUCCC – James researchers have discovered a combination of drugs that shows promise in treating it. In this project, scientists seek to understand how to make this combination most effective while also reducing potential side effects. The drugs have already undergone some clinical evaluation, and the scientists hope this work will result in an early-stage clinical trial to test this combination therapy in patients with advanced cancer.

Understanding Suppressor Cells' Role in Cancer Therapy



Xue-feng Bai, PhD,
College of Medicine, Department of Pathology; OSUCCC – James Translational Therapeutics Program

Cells of the immune system called myeloid-derived suppressor cells (MDSC) can inhibit the body's immune response to foreign and transformed cells. Scientists therefore believe that MDSC play an important role in cancer progression.

Researchers designed this study to gain insights into the role of MDSC and a natural antitumor substance called IL-27 in cancer progression. They also hope to identify molecular targets for the development of therapies that will capitalize on both mechanisms and ultimately improve cancer treatment.

Improving Immune-Based Treatments for Cancer



William Carson, MD,
College of Medicine, Department of Surgery; OSUCCC – James Translational Therapeutics Program

This project focuses on understanding and improving mechanisms by which the immune system can recognize and eliminate cancer cells. This research team will look at how immune-suppressor cells function and which suppressor cells are elevated in cancer patients.

The researchers hypothesize that the effectiveness of immune-based anticancer treatments could be improved by eliminating or “turning off” these suppressor cells. Information gleaned from this study may help scientists reduce the side effects that patients experience as a result of current and new immunotherapies. //

TRAINING THE NEXT GENERATION



Pelotonia Fellowships Support & Encourage Young Cancer Researchers

Each year, the Pelotonia Fellowship Program allots \$2 million to support promising Ohio State students in any discipline or level of scholarship who want to conduct cancer research under the guidance of faculty mentors at the OSUCCC – James.

Since the program began in 2010, it has awarded more than \$15 million in fellowships for

479 cancer research projects undertaken by students, including 223 undergraduates, 143 graduates, 107 postdoctoral fellows and six professional students. The program also has provided international research experiences for 21 Ohio undergrads in India and Brazil, and it has brought 14 students from India and Brazil to contribute to cancer research in Ohio State labs.

The fellowships are peer-reviewed and issued by a committee of faculty cancer researchers chaired by Rosa Lapalombella, PhD, associate professor in the Department of Hematology at Ohio State and member of the Leukemia Research Program at the OSUCCC – James. On the next two pages are profiles of three Pelotonia fellowship recipients.



Manuel Torres

Since Manuel Torres discovered his passion for medicine and research, his life goal has been to “make a real difference for underrepresented cancer patients.”

The Pelotonia Fellowship Program gave him his first opportunity to do that.

Working in the lab of David Carbone, MD, PhD, director of the Thoracic Oncology Program at the OSUCCC – James, Torres focused on studying the Brazilian lung cancer population in partnership with the National Cancer Institute of Brazil (NCIB) and Luis Araujo, MD, who leads the NCIB study.

“The Brazilian population has a diverse genetic history that represents a range of people from across the world, making it a great model to study the interaction between genetic ancestry and the incidence of cancer-driving mutations in lung cancer patients,” says Torres, a native of Puerto Rico who earned his undergraduate degree in Molecular Genetics at Ohio State and recently joined Northwestern University’s Medical Scientist Training Program in pursuit of an MD/PhD.

“Understanding how patients with diverse genetic backgrounds are differentially predisposed to cancer after acquiring these mutations could (enable doctors to provide) them and many others with personalized therapies tailored to their genetic history,” Torres says.

His project involved receiving and processing tumor samples from Brazilian patients on a rolling basis at Ohio State. The researchers used DNA sequencing technology to look for correlations between “ancestry-informative genetic markers” and mutations that drive cancer progression in the samples. They hoped to uncover associations that might be used in the clinical setting.

Torres is grateful for the time he spent in Carbone’s lab. “I received exposure to tasks such as grant writing and publishing that will be important later,” he says. “That this exposure came from such talented scientists and physicians was a blessing in itself.”

He hopes eventually to return home and help train the next generation of Puerto Rican scientists—and perhaps someday lead the University of Puerto Rico Comprehensive Cancer Center—but those are long-term dreams. “First, I want to treat the Latino community in the mainland and gain the experience required to achieve my goals.”

As a Team Buckeye rider in Pelotonia, his most memorable moment was just before the start of the event, “when I got to see the uncountable amount of people who were excited to participate in such a good cause. It was inspiring and humbling.”



Luxi Chen

Luxi Chen’s Pelotonia fellowship project yielded a discovery that could result in new ways to boost the immune system’s ability to fight cancer.

“We found a novel precursor of natural killer (NK) cells, which are immune cells that can directly target and kill cancer cells,” says Chen, a fourth-year doctoral student who is a native of China but grew up in Canada and San Jose, Calif. She earned her undergraduate degree in biochemistry at UCLA.

“By studying how this precursor develops into a mature NK cell, we can find new ways to boost our immune system to fight cancer,” she adds, noting that her study focuses on acute myeloid leukemia but could apply to other cancers. “The idea of having a wide range of applications for this knowledge, and of possibly finding cures, is deeply fulfilling, both professionally and personally.”

Chen is mentored on her project by former OSUCCC Director and James CEO Michael A. Caligiuri, MD, who is now at City of Hope National Medical Center in Duarte, Calif., but remains her adviser on

record. Aharon Freud, MD, PhD, of the Leukemia Research Program at the OSUCCC – James, is her co-adviser.

Their study resulted in a paper that was submitted for publication in the journal *Immunity* with Chen as first author, and Caligiuri and Freud as corresponding authors.

Chen is on track to earn her PhD in 2019. She plans to return to medical school for two years after that to earn her MD. “I would like to become a physician-scientist and pursue a career in hematology/oncology,” she says.

2018 marks Chen’s fifth straight year of participating in Pelotonia with Buckeye Student Riders, a group within the Team Buckeye superpeloton. This year she chose the route from Columbus to Pickerington. A well-rounded athlete who enjoys outdoor and indoor cycling, swimming, running and tennis, she looks forward to each Pelotonia.

“My favorite part of the ride is hearing the resounding cheers of families, friends and supporters in the middle of an otherwise quiet country road as riders pass by,” Chen says. “This connection between community and riders inspires and encourages my research endeavors.”

Editor’s Note: A story about Luxi Chen’s Pelotonia-funded research appeared in a recent edition of Frontiers magazine with an incorrect photo. Her correct photo appears with this story. We regret this error.



Lindsey Brinton, PhD

Lindsey Brinton’s intense curiosity about how things work—and why they sometimes don’t—has fueled her career in cancer research.

“I was always an inquisitive child,” Brinton says. “I have a strong passion for math and science, and a fascination with how the body functions and malfunctions, so I was easily taken in by the challenge of better understanding how cancer works.”

After earning her PhD in biomedical engineering at the University of Virginia, Brinton came to Ohio State in 2016 as a postdoctoral fellow with Rosa Lapalombella, PhD, John C. Byrd, MD, and James S. Blachly, MD—all members of the Leukemia Research Program at the OSUCCC – James. Brinton studies the DNA of patients with leukemia, focusing on a gene called *BIRC6* that has been found to be different in some patients and thus represents a promising therapeutic target.

With support from her Pelotonia fellowship, Brinton is “testing to see how many of our patients were born with this change and how many acquired it later. I want to understand how this gene

contributes to leukemia and how we can use this information to better treat patients.” Lapalombella is her mentor for this work.

Brinton says her team uses a genomic engineering technology called CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) “to create an endless supply of cells to study that have the same changes as our patients, so we can discover which functions are disrupted. We also test how the cells respond to chemotherapy drugs, and we find characteristics we may be able to exploit for new therapies.”

Brinton hopes to one day lead her own laboratory, but for now she is happy working with her team at Ohio State and grateful for the support she receives from Pelotonia.

She rode in Pelotonia 17, but this year she was a virtual rider because she recently had a baby. (She and her husband Travis have three children, including a 5- and a 2-year-old.)

Her zest for understanding cancer mechanics also bears a personal dimension.

“Since I began researching cancer, I have lost both of my grandpas to this disease, as well as a friend who lived his life to the fullest and died way too young,” she explains. “So for me, it comes down to channeling my curiosity into helping patients and their loved ones by creating better treatments.”

NEW HOPE

Pelotonia Supports Clinical Research at the OSUCCC – James



Clinical research studies people. It includes clinical trials that investigate the safety and effectiveness of new therapies, as well as studies that make observations of people to better understand and ultimately solve medical problems. In this way, clinical research improves cancer care. Here are two examples of clinical research at the OSUCCC – James that are supported by Pelotonia funds. To learn more about clinical trials available at Ohio State, call The James Line at **800-293-5066** or **visit cancer.osu.edu**.

Learning How Women With Breast Cancer Make a Critical Decision

A growing number of women who develop cancer in one breast are choosing to have the unaffected breast removed also. The procedure, called contralateral prophylactic mastectomy (CPM), is typically appropriate for women at high risk for breast cancer, such as those with a strong family history

of the disease or with a mutation in a breast cancer gene.

But a rising number of women with sporadic (nonhereditary) breast cancer are also requesting it. Over the past decade, rates rose to 12 percent, up from 2 percent, among early-stage breast cancer patients, and to 33 percent among younger breast cancer patients. Women say they choose the procedure to reduce fears of developing cancer in the second breast and for greater control over appearance.

What is unclear is how well women understand the risks of CPM, which can include surgical complications, longer recovery time, a more far-reaching body image, impaired sexual experiences and greater financial cost. It's also unknown whether the procedure improves a woman's quality of life and how it affects survival.

Clara Lee, MD, associate professor of Plastic Surgery and member of the OSUCCC – James Cancer Control Program, is leading a Pelotonia-funded clinical trial to better understand how women choose to have the procedure.

"We want to understand how patients make decisions about CPM, and how patients and providers communicate about the procedure," Lee says. "Patients appear to initiate discussions about CPM, and healthcare providers seem somewhat reluctant to discuss or offer it. But we don't really know what patients and providers are actually saying to each other."

Lee and colleagues are studying how women with early-stage breast cancer make treatment decisions and how discussions they have with their oncologists affect those decisions. They also are examining the women's knowledge about CPM, their treatment preferences and their quality-of-life expectations.

The two-year study involves 77 women undergoing treatment for breast cancer. The researchers are developing and testing a smart-phone application that study participants use to record the conversations they have with their oncologists. The researchers will evaluate those discussions for informed decision-making and patient and provider interaction.

"Past studies like this were done by having a researcher record the conversations," Lee says. "Empowering patients to do the recordings themselves enables us to include patients from all kinds of places—not just academic centers—and to include a wider range of oncology specialists. Those are both critical things for doing more valid research."

Lee's collaborators include specialists in surgical oncology, radiation oncology and bioinformatics, and faculty in integrated systems engineering in the College of Engineering, the College of Public Health and the School of Communications. She and her colleagues believe their findings will help clinicians better assist patients in making informed decisions about their care.

Improving an Alternative Treatment for Early Lung Cancer

Lung cancer is the leading cause of cancer-related deaths in the United States and worldwide. Of the more than 200,000 new lung cancer cases diagnosed each year in this country, about 85 percent are a type called non-small cell lung cancers (NSCLC).

About 15 percent of NSCLC cases are diagnosed at an early stage. Surgery is the best treatment option for these early cases, and 60-70 percent of patients are alive after five years. Sometimes, though, surgery isn't an option for these patients, such as those who are medically frail. These patients are typically treated with radiation therapy, but their survival rates tend to be lower than for those treated with surgery. This is likely due to pre-existing medical conditions that limit their life expectancy.

The problem is that the dose of radiation delivered to many lung tumors must be reduced to protect nearby vital structures, such as the heart and aorta. "This results in lower rates of tumor control and poorer clinical outcomes," says Terence Williams, MD, PhD, associate professor of Radiation Oncology.

Williams and Nicholas Denko, PhD, MD, also a professor of Radiation Oncology, have designed a Pelotonia-funded phase I clinical trial to address the problem.

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NEW HOPE

They are testing the use of a drug that makes lung tumors more sensitive to lower doses of radiation. If it works as planned, it will enable lower-dose radiation to kill more tumor cells. The researchers call it “biologic dose-escalation.”

“We are using a drug to make the tumor more sensitive to radiation as a novel way to improve tumor control in patients who cannot have full-dose treatment,” Williams says.

The drug Williams and Denko are studying is an FDA-approved agent called papaverine. It’s a muscle relaxant that has been used for more than 100 years and

has an excellent safety profile. Earlier laboratory studies by Denko showed that papaverine reduces oxygen consumption in cancer cells, making it more available in the tumor microenvironment. Low oxygen levels are an established mechanism by which radiation works less effectively.

The researchers believe that the drug will help overcome a form of resistance to radiation that occurs in solid tumors. It happens because solid tumors have poor blood circulation, which leaves many areas of a tumor poorly oxygenated, or “hypoxic,” and low-oxygen levels protect cancer cells from being killed by radiation. In fact, it can take a radiation dose that is two to three times higher to kill hypoxic cancer cells compared with fully oxygenated cancer cells.

“Based on our preclinical studies of papaverine, we proposed a phase I trial in patients with NSCLC to test the safety of the drug in combination with radiation,” Williams says. “We believe papaverine could dramatically improve tumor control after radiation, with minimal damage to normal tissue. Thanks to Pelotonia, we can test our hypothesis.”

The Williams and Denko study could have broad implications. “If we can reverse the effects of tumor-induced hypoxia and improve the success of radiotherapy in these NSCLC patients,” Williams says, “it might also apply to many other tumor types.”



STATEWIDE INITIATIVES

Pelotonia Dollars Help OSUCCC – James Target Colorectal, Endometrial and Lung Cancers in Ohio



Pelotonia funds are helping the OSUCCC – James change the landscape of cancer care by supporting three statewide initiatives that promote early detection and better outcomes for patients with colorectal, lung and endometrial (uterine) cancers in Ohio.

These initiatives extend the OSUCCC – James’ individualized screenings, education and care throughout the state via partnerships with a network of 50 community hospitals. The overall goal is to elevate cancer care and reduce healthcare costs while saving lives.

Beating Lung Cancer – in Ohio (BLC-IO)

BLC-IO has two aims: to evaluate the effect of advanced gene testing combined with expert advice on lung cancer treatment and patient survival, and to improve smoking-cessation rates among smokers with lung cancer and their family members and improve patients’ quality of life. BLC-IO is funded with \$3 million in Pelotonia money.

The effort is led by Peter Shields, MD, deputy director of the OSUCCC, David Carbone, MD, PhD, director the Thoracic Oncology Center at the OSUCCC – James, Mary Ellen Wewers, RN, PhD, MPH, and Barbara Andersen, PhD. Wewers and Andersen are in the Cancer Control Program at the OSUCCC – James.

A three-year period of patient recruitment began in March 2017. Project leaders anticipate that more than 2,000 newly diagnosed patients with stage IV non-small cell lung cancer will enroll in BLC-IO via the community hospital network. Each enrollee will receive free testing for more than 300 genes in their cancer specimens, and the local physicians who treat them will receive expert support for interpreting test results and determining treatments.

In addition, the BLC-IO will provide smoking-cessation support for up to three years to all participating lung cancer patients and family members. Researchers will test different models for smoking-cessation support in collaboration with primary care physicians.

Ohio Prevention & Treatment of Endometrial Cancer (OPTEC)

Women with Lynch syndrome (LS), a cancer-causing condition that occurs when a person inherits a mutation in one of four genes, have a 40-60 percent lifetime risk of endometrial cancer. OPTEC aims to recruit up to 700 women with endometrial cancer from at least 25 partner hospitals and to screen them for LS and other inherited genetic mutations that raise the risk of endometrial and other cancers. Tumor samples will undergo molecular profiling to guide and personalize treatment according to each patient's tumor characteristics.

OPTEC was launched by the OSUCCC – James in 2017 and is being funded through \$1.25 million in Pelotonia dollars. The initiative is led by David Cohn, MD, director of the Division of Gynecologic Oncology, and geneticist Paul Goodfellow, PhD, with multiple collaborators from the OSUCCC – James and Nationwide Children's Research Institute.

Patients identified with LS and their at-risk family members will be educated about the importance of genetic testing and cancer-prevention strategies based on their highest risk of LS-associated cancers. Those whose tumors have defective DNA mismatch repair will be considered for immunotherapy clinical trials for endometrial cancer.

OPTEC will conduct its LS screening with a novel one-step genetic sequencing technique developed by Goodfellow and Elaine Mardis, PhD, a geneticist at Nationwide Children's Research Institute. Genomic profiling also will help identify patients most likely to benefit from new medical therapies, including immunotherapy drugs that target certain proteins.

Ohio Colorectal Cancer Prevention Initiative (OCCPI)

The OCCPI began in 2013 and has involved \$4.3 million in Pelotonia funds over five years to establish the 50-hospital network—which also serves the other initiatives—and to set the stage for screening newly diagnosed colorectal cancer (CRC) patients and their biological relatives for Lynch syndrome (LS).

People with LS are very likely to develop CRC, endometrial, ovarian, stomach or other cancers. The OCCPI screenings were designed to identify patients and family members who may be at risk of developing these cancers so they can take precautionary measures, including heightened surveillance for early detection.

“Increased monitoring of these patients, through such procedures as annual colonoscopies starting at age 20 to 25, can save lives by catching precancerous polyps early and removing them before cancer develops,” says OCCPI

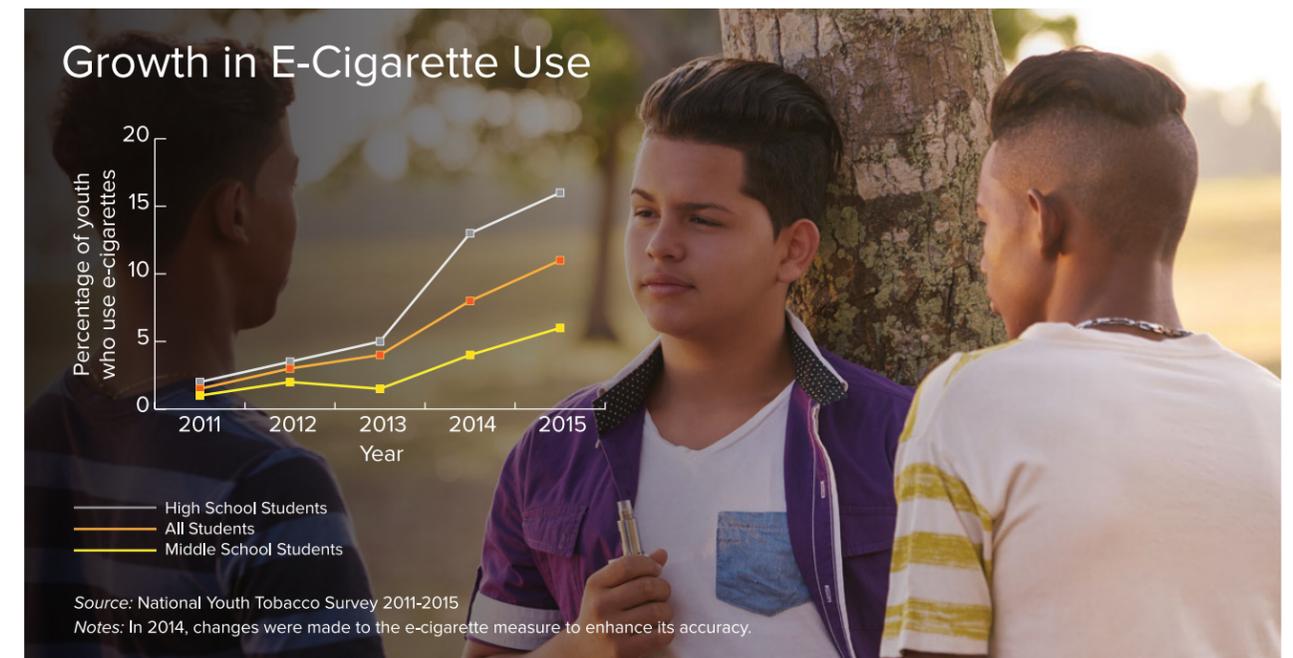
principal investigator Heather Hampel, MS, LGC, associate director of the Division of Human Genetics at Ohio State.

The OCCPI technically has ended, but Pelotonia money is still covering some costs through 2018 to collect and analyze data and to close the project. Hampel says the screening effort enrolled 3,346 newly diagnosed CRC patients, of whom 143 tested positive for LS. She also reports that 204 of their relatives tested positive, while another 101 CRC patients were found to have a hereditary cancer syndrome other than LS.

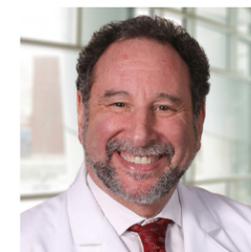
She and colleagues estimate the OCCPI will save about 1,000 years of life and provide some \$32 million in benefit to the community because of the lives it has saved in Ohio through early diagnosis of LS and, consequently, a reduced need for cancer treatment.

“Our study findings demonstrate the need and value of screening early-onset CRC patients,” Hampel says, noting that she and colleagues are working to launch this screening approach nationally. “We believe the OCCPI can serve as a roadmap for other states to implement LS screening as well.”

GROUNDBREAKING ANSWERS TO PRACTICAL QUESTIONS



Pelotonia funds support studies by OSUCCC – James researchers that will improve cancer prevention and treatment. Here are two examples.



Peter Shields, MD



Mark Wewers, MD

Learning How Electronic Cigarettes Affect Lung Health in Young People and Formerly Never-Smokers

OSUCCC – James researchers Peter Shields, MD, and Mark Wewers, MD, want to learn how electronic cigarettes, or e-cigs, affect lung health compared with traditional cigarettes. They want to know, for example, whether smokers who turn to e-cigs instead of just quitting are harmed by them, and whether e-cigs harm kids who were never smokers.

Pelotonia funds are helping them and their colleagues find the answers.

“E-cigs are likely to be safer than cigarettes for long-term use, but we don't know how much safer,” says Shields, a thoracic oncologist, cancer control researcher and deputy director of Ohio State's Comprehensive Cancer Center. “Are they similar to cigarettes or very different? Can they be used like nicotine-replacement therapy and other conventional aids to help people quit cigarettes? How harmful are they for adolescents, young adults and others who were nonsmokers but have started using e-cigs? We need to know the answers to such questions.”

The study involves 72 participants who fit into one of three categories: current cigarette smokers, e-cig users or nonsmokers.

The researchers are using bronchoscopy to directly assess the effects of tobacco and e-cig use on the lungs of the volunteers. During this outpatient procedure, a doctor inserts a thin tube through the nose or mouth to view the airways. A sample of lung cells is collected from fluid in the lungs to evaluate differences among the groups. Participants also provide their demographic information, medical history and tobacco history.

Nonsmoker volunteers are asked to use nicotine-free and flavor-free e-cigs for one month before undergoing a second bronchoscopy so researchers can observe the effects, if any, of e-cigs on the lungs.

“Using bronchoscopy, we can see in real time how the lung tissue of nonsmokers, e-cig users and traditional cigarette smokers differs,” Shields says. “And Pelotonia is helping us gain this knowledge. We’re using Pelotonia funds to help support the critical bronchoscopy portion of the study.”

The researchers are also looking at how e-cig use affects the immune system. “This could be an important indicator of negative health impacts and give us clues about the changes in lung tissue that lead to future lung diseases,” Shields says.

“Anyone thinking about using e-cigs should have the information about risks and benefits, information that is not known today,” he adds. Knowledge gained from Shields’ and Wewers’ study will help the FDA develop policies to make e-cigs safer and to regulate their marketing.

Idea Grant Leads to a Clinical Test That Detects Fusion Genes



Sameek Roychowdhury, MD, PhD

A Pelotonia Idea Grant has helped researchers at the OSUCCC – James develop an assay that identifies a peculiar but important change that often contributes to cancer growth.

The assay is called OSU-SpARKFuse (Ohio State University-Spanning Actionable RNA Kinase Fusions), and it detects a change in cancer cells called gene fusions.

Gene fusions occur when a chromosome breaks apart and a piece of it becomes attached to another chromosome. Sometimes, such “translocations” join two genes together, resulting in one abnormal gene that plays a predominant role in driving cancer-cell and tumor growth.

For this reason, drugs are being developed that block fusion-gene activity, and assays are available to detect their presence in biopsied

tumor tissue. These tests, however, require knowledge about the genes that are involved in the fusion. OSU-SpARKFuse, on the other hand, is capable of detecting fusions even when only one of the two genes is known, so the assay can discover previously novel fusions.

“We designed OSU-SpARKFuse to identify patients who are eligible for new therapies that target gene fusions,” says Sameek Roychowdhury, MD, PhD, associate professor in the Division of Medical Oncology at Ohio State, who led development of the assay. “It is an accurate, reproducible, cost-effective assay that detects fusions across many genes and from the small samples of tumor tissue obtained by biopsy.

“Pelotonia funding was critical to the development of SpARKFuse, and it helped our team obtain a four-year grant from the National Cancer Institute,” he adds. “This has subsequently helped patients become eligible for clinical trials at The James—and that’s why we ride in Pelotonia, for patients.”

OSU-SpARKFuse can provide other genetic information as well, including gene-expression data, single-nucleotide changes, alternative splicing events and resistance genes. “We believe the clinical use of OSU-SpARKFuse will help expand our knowledge of gene fusions in solid tumors, and it could improve patient care by detecting fusions that we can target therapeutically,” Roychowdhury says. //

INSTRUMENTS OF DISCOVERY

Digital Pathology Update

Pelotonia Dollars Support Purchases of Equipment & Development of Techniques

Traditionally, pathologists diagnosed cancer by placing biopsy specimens on glass slides and examining them under a microscope. But glass slides are difficult to store, retrieve, transport and share with colleagues.

In 2017 the OSUCCC – James initiated a comprehensive digital pathology program. Digital pathology involves taking tissue mounted on microscope slides and scanning them to produce digital images that have the same diagnostic detail as the original slide. With a few clicks, a pathologist can call up a patient’s virtual biopsy, paired with clinical information, to quickly get an integrated picture of the patient’s unique cancer and thus enable faster delivery of optimal therapy.

In addition, Pelotonia funds have enabled the digital pathology service to scan more than 570,000 tumor sections stored on glass slides from 50,000 past cancer cases. This digital archive, which includes associated clinical data minus all identifying patient information, is available to cancer researchers worldwide.

“Thanks to Pelotonia, those specimens will see new life and contribute to the discovery of new biomarkers and new ways to more accurately diagnose cancer,” says Anil Parwani, MD, PhD, MBA, who leads the digital pathology project for the OSUCCC – James and the Department of Pathology, and directs anatomic pathology at Ohio State’s Department of Pathology.

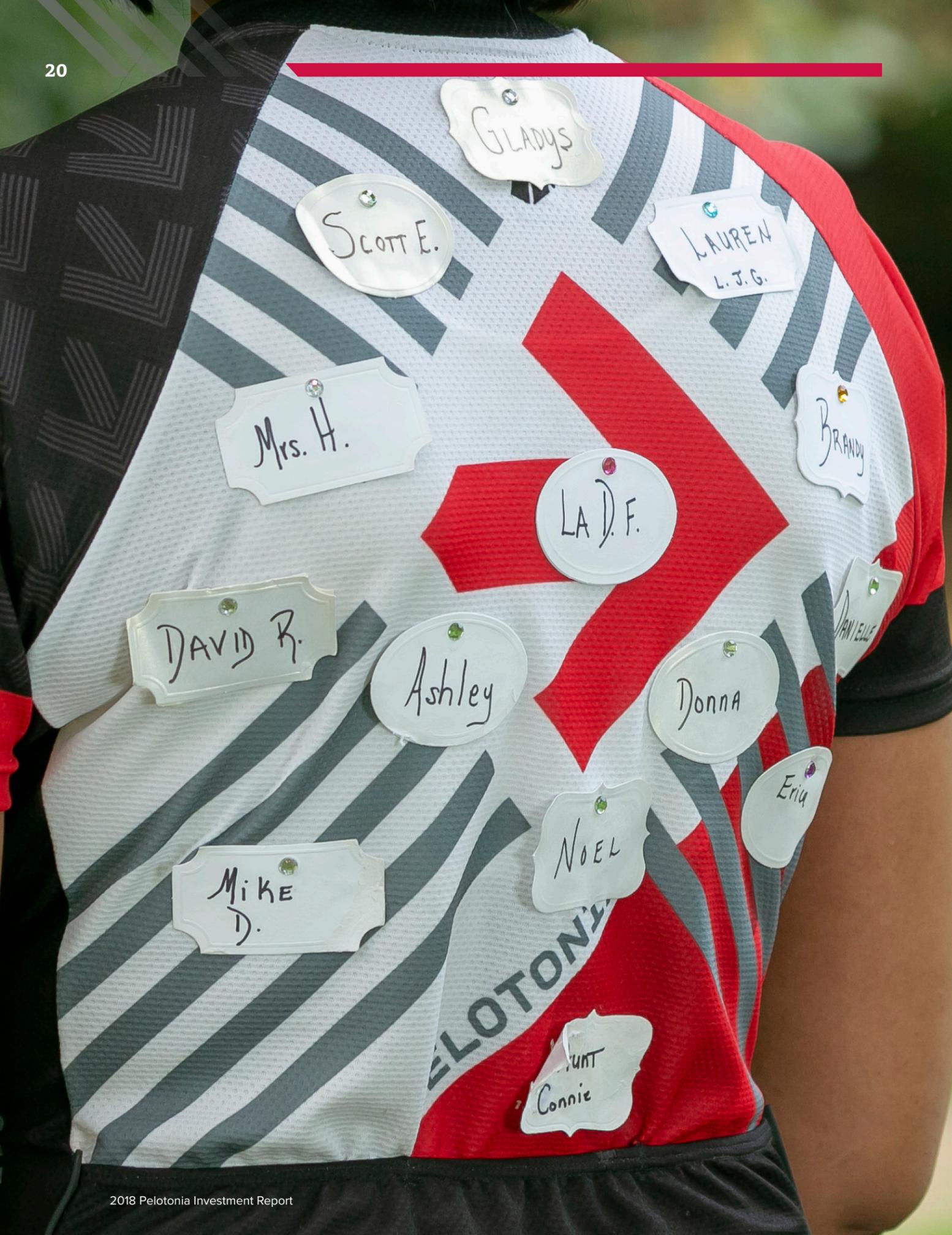
In a related project, Wendy Frankel, MD, chair of the Department of Pathology, is using a Pelotonia Idea Grant to develop image-analysis techniques that will accurately assess tumor budding in digital images of colorectal cancer tissue sections. Tumor budding happens when individual or small clusters of tumor cells pinch off, or bud, from the front edge of an invading tumor. Colorectal cancers that show cancer-cell budding may be aggressive, spread to lymph nodes, recur and have worse outcomes.

“Tumor budding can be an independent prognostic factor in colorectal cancer and help determine a patient’s treatment,” says Frankel, whose research team includes other pathologists, image analysis scientists and a biostatistician.

Frankel and colleagues will also compare their computer-assisted evaluation of tumor budding with manual evaluation. Last, they will correlate tumor budding with clinical and pathological features already collected by the Ohio Colorectal Cancer Prevention Initiative, a statewide Pelotonia-supported project that involved 50 Ohio hospitals. //

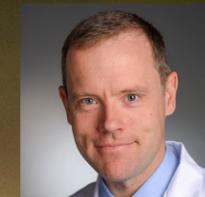
Stacking the 570,000 slides digitized by the Digital Pathology Service would create a column 19 times taller than The James.





BRINGING THE BEST RESEARCH TO OHIO STATE

Some of the brightest minds in cancer research are attracted to the OSUCCC – James and its vast array of resources. Pelotonia dollars help these researchers continue their groundbreaking work when they arrive. Among the many recent recruits are these prominent scientists:



Brad Blaser, MD, PhD,

is an assistant professor in the College of Medicine, Department of Internal Medicine, Division of Hematology. He also is a member of the Leukemia Research Program at the OSUCCC – James. He is a medical scientist whose research interest involves identifying factors in the hematopoietic niche that promote the development of myeloid neoplasia.



Nicole Grieselhuber, MD, PhD,

is an assistant professor in the College of Medicine, Department of Internal Medicine, Division of Hematology and Division of Medical Oncology, where she conducts research in acute myeloid leukemia (AML). Her research interests include molecular mechanisms of leukemogenesis, pharmacology of targeted inhibitors and applying genomic technologies to patient care.



Edmund Folefac, MBChB,

is an assistant professor in the College of Medicine, Department of Internal Medicine, Division of Medical Oncology. He specializes in genitourinary cancers, melanomas and lung cancers. His research focuses on smoking cessation in the context of preventing lung cancer, and on screening, healthcare efficiency, cancer and aging, and personalized medicine.



Amanda Hummon, PhD,

is an associate professor in the College of Arts and Sciences, Department of Chemistry and Biochemistry. Her research interests involve analytical chemistry and chemical biology, with a focus on cancer biology. Her team develops analytical methods to evaluate the transcriptome and the proteome in cancer cells, while exploring deregulation in cancer-associated signal transduction pathways.

continued...

BRINGING THE BEST RESEARCH TO OHIO STATE



Zachary Schultz, PhD, is an associate professor in the College of Arts and Sciences, Department of Chemistry and Biochemistry. His team focuses on developing tools for identifying molecules relevant to biomedical diagnostics and other applications. To do this, the team builds and develops instrumentation that takes advantage of chemical properties to characterize complex biologic samples.



Gina Sizemore, PhD, is an assistant professor in the Department of Radiation Oncology and member of the OSUCCC – James Molecular Biology and Cancer Genetics Program. Her research integrates *in vitro* and *in vivo* modeling of the brain metastatic tumor microenvironment (TME) to provide mechanistic insight into how the brain metastatic TME contributes to breast cancer metastatic progression. Current studies aim to elucidate whether platelet-derived growth factor receptor-beta (PDGFR β) signaling is a promising pathway for diagnostic and/or therapeutic purposes for metastatic breast cancer patients.



Steven Sizemore, PhD, is an assistant professor in the Department of Radiation Oncology and member of the OSUCCC – James Molecular Biology and Cancer Genetics Program. His research focuses on elucidating the mechanisms of cancer metastasis and developing therapies to improve outcomes for patients with metastatic disease. Metastatic breast cancer and metastatic soft tissue sarcoma are the areas of concentration for his research.



Hiral Shah, MD, is an assistant professor in the College of Medicine, Department of Internal Medicine, Division of Medical Oncology, where she specializes in treating patients with melanoma and other cutaneous malignancies. Her research focuses on early-phase clinical trials using immunotherapy for treatment of cutaneous malignancies. She also works to identify predictive biomarkers in melanoma patients who develop brain metastasis.



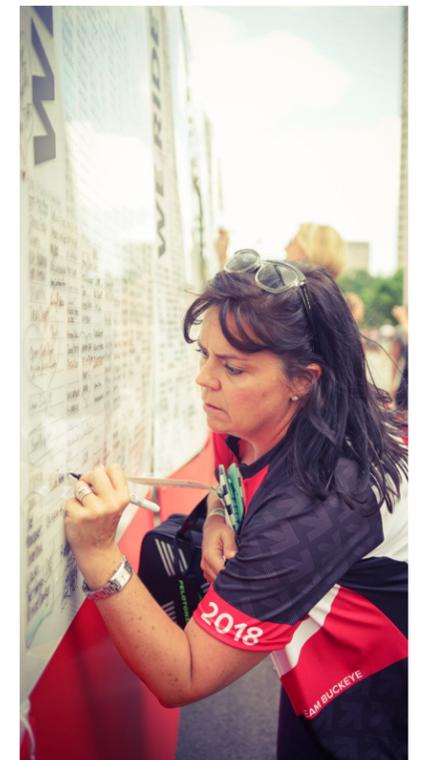
Philip Tschlis, MD, is a professor in the College of Medicine, Department of Cancer Biology and Genetics. He also serves as co-leader of the Molecular Biology and Cancer Genetics Program at the OSUCCC – James. His lab focuses on using insertional mutagenesis and other genetic strategies to identify genes involved in causing cancer or regulating phenotypic changes in tumor cells. He and colleagues have identified and exploited a number of genes implicated in cancer, including *Akt1*, *Tpl2*, *Gfi-1* and *Gfi-1B*.



Allan Tsung, MD, will become director of the Division of Surgical Oncology in Ohio State's College of Medicine on Jan. 1. He comes to Ohio State from the University of Pittsburgh Medical Center (UPMC), where he was the Raizman-Haney Endowed Chair and a professor in the Department of Surgery. He also directed the Liver Cancer Program at the UPMC Hillman Cancer Center, led the UPMC Regional Therapy Program for primary and metastatic liver cancers, and directed the Biospecimen Repository and Processing Core of the Pittsburgh Liver Research Center.



Jing "Jenny" Wang, PhD, a scientist who studies molecular mechanisms and therapeutic targets of colon cancer metastasis and drug resistance, joined the Ohio State College of Medicine faculty on Aug. 1 as a professor in the Department of Cancer Biology and Genetics. She was recruited from the University of Nebraska Medical Center, where she was a professor in the Eppley Institute for Research in Cancer and Allied Diseases. Her research focuses on developing effective therapies for patients with advanced colon cancer.





For more information about Ohio State's cancer program, visit cancer.osu.edu.

For more information about Pelotonia, visit Pelotonia.org.

Looking Ahead to Pelotonia 19

Now is a good time to start planning for Pelotonia 19, which will take place on the weekend of Aug. 2-4 on assorted routes between the Columbus area and Gambier, Ohio, (home to Kenyon College) as the 11th installment of this annual grassroots cycling event. Everyone is encouraged to ride in, donate to or volunteer for this spectacular endeavor as it enters its second decade of raising money for cancer research at the OSUCCC – James. Registration for Pelotonia 19 will open in early 2019. Watch for details on www.Pelotonia.org.

Ride. Donate. Volunteer.

Pelotonia 19
Friday-Sunday, Aug. 2-4, 2019
Pelotonia.org

The James



THE OHIO STATE UNIVERSITY
COMPREHENSIVE CANCER CENTER