TURNING CANCER DISCOVERIES INTO TREATMENTS

FRONTIERS

PELOTONIA SPECIAL EDITION 2016

The James

THE OHIO STATE UNIVERSITY
COMPREHENSIVE CANCER CENTER

NCI Comprehensive Cancer Center
A Cancer Center Designated by the National Cancer Institute

THE OHIO STATE UNIVERSITY COMPREHENSIVE CANCER CENTER–JAMES CANCER HOSPITAL AND SOLOVE RESEARCH INSTITUTE
Excitement builds with the annual approach of Pelotonia weekend, but everyone associated with this amazing event knows that it’s really a year-round venture.

Pelotonia, which began in 2009, has raised more than $106 million for cancer research at Ohio State. The event hinges not only on a climactic two-day bicycle tour each August by thousands of cyclists on routes of up to 180 miles between the Columbus area and Gambier, Ohio, but also on an abundance of grassroots fundraising that takes place throughout the year.

Besides riders and virtual riders seeking pledges and donations to support their ride or peloton (riding group), this fundraising effort comprises a multitude of events and initiatives—some large, some small, some traditional and some incredibly creative. The one thing they all have in common is their invaluable contribution toward Pelotonia’s one goal: end cancer.

Here are four examples of fundraising events created by members of Team Buckeye, the official superpeloton of The Ohio State University:

- A Taste of Pelotonia, in which delicious cuisines prepared by various Columbus restaurants and catering companies are available for sampling for a few hours at the OSUCCC – James;
- A huge golf outing coordinated by the Bo’s Tire Barn peloton that raises more than $20,000 per year;
- Sync Cancer, a peloton created by the Ohio State Synchronized Swim Team to honor a former teammate who died of breast cancer—members of this peloton are virtual riders who participate by swimming rather than riding a bike;
- Movie Night in the ‘Shoe, a popular event staged by the OSU Athletics peloton that enables guests, for just $5 apiece, to sit on the field at Ohio Stadium and watch a current-release movie on the giant scoreboard.

Imaginative fundraisers aren’t solely the domain of Team Buckeye—far from it. Events sponsored by Pelotonia’s many other pelotons, riders and family members range from designated “jean days” at work, to Vacation Bible School collections, to poker runs, to dog kisses, in which people pay to smooch a pooch owned by a young girl whose parents ride in Pelotonia and who donates the proceeds to our cause.

The ambitious creativity of Pelotonia participants perfectly matches our drive to pursue a cancer-free world. I believe we’ll get there some day. It’s a long haul, and I’m grateful to all who help lighten our shared journey.
FEATURES

06 RESEARCH HIGHLIGHTS
Examples of Innovative Pelotonia-Supported Studies at the OSUCCC – James

07 TRAINING THE NEXT GENERATION
Pelotonia Fellowships Support & Encourage Future Cancer Researchers

09 CULTIVATING INNOVATION
Pelotonia idea grants nurture original ideas to accelerate progress against cancer

14 FROM IDEAS TO IMPACT
Discoveries Made With Pelotonia Support

FINANCIAL REVIEW

04 Pelotonia 7-Year Total Exceeds $106 million

05 6-Year Pelotonia Financial Summary

RIDER PROFILES

11 Oncologic Plastic Surgeon Rides to Restore

12 Pelotonia Helped Shape Researcher’s Career

21 Cancer Survivor’s Ride is Replete With Reflection

NEW HOPE

16 Dollars Raised by Pelotonia Riders, Volunteers and Virtual Riders Support Cancer Research at the OSUCCC – James

18 Drug Development Institute

20 Super Cytometry

23 A Pelotonia-funded Clinical Trial for Cancer Patients With Depression

BRINGING THE BEST RESEARCH TO OHIO STATE

22 Meet Eight Renowned Senior Researchers Recruited With Pelotonia Funding

ON THE COVER:
Community members of all ages express thanks to Pelotonia riders

Read Frontiers online or download an issue at http://cancer.osu.edu/Frontiers.
Pelotonia 7-Year Total Exceeds $106 Million

Riders, virtual riders and donors in Pelotonia 15, the seventh installment of an annual grassroots bicycle tour that generates money for cancer research at Ohio State, raised a record $23,659,675 and boosted the seven-year total for this event to $106,055,015.

Pelotonia money supports projects addressing many aspects of cancer, including diagnosis, treatment, psychosocial issues, prevention, accelerated drug development, and initiatives that span Ohio and the nation to change the landscape of cancer care.

Key Pelotonia Sponsors

Major Funding Partners
Huntington
L Brands Foundation
Richard and Peggy Santulli

Supporting Funding Partners
AEP
Nationwide

Notable Funding Partners
Cardinal Health
Harold C. Schott Foundation
Scotts Miracle-Gro
Kenyon College

The 2015 Pelotonia total outdistanced the 2014 tally by more than $2.5 million. Thanks to Pelotonia’s major funding partners – including L Brands Foundation, Huntington, and Peggy and Richard Santulli—every cent raised by riders, virtual riders and donors goes directly to cancer research at the OSUCCC–James.

Pelotonia staff presented a check for the Pelotonia 15 total to OSUCCC Director and James CEO Michael A. Caligiuri, MD, at a Nov. 18, 2015 ceremony at The Schottenstein Center—a ceremony that included a musical performance by special guest Sheryl Crow.

“As a cancer survivor, it was incredibly meaningful for me to be a part of Pelotonia’s check presentation,” Crow says. “This community has already achieved so much for cancer research, but they continue to go above and beyond each and every year with one goal in mind. Their fundraising efforts have made such an impact on cancer research, and they show no signs of slowing down.”

Pelotonia 15 notable numbers

7,981 riders from 40 states, 10 countries
3,899 virtual riders
2,770 volunteers
277 registered pelotons (riding groups)

Team Buckeye, Ohio State’s official superpeloton

2,494 Team Buckeye members
85 individual pelotons
758 virtual riders
274 volunteers

Team Buckeye Fundraising Total:

$2.9 million

Total Participation
Riders, virtual riders and volunteers

Total Funds Raised
Seven-Year Total $106,055,015
Pelotonia generated more than $82 million in its first six years through rider pledges and donations. Thanks to the event’s major funding partners, every dollar raised by riders, virtual riders and donors is used to advance cancer research, as shown in the bar graph to the left.

**Bringing Knowledge to Bear in the Fight Against Cancer**

Pelotonia research funding has been allocated to investigators in multiple 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
- Nationwide Children’s Hospital
- Cincinnati Children’s Hospital Medical Center

**Investing in the Next Generation: Pelotonia Fellowship Program**

The Pelotonia Fellowship Program has awarded more than $11 million in funding for 399 peer-reviewed cancer research projects undertaken by Ohio State students working in the labs of faculty mentors. The trainees are students in multiple disciplines and at all levels of scholarship: undergraduate, graduate, medical school, postdoctoral and international scholars.
Research Highlights

Pioneering Pelotonia-Supported Studies at the OSUCCC – James

Gaining Insights into Radiation Resistance in Brain Cancer

Radiation is often used to treat glioblastoma, the most lethal form of brain cancer. The treatment kills the great majority of the cells it strikes, but it usually can’t kill them all because radiation doses are limited by the need to minimize damage to healthy brain cells.

But in surviving glioblastoma cells, radiation treatment can trigger changes that promote tumor recurrence and make the cells resistant to further radiation therapy.

Why this happens is poorly understood, but a new study by OSUCCC – James researchers and supported in part by Pelotonia provides new and important insights into the cause of problem.

It also identifies molecules that could be targeted by future drugs to perhaps prevent recurrence.

The study by Divya Kesakurti, PhD, a postdoctoral fellow working in the lab of Vinay Puduvalli, MBBS, professor of Neurology, director, Division of Neuro-Oncology, and colleagues, was published in the journal *Oncogene*.

The finding reveals molecular changes that lay the groundwork for tumor recurrence and radiation resistance in glioblastoma. It is known that radiation produces molecules in cells called reactive oxygen species that usually play an important role in killing cancer cells. But sustained levels of these molecules after radiation can promote tumor growth.

Kesanakurti and Puduvalli’s study found that glioblastoma cells that survive radiation have high levels of a molecule called PAK4. PAK4 then activates specific genes in tumor cells that increase reactive oxygen species and give the surviving cancer cells features of a more primitive and aggressive form of cell called a mesenchymal cell.

Glioblastoma cells that revert to this more primitive cell type grow faster and form tumors that are more aggressive and more resistant to radiation.

“Our results are the first evidence that PAK4 is involved in the radiation-induced transition of glioma cells to this more aggressive cell type, and they suggest that the therapeutic targeting of PAK4 might overcome radiation resistance in glioblastoma,” Puduvalli says.

Teaching the Tango to Improve Balance

Nearly four out of 10 cancer patients treated with multidrug chemotherapy develop nerve damage that can cause pain, numbness and muscle weakness in the extremities and impair balance.

Patients with this condition—called chemotherapy-induced peripheral neuropathy, or CIPN—often have impaired balance and difficulty standing and walking. CIPN often resolves a few months after chemotherapy ends, but until then, patients are at risk for injurious falls, and many use a cane or walker.

There are no good treatments for the condition, but Marie “Mimi” Lamanitia would like to change that.
Pelotonia Fellowships Support and Encourage Future Cancer Researchers

Each year the Pelotonia Fellowship Program allots $2 million to help promising Ohio State students in any discipline or level of scholarship who want to conduct cancer research in the labs of OSUCCC – James faculty mentors. Since the program started in 2010, it has awarded 399 student fellowship grants to 179 undergraduates, 114 graduates, six medical students, 86 postdoctoral fellows and 14 international scholars. The fellowships are peer-reviewed and issued by a committee of faculty cancer researchers chaired by Gustavo Leone, PhD, associate director for basic research at the OSUCCC – James, and co-chaired by Janice Kiecolt-Glaser, PhD, of the OSUCCC – James Cancer Control Program. Here’s a look at three recent Pelotonia fellowship recipients and their research:

Sophia Maharry

A sophomore majoring in biomedical science and French, Sophia Maharry studies the impact of an NRAS gene variant in acute myeloid leukemia (AML). She works in the lab of Albert de la Chapelle, MD, PhD, who with a team of colleagues discovered five variants of NRAS, a gene involved in the development and progression of many cancers. “We are investigating the effects of the smallest NRAS variant, isoform 5, in AML,” Maharry says, noting that her mentor for this work was Ann-Kathrin Eisfeld, MD, a postdoctoral fellow and a previous Pelotonia awardee in the de la Chapelle lab. “Experiments have shown this variant leads to more aggressive growth of cancer cells. If we can learn its role in disease progression, we can establish better targeted therapies.”

Maharry also was first author of a manuscript involving another project in the de la Chapelle lab on the role of microRNA-3662 in blood cell formation and AML. The manuscript, for which de la Chapelle, Clara D. Bloomfield, MD, and Eisfeld were co-senior authors, was accepted for publication in the journal Cancer Discovery.

Maharry, who plans to pursue an MD/PhD and “combine my passions for cancer biology, patient care and Francophone studies,” says she was “beyond grateful to receive a Pelotonia fellowship for my work.” 2016 will mark her fourth year as a Pelotonia rider. “While the ride is long and very hilly at times, the feeling of unity among everyone involved makes it worth it year after year.”

(continued on page 8)
Mark Calhoun

Graduate student Mark Calhoun, who earned his undergraduate degree in biomedical engineering at Rose-Hulman Institute of Technology in Terre Haute, Ind., and is pursuing a PhD at Ohio State, is investigating how physical forces acting on tumor cells, such as pressure and fluid flow, affect their ability to invade brain tissue. This information may help find a way to inhibit the invasive nature of glioblastoma, the deadliest form of brain cancer.

“Chemotherapy drugs are our most versatile way to attack a tumor, and better drugs translate to better outcomes,” says Calhoun, who works in the lab of Jessica Winter, PhD. “Drug discovery starts with identifying potential targets, and the tumor microenvironment, or the environment that the cell ‘sees,’ provides a wealth of opportunity. The goal of this project is to mine those drug targets and pave the way to new drugs.

“As engineers in the fight against cancer, the greatest contributions we can make are in modeling facets of the tumor that biologists traditionally have not been able to do,” he adds. “The really cool part of the project for me is using my skill set in a way that’s useful to the public good.” Calhoun rode 100 miles in Pelotonia 15 and plans to ride 180 this year. “It’s an honor to be on the receiving end of all the hard fundraising work that this huge community has done, and then to turn that around and give back to the community and to patients.”

Eason Hildreth, DVM, PhD

Postdoctoral fellow Eason Hildreth, DVM, PhD, is studying ways to inhibit or better treat breast cancer metastasis (spread) and growth in bone. Hildreth, who works in the lab of Michael Ostrowski, PhD, says breast cancer cells that spread to bone cause a massive activation of normal bone cells called osteoclasts, whose usual role is to break down bone so new bone can form. However, increased osteoclast activation causes accelerated bone removal, leading to bone loss, pain and fracture.

“Our research is focused on inhibiting the development and growth of bone metastases and also overcoming the limitations of current treatment methods,” Hildreth says, adding that, using a mouse model of human breast cancer in which malignant cells spread to the lung, liver, bone and brain, “We are looking at a new way to reduce osteoclast function that may also be used to inhibit or treat metastases to other organ systems.”

Hildreth, who earned his DVM at North Carolina State University in 2004 and his PhD at Ohio State in 2014 before joining the Ostrowski lab, rode in Pelotonia 15 and plans to ride this year. “I will continue to raise money for years to come for Pelotonia because it is an excellent organization and cause,” he says. “To be selected for a Pelotonia fellowship was a great honor that I am thankful for every day.”
Cultivating Innovation

Pelotonia idea grants nurture original ideas to move progress

All the money raised by Pelotonia cyclists supports cancer research at The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James).

Part of that money supports OSUCCC – James idea grants, which provide two years of support to teams of OSUCCC – James scientists. The grants are competitive. The researchers propose studies that will break new research ground and generate data that will help them garner grants for larger, more definitive studies.

Since the program’s inception, funding has been awarded to 89 research teams. The collaborating researchers come from several Ohio State colleges and departments and three academic institutions, including Nationwide Children’s Hospital.

Idea grants are designed to break new ground and hasten the development of safer, more effective treatments and improved prevention strategies. Here are three examples of the Pelotonia idea grants awarded in 2015.

Developing More Precise Treatments for Prostate Cancer

Male hormones such as testosterone are known as androgens. Decades of research have shown that androgens are necessary for the development and progression of prostate cancer. The hormones bind to androgen receptors in prostate-cancer cells, and the hormone-receptor complex then activates a set of genes that cause the cancer cells to grow.

Drugs that block androgen receptors so that androgen hormones can’t activate them can often control the disease for a time, but prostate tumors eventually develop a capacity to grow without help from androgen hormones. At that point, antiandrogen drugs lose their effectiveness.

To improve the treatment of any cancer, it is essential to understand the biology of the disease. For prostate cancer it was believed that when an antiandrogen drug is bound to androgen receptors, the drug-receptor complex blocks the same cancer-promoting genes that are activated by the hormone-receptor complex.

However, recent research by these OSUCCC – James investigators found that antiandrogen-receptor complexes actually activate a different set of genes that include cancer-promoting genes.

With help from a Pelotonia idea grant, these researchers are carrying out studies that are based on this new understanding of prostate-cancer biology. Their work could bring new knowledge about how androgens promote prostate-cancer growth and how resistance develops to particular antiandrogen drugs.

Their ultimate goal is to identify therapeutic targets in prostate-cancer cells and to develop more precise, personal and effective treatments for prostate cancer.

Searching for the Source of CLL

Natarajan Muthusamy, DVM, PhD, professor of Medicine
Chronic lymphocytic leukemia (CLL) is the second most common leukemia in the United States, with an estimated 14,600 new cases in 2015, along with 4,650 deaths from the disease. Great progress has been made in the treatment of CLL—including promising targeted agents such as ibrutinib, which was developed with much assistance from research at the OSUCCC – James, work that was supported in part by Pelotonia funds. But even with these advances, the disease remains incurable. CLL patients invariably relapse, and relapsed CLL is particularly resistant to treatment. Furthermore, why and how a relapse occurs is poorly understood. The problem is challenging in part because the source of the cell from which CLL originates remains unknown.

The existence of a leukemic stem cell is widely accepted in acute myeloid leukemia and certain other leukemias, but the existence of a CLL stem-like cell remains controversial. This OSUCCC – James research team is using a Pelotonia idea grant to hunt for the elusive cell in bone marrow samples from CLL patients using a 3D nanochannel electroporation technique in combination with molecular probes. The new nanotechnology platform will better enable them to identify rare cells that display a particular combination of marker molecules.

The researchers hypothesize that the rare cells will include the elusive CLL stem cell and early progenitor cells. Their findings will pave the way for the development of new drugs and therapeutic strategies for treating people with relapsed leukemia.

Improving a Mobile Health Intervention for HPV Vaccination

Human papillomavirus (HPV) is the most common sexually transmitted infection in the United States, with the highest rates of infection in young adults. HPV infection can cause cancers of the cervix, vagina, vulvar, oropharynx, anus and penis, as well as genital warts. HPV vaccines are safe and effective. However, HPV vaccination rates among young adults are low, even though their risk of acquiring HPV is high. It is recommended that girls and boys receive the HPV vaccine before becoming sexually active, ideally at age 11 or 12. Catch-up vaccination may be given through age 26. Wide use of the vaccine may prevent an estimated 22,000 cases of cancer and more than 300,000 cases of genital warts annually in the United States.

These OSUCCC – James researchers are using a Pelotonia idea grant to increase the use of the vaccine by improving how information about HPV-associated diseases and HPV vaccines is provided to young adults. Currently, 18 percent of females ages 20 to 24 are infected with a vaccine-preventable HPV type (type 16, 18, 6 or 11). But HPV vaccination rates are especially low among young adults ages 19 to 26. Only about 40 percent of females and 8 percent of males have received the first dose of the three-dose series (2014); fewer females and males have completed the three-dose HPV vaccine series.

Working with Ohio State’s Wilce Student Health Center and with Ohio State students, the researchers are developing and pilot testing gender-specific targeted animated videos about the benefits of HPV vaccination. The study will be conducted using a mobile-friendly website. The researchers will obtain preliminary data on whether the targeted video increases the number of young adults who receive the HPV vaccine. They think vaccine use will be higher among those who watch the video compared with those given standard HPV vaccine information. Findings from this study could lead to a randomized clinical trial to test the efficacy of this HPV-vaccine intervention at several universities, which could lead to widespread use.
Roman Skoracki, MD, came to the OSUCCC – James about two years ago from The University of Texas MD Anderson Cancer Center.

He has two children, 8 and 11. “We love Columbus. It’s a very family-oriented, friendly city,” he says. “Something I didn’t appreciate about Columbus at first was the focus on cancer research,” he says. “Seeing the community come together for Pelotonia is extraordinary”

Skoracki is a professor of Plastic Surgery and chief of the Division of Oncological Plastic Surgery. His clinical expertise includes reconstructive microsurgery of the head, neck and breast, surgical treatment of lymphedema and sarcoma reconstruction.

He specializes in microvascular surgery—the meticulous sewing together of pin-head diameter blood vessels using tiny needles and ultrafine sutures. He is one of very few surgeons in the country performing microvascular surgery to treat lymphedema, a painful swelling of a limb caused by the buildup of fluid when lymphatic vessels are damaged or removed during surgery.

Skoracki’s goal is to improve patient outcomes physically and psychologically. His research focuses on improving outcomes in head and neck cancer reconstruction and on the surgical treatment of lymphedema.

This procedure re-routes lymphatic channels to allow proper fluid drainage or re-introduces lymph nodes to the affected region. (The James is one of a few hospitals in the country that has a comprehensive lymphedema team and program for cancer patients.) He is also helping to develop an education initiative for breast-cancer patients anticipating reconstruction.

He rode his first Pelotonia last year, tackling the 100-mile route. “It was incredible,” he says. “I hadn’t ridden a bike for 10 years, and I’m getting older, so it took preparation—I also took advantage of rest stops and drafted behind friends and colleagues. The energy level and support from everyone along the way made the ride go by faster than I thought it would.”

He rides with colleagues from the Department of Plastic Surgery’s Riders to Restore peloton, which includes patients and staff. “The name comes from what plastic surgery is intended to do: restore and make whole what has been taken away,” Skoracki explains.

In the clinic, he works with cancer patients from diagnosis forward. “I especially enjoy getting to know my patients and accompanying them on their journey to recovery.”

He rides in Pelotonia to honor his patients and the strength they show during recovery, and to honor a close friend who recently died of cancer.

“I’ve had the privilege of caring for cancer patients for more than 15 years. It’s a privilege because these patients are incredibly courageous and a daily inspiration to me. They may be losing their hair, they
Emily Smith expected to follow her interest in infectious diseases when she entered Ohio State’s graduate program in 2012. But her academic adviser recommended that she first try something different. “OK, fine, fine,” Smith told herself.

She spent more than a month in the Division of Hematology, then reported back to her adviser, Joanne Turner, PhD, professor of Microbial Infection and Immunity. “I tried the rotation,” she said, “and I’ve decided to stay there.”

Hematology offered an opportunity to study the pathogenesis of disease while doing the biochemistry that she enjoyed.

She also watched the physicians interact with patients. “It was a level of care above and beyond what I had seen before,” she says.

She chose to work in the laboratory of Robert Baiocchi, MD, PhD, associate professor of Hematology. She was drawn to his research and to the care he took with patients. “Dr. Baiocchi wants patients to understand all their options; it’s not a 30-second ‘This is what’s happening and we’re done.’ It’s pretty remarkable,” Smith says.
She registered for Pelotonia 2013 on Mother’s Day. “Later that week, Mom phoned to say she had been diagnosed with uterine cancer,” Smith says. The news crystalized her decision to study cancer. “If there was ever a sign, that was it.”

(Smith reports that her mom was diagnosed early and is doing fine.)

Smith signed up for the 25-mile ride. “I like to be active. I like to run. I like to be outside. But I’m not a cyclist by nature,” she acknowledges.

When the big morning arrived, she was apprehensive as she joined the other riders at the Pelotonia starting line.

“I didn’t know what to expect...then I was overwhelmed,” she says. “When you’re at that starting line with everyone, there’s a feeling of excitement. Everyone is there for the same reason; we all want to see a cure for cancer. It was very emotional.”

She also realized something else. “Normally, as a lab researcher I would never see patients,” Smith says. “But at Pelotonia events, people would come up and thank me for doing the research that I’m doing and for listening to their stories and interacting with them. That means a lot.”

She talked of these experiences with Baiocchi, too. “His response was always, ‘Well, you know, Emily, you can see your research applied to patients and witness the direct impact in the clinic if you’d get your medical degree.’

“I love research, I love the bench, I love doing the hands-on work,” Smith says. “I knew I wanted to do something that would help people and make an impact. But seeing the physicians and seeing that I could do both has really influenced my career path in that I do plan to get my MD after I finish my PhD.”

Back in the laboratory, Smith’s work with Baiocchi held a bonus: It involved an infectious agent, a virus. Her work focuses on a protein called PRMT5 and how it drives a healthy B cell to become a lymphoma cell during Epstein-Barr virus infection. Furthermore, Smith applied for and received a graduate-student Pelotonia fellowship to help support her research.

“When I served on the executive board for Team Buckeye Student Riders, I gave talks to student groups, and I always told them that if you ride in Pelotonia one year, you’ll be back to ride again. “It’s because of the people you meet and the feeling that everyone shares the same passion: to end cancer. It is very emotional.”
From Ideas to Impact

Discoveries Made With Pelotonia Support

Pelotonia funds help support groundbreaking preliminary studies at The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James). They produce data and publications that can lead to grants for larger studies. In this way, Pelotonia funds advance cancer treatment and improve patient care. Here are three examples of that work.

E-Health Program to Reduce Obesity in Appalachia

A 2010 idea grant enabled a team of OSUCCC – James researchers to develop and implement an intervention to reduce obesity and cancer incidence by promoting a healthy diet, exercise and screening in some of the most impoverished areas of America, including Ohio Appalachia.

The project developed a faith-based healthy eating and physical activity intervention called Walk by Faith. The goal was to reduce weight and cancer risk among overweight and obese residents of Ohio Appalachia by encouraging greater physical activity and dietary changes.

Results indicate that participants lost weight, especially if they walked, participated in the educational sessions and used a pedometer to track daily steps.

“The effort has helped many people lose weight, enabling them to discontinue some medications,” says OSUCCC – James researcher Electra Paskett, PhD, MSPH, The Marion N. Rowley Chair in Cancer Research, director of the Division of Cancer Prevention and Control, and associate director for Population Sciences.

“In the screening education arm of the study, one person was diagnosed with early-stage melanoma, which probably would have been diagnosed at a later stage without our study. This person might not be alive today or have the same quality of life.”

In addition, Paskett says, “The procedures and interventions we developed can be used in the community to contribute to living in a cancer-free world.”

Reducing Chemotherapy-Induced Cognitive Deficits

In 2012, Maryam Lustberg, MD, MPH, assistant professor in the Division of Medical Oncology, and Courtney DeVries, PhD, professor of Neuroscience and Psychology, received an idea grant to investigate why nearly one-third of breast-cancer patients who receive chemotherapy report problems with memory, concentration, attention and understanding during and after treatment.

Chemotherapy-induced cognitive deficits, sometimes called “chemo brain,” can be a problem for patients treated for malignancies that include breast, ovarian and prostate cancers.

Chemotherapy, commonly used to treat women with breast cancer,
can have mental side effects that can last up to 10 years and affect social interactions, work performance and the ability to read or drive, the researchers say.

Lustberg and DeVries used the idea grant to investigate how chemotherapy activates brain cells called microglia, which are implicated in the problem. “We believe that certain chemotherapy regimens can lead to localized inflammation that involves the microglia and alters brain-cell structure and function, which in turn causes cognitive problems,” DeVries says.

“We believe our research is the first to test the idea that inflamed neurons contribute to the development of cognitive impairments in chemotherapy patients,” she adds. “Having a mechanistic explanation for the problem is essential for developing targeted therapies to treat it.”

The data they obtained from their Pelotonia-supported studies enabled them to obtain a multi-investigator, four-year, $2.15 million National Cancer Institute grant led by OSUCCC – James researcher Tonya Orchard, PhD, assistant professor in the College of Education and Human Ecology at Ohio State. The animal study investigates whether omega-3 supplementation would reduce chemotherapy-induced cognitive deficits.

“We hope to find that high omega-3 fatty acids will reduce neuroinflammation and lessen chemotherapy-induced cognitive deficits,” Lustberg says. “These are the first steps in establishing a strategy for preventing chemotherapy-induced cognitive dysfunction, which could vastly improve quality of life for cancer survivors.”

Learning Whether Black Raspberries Can Inhibit Oral Cancer

An idea grant was awarded in 2012 to a multidisciplinary team of OSUCCC – James researchers led by Yael Vodovotz, PhD, professor of Food Science and Technology, to further develop a food-based approach for preventing oral cancer in people at high risk for these diseases and for improving their treatment.

The research team also included Steven Clinton, MD, PhD, in the College of Medicine, Christopher Weghorst, PhD, in the College of Public Health, and Steven Schwartz, PhD, in the College of Food, Agricultural and Environmental Sciences.

Cancer of the oral cavity is a devastating disease that can affect speech and swallowing, as well as often being fatal. In 2012, an estimated 529,000 people worldwide were diagnosed with oral cancer, and 292,000 people died of the disease. The 50-percent five-year survival rate has remained largely unchanged for decades.

The researchers studied the use of a highly concentrated form of black raspberries, which research has shown have significant anticancer activity. The team’s Pelotonia grant supported a two-week clinical trial of 60 healthy adults who consumed black raspberry confections at two doses and in three forms.

The researchers wanted to learn which form most effectively releases the berries’ natural cancer-fighting phytochemicals into the mouth and which form trial participants found most palatable.

A gummy form was found most acceptable. It released black raspberry phytochemicals at an acceptable rate and also provided users with an acceptable texture and sensory experience.

“This controlled release form of confection may have great applications in various types of disease-prevention clinical trials,” Vodovotz says.

The grant led to a five-year, $3.1 million grant from the National Cancer Institute to study whether a black raspberry drink will help prevent oral cancer. The study focuses on how the bacterial communities in the mouth—the oral microbiome—might influence the effect of the berries. The study was described in the spring 2016 issue of Frontiers, available at cancer.osu.edu/frontiers.
New Hope

Dollars raised by Pelotonia riders, volunteers and virtual riders support cancer clinical trials at the OSUCCC – James

Clinical trials are the gold standard for evaluating the safety and effectiveness of innovative new therapies in humans. Here are two examples of Pelotonia-supported clinical trials under way at the OSUCCC – James.

A Cancer-Killing Virus for Treating Solid Tumors in Children

OSUCCC – James researcher Timothy Cripe, MD, PhD, chief of the Division of Hematology and Oncology, and Blood and Marrow Transplantation at Nationwide Children’s Hospital, is leading a clinical trial he believes will help children with solid tumors that occur outside the brain.

The cancers include neuroblastoma, which occurs in children age 17 months on average and arises from immature nerve cells; sarcomas, or tumors of muscle and other soft tissue; and osteosarcoma, tumors that develop in bone.

“We’ve made progress in treating these types of cancers, but we’ve essentially reached the maximum benefit from surgery, chemotherapy and radiation,” Cripe says. “We need new types of therapies for these patients, particularly those with metastatic disease.”

Cripe’s phase I trial is testing the use of a cancer-killing virus, also called an oncolytic virus, that selectively kills cancer cells while doing little damage to healthy cells. The virus replicates in cancer cells, which causes them to burst, killing the cancer cells and spreading the virus to adjacent tumor cells.

In addition, studies in animals suggest that the bursting cells release cancer-cell specific molecules that stimulate the immune system to attack the tumor. The therapy therefore kills cancer cells both directly and indirectly through an immune response.

The virus is a modified herpes simplex virus type 1. A similar type of weakened virus has been approved by the Food and Drug Administration to treat melanoma in adults. “Our trial is designed to learn if this type of treatment is safe in children and young adults,” Cripe says.

The trial is open to patients aged 7 to 30 with any type of solid tumor located outside the brain.

Timothy Cripe, MD, PhD
and central nervous system. (The trial does not accept leukemia or lymphoma patients.)

The study has two parts. In part one, the virus is injected directly into the patients’ tumors. In part two, patients receive an infusion of the virus into a vein. “The idea is that the bloodstream will carry the virus to metastatic tumors anywhere in the body and kill them,” Cripe says.

“This is a new type of therapy for childhood solid tumors. We believe it will provide another option for treatment of these cancers and in the future should be able to be combined with standard treatments.

“Pelotonia is supporting the systemic testing of the virus, which is important for patients with metastatic disease,” Cripe says. “We are the only ones in the world using this virus systemically. We’re hoping it will open an entirely new era of cancer therapy that is more effective and safe.”

Learn more about childhood cancer in a video by Timothy Cripe, MD, PhD, at http://go.osu.edu/BWbD

Seeking a Gentler Therapy for AML

Acute myeloid leukemia (AML) is the most common form of acute leukemia in the United States. Some 20,800 new cases were expected in 2015, along with nearly 10,500 deaths from the disease.

An early-stage clinical trial supported in part by Pelotonia funds and led by principal investigator Sumithira Vasu, MBBS, assistant professor in the Division of Hematology, is evaluating the feasibility and safety of an innovative immune therapy for AML. The therapy was developed by Vasu and colleagues in the OSUCCC – James Leukemia Research Program.

The therapy is designed for older patients and people who cannot withstand the rigors of stem-cell transplantation, which is currently the most effective treatment for many cases of AML.

The need for new therapies is critical. Only about 40 percent of AML patients under age 65 achieve long-term remission. The survival rate is worse in patients age 65 and older, who often develop subtypes of AML that are harder to achieve remission and more likely to recur. Also, older patients often have other medical problems that leave them less able to tolerate chemotherapy. Hence, only about 10 percent of older AML patients are alive five years after diagnosis without an allogeneic (from a donor) transplantation.

The treatment being studied by Vasu and her colleagues in the OSUCCC – James Leukemia Research Program is carried out in four steps over 16 days. First, participants receive low doses of fludarabine, a drug that mildly suppresses the immune system. That is followed by:

• Low doses of an anticancer drug called decitabine;
• An infusion of immune cells called natural killer (NK) cells that were obtained from a compatible donor;
• Several doses of a drug that stimulates NK-cell growth.

The researchers hypothesize that the fludarabine will help the patient’s immune system accept the NK cells, and the decitabine will make AML cells more susceptible to killing by NK cells.

“Though additional clinical testing will be necessary, we believe this therapy could help more patients achieve remission,” Vasu says.

In addition to this clinical trial, Pelotonia funds helped Vasu and William Blum, MD, and Natarajan Muthusamy, DVM, PhD, both professors in the Division of Hematology, study patient samples to help develop a novel combination regimen for patients older than 60 years.

Using samples from patients who generously donated samples as part of clinical trials using decitabine led by Blum, the study showed that decitabine also modulates leukemia cells and makes them more susceptible to killing by NK cells and to antibodies that depend on NK cells for killing. These preclinical studies were published recently in the journal Blood and led to an international, multicenter trial evaluating the combination of decitabine and a novel antibody that relies on NK cells for killing AML cells. This trial is expected to be open in the fall of 2016.
Pelotonia Funds Are Translating OSUCCC – James Discoveries into New Cancer Treatments

The Drug Development Institute (DDI) is a biotech-like institute embedded in The Ohio State University Comprehensive Cancer Center. The DDI identifies promising anticancer agents discovered by OSUCCC – James researchers, advancing them through the pharmaceutical development process with the goal of partnering with industry to deliver new therapies to patients.

The DDI was founded by Michael A. Caligiuri, MD, director of Ohio State’s Comprehensive Cancer Center and CEO of The James Cancer Hospital and Solove Research Institute, and by Timothy Wright, a former executive of several pharmaceutical companies and chair of the DDI External Advisory Board, in 2010. The DDI was organized to address the developmental gap that exists between discoveries made in the academic lab and the conversion of those discoveries to new therapies in patients. The DDI utilizes its extensive industry drug-development experience to substantially reduce the risks, time delays and costs of advancing basic research breakthroughs into treatments. This de-risking approach is done in partnership with Ohio State research teams and places strong emphasis on multidisciplinary collaboration. By bringing an industry-focused perspective to investment and management decisions, the DDI ensures that research programs have a high likelihood of success.

Here are four examples of OSUCCC – James anticancer agents currently in development by the DDI with support from Pelotonia funds.

Activated B-cells for Cancer Immunotherapy

OSUCCC – James researchers have developed an anticancer vaccine that uses B lymphocytes, or B cells, the type of immune cells best known for fighting infections by releasing antibodies. B cells in this new vaccine are used to fight cancer by boosting the patient’s immune system. The researchers have already shown that these B cells can attack tumors and dramatically decrease their size. They now aim to establish that these B cells promote the rejection of established tumors and tumors that generate a poor immune response. The researchers believe that their approach can overcome the limitations of related immune therapies currently on the market or in clinical trials testing.
Multivalent Notch Ligands for Cancer Immunomodulation

Low numbers of Notch signaling receptors on the surface of immune cells weaken the immune response against cancer cells. Researchers at the OSUCCC – James are synthesizing molecules that interact with Notch receptors and modulate Notch signaling. They believe that the molecules could work as anticancer agents by helping the immune system recognize and react against tumor cells that arise in the body. Currently, they are synthesizing the novel molecules and testing them in the laboratory. The next step is to identify a set of candidate molecules that will be assessed for safety and effectiveness in animal cancer models.

A Novel MRI Imaging Agent

A practical, safe method for expanding the use of MRI to visualize tumors a quarter-inch or smaller in size would greatly help doctors detect cancer earlier. OSUCCC – James researchers are developing a technology that uses submicroscopic particles that assemble themselves into larger molecules in the acidic conditions around a tumor. There, the molecules enlarge 20 to 100 times their size and self-assemble into tiny fibers that remain in the tissue surrounding the tumor. Attaching a label to the molecules would make them a cancer-targeted MRI-imaging agent. The technology might work with a broad range of cancers and could be particularly useful for detecting small, early lung cancers. The same technology might also work for delivering drugs or radiotherapy to tumors.

Epigenetic Inhibitors for Cancer Treatment and Autoimmune Disease

Protein arginine methyltransferases (PRMTs) are a family of enzymes that regulate a wide variety of cellular functions and are frequently associated with many human cancers. Recently, increasing evidence suggests that PRMT5, an important member of the PRMT family, is a potential oncoprotein and thus may cause cancer. Thus, PRMT5 is an important target for therapeutic strategies. OSUCCC – James researchers are evaluating PRMT5 inhibitors for the therapeutic treatment of glioma, hematologic malignancies and autoimmune diseases. Ohio State is a center of excellence in PRMT5 research and is leveraging these resources to develop a targeted PRMT5 inhibitor. Currently no PRMT5 inhibitor exists in any stage of clinical development, giving the OSUCCC – James an opportunity to develop a first-in-class therapeutic.
Super Cytometry

A technology called flow cytometry has been a mainstay of cancer research for decades. It tells researchers what type of cells they are looking at.

The method uses antibodies that bind with certain molecules that might be on or inside cells. Each of the antibodies emits a certain color of light when exposed to a laser beam. The cells are run through a flow-cytometer, which counts cells based on the colors of light they emit.

But the technique has limitations. “When using multiple antibodies, the colors bleed into one another, making it hard to label even 10 molecules in cells,” says OSUCCC – James researcher Gregory Behbehani, MD, PhD, assistant professor of Medicine in the Division of Hematology.

For example, it’s important to identify leukemia progenitor cells, often called leukemia stem cells, which are present in very small numbers, he says. “Less than 5 percent of the cells present in a sample are leukemia stem cells, and we must look at 7-10 markers just to identify them. That doesn’t leave much room for asking questions when using traditional flow cytometry.”

Fortunately, Pelotonia funds have enabled Ohio State’s cancer program to purchase a mass cytometer, a state-of-the-art instrument that identifies and sorts cells without relying on light.

In mass cytometry, the same antibodies are again used to identify telltale molecules on cells, but the antibodies are linked to heavy metals that are never present in cells.

The instrument vaporizes the cells into clouds of ionized atoms and then separates the metal ions that were attached to the antibodies bound to the cells according their molecular weight. This separation can be performed at very high resolution, allowing the presence of the antibodies to be detected and eliminating the problem of color overlap. “The new system allows us to measure 30 to 50 molecules on cells,” Behbehani says.

He has already used the instrument to study why some people with a subtype of acute myeloid leukemia (AML) called core-binding factor AML are cured with chemotherapy, while people with an AML subtype that features a mutation called FLT3 ITD are not.

The 2015 study was published in the journal Cancer Discovery, with a commentary. Among its many findings, it showed that in patients with leukemia subtypes that are typically curable, 7-8 percent of leukemia precursor cells are undergoing cell division at any one time, which would make them sensitive to chemotherapy.

But only about 0.5 percent of those progenitor cells are dividing at any one time in patients with FLT3 ITD mutations. “So those cells are growing very slowly, making them much less sensitive to chemotherapy,” Behbehani says. “Patients with this leukemia subtype go into remission, but their disease usually relapses, making it very difficult to cure.

“In the future,” he says, “we hope to use instruments like this one to further personalize treatments and cure more patients.”

Gregory Behbehani, MD, PhD

Palak Sakhi, MS, research associate in the laboratory of Gregory Behbehani, MD, PhD, with the Helios mass cytometer purchased with Pelotonia funds.
RIDER PROFILE: Kent Rinker

A Ride Replete with Reflection

The only time Kent Rinker thinks about surviving cancer is during his annual Pelotonia ride. He also thinks about his father and several friends who had cancer but were “not as lucky and are no longer with us.”

“That is why this ride is so emotional for me,” says Rinker, 68. “The fact that I can ride with my family makes it a special day as well.

“The distance I choose to ride might be difficult, but it is nothing compared to what cancer patients deal with daily.”

Rinker, a retired public mutual fund manager with Diamond Hill Capital Management, began riding in Pelotonia in 2010 after being encouraged by a younger colleague and active cyclist at Diamond Hill who had ridden in the 2009 inaugural Pelotonia.

Rinker and his wife Nancy, daughters Julie and Kelly, son Nick, daughter-in-law Jessie and son-in-law Tom have all ridden as part of the Diamond Hill peloton (Julie also works there).

“I have been hooked ever since my first ride,” he says, noting that he and Julie have since ridden 100 miles together four times; last year they rode 75 again, mainly because he was suffering from a bad left knee. Although his knee still troubles him, he plans to once again ride 100 miles this year, accompanied by his daughter Julie, his son and their spouses.

Rinker learned 10 years ago that he had prostate cancer while in Florida. Severe pain in his groin sent him to an emergency room. Later, a urologist, suggested a biopsy that detected cancer. Rinker then sought opinions from urologists at other locations, including The James.

Eventually he had his prostate removed via robotic surgery. He required no follow-up therapy, and he has had no recurrences.

“I always felt and hoped that I would be cancer-free,” he says. “I was optimistic and never depressed. I treated the news as if it were a small bump in the road of my life. Fortunately, that’s all it was, and my wife, family and friends were very supportive.”

He feels lucky to be a survivor but doesn’t dwell on it. Rather, he thinks of others, such as a man on another continent for whom he became a bone marrow donor some 20 years ago. Rinker went to The James for the donation procedure, which he says “could not have gone better.”

Rinker wished to contact the recipient and, following donation confidentiality policies, he did so after a one-year waiting period. The two have kept in touch; Rinker plans to visit the recipient next year.

In addition, Rinker and his family think of a niece who was diagnosed with a rare cancer called leiomyosarcoma. When the Rinkers inquired about research funding for this disease, retired James Director Emeritus David Schuller, MD, introduced them to Raphael Pollock, MD, PhD, a sarcoma specialist who had been recruited from MD Anderson Cancer Center to Ohio State with the support of Pelotonia funds to aid his research.

“A driving factor in his decision to come here was research dollars raised by Pelotonia,” Rinker says. “This doctor is one of the best in the world, and he is here because of Pelotonia and the work being done at The James.

“Unfortunately,” he adds, “our niece died last December. We will continue to ride in her honor.”
Bringing the Best Research to Ohio State

The OSUCCC – James attracts some of the brightest minds in cancer research, and Pelotonia dollars help them continue their studies when they arrive. Among those recruited in 2015-16 are these prominent senior researchers:

Daniel Jones, MD, PhD, professor, vice chair and director of molecular pathology in the Department of Pathology, and director of molecular pathology for the OSUCCC – James. Jones came to Ohio State from Quest Diagnostics Nichols Institute, where his group developed more than 100 oncology, genomics and pathology assays.

Anil Parwani, MD, PhD, MBA, professor, vice chair and director of anatomic pathology in the Department of Pathology. In the OSUCCC – James, he directs the digital pathology service, enabling expansion of precision cancer medicine. His research focuses on molecular markers in bladder, prostate and kidney cancers. Parwani came to Ohio State from the University of Pittsburgh.

Sharyn Baker, PharmD, PhD, professor and chair of the Division of Pharmaceutics and Pharmaceutical Chemistry in the College of Pharmacy, and holder of the Gertrude Parker Heer Chair in Cancer Research. Baker came to Ohio State from St. Jude Children’s Research Hospital. Her research interests include anticancer drug development.

Alex Sparreboom, PhD, professor in the College of Pharmacy’s Division of Pharmaceutics and Pharmaceutical Chemistry. Sparreboom, who came to Ohio State from St. Jude Children’s Research Hospital, studies factors contributing to chemotherapy side effects and how to reduce them.

Rajgopal Govindarajan, DVM, PhD, associate professor in the College of Pharmacy’s Division of Pharmaceutics and Pharmaceutical Chemistry. He was recruited from the University of Georgia. His goal is to understand factors that make tumors more or less sensitive to chemotherapy, and microRNA drugs.

Cheryl Taylore Lee, MD, professor and chair of the College of Medicine’s Department of Urology. Lee, an expert in outcomes research and comparative studies, was recruited from the University of Michigan to lead Ohio State’s urology, uro/gynecology and uro/oncologic programs.
Beating the Blues

_A Pelotonia-funded clinical trial evaluates an online therapy for cancer patients with depression_

“Beating the Blues” is an online intervention designed to treat depression and anxiety. It is based on cognitive-behavioral therapy, and it provides ways to better manage mood, stress and anxiety, the researchers say.

The trial is funded by a Pelotonia postdoctoral fellowship awarded to Marlena Ryba, PhD, a postdoctoral researcher in the laboratory of OSUCCC – James researcher Barbara Andersen, PhD, professor of Psychology and a Distinguished University Professor.

“Promising findings indicate that this intervention may be suitable for a range of patients in diverse settings,” says Ryba, principal investigator for the trial. “Our trial is designed to determine whether Beating the Blues is effective in reducing depression in people with cancer.”

Depression affects 10 to 50 percent of cancer patients. Yet, it often goes undiagnosed, and when diagnosed, it is often undertreated.

“Depression can be a risk factor for premature mortality in cancer patients, and the need for psychosocial intervention can be important,” says OSUCCC – James researcher and principal investigator Barbara Andersen, PhD, professor of Psychology and a Distinguished University Professor.

Beat the Blues consists of eight weekly sessions, each session lasting 45 minutes to an hour. For more information, contact beatingtheblues@osu.edu, phone 614-292-6874 or visit [http://studysearch.osumc.edu/studies/2272](http://studysearch.osumc.edu/studies/2272)
Year after year, through the dedication of our Riders, Virtual Riders, Volunteers, and Donors, Pelotonia continues to grow.

THANK YOU FOR MAKING AN IMPACT.

FOR MORE INFORMATION, PLEASE VISIT PELOTONIA.ORG/IMPACT

INSIDE THE NEXT FRONTIERS

SLOWING GROWTH
Choking off energy supplies and derailing metabolism in malignant cells are promising and novel strategies for treating cancer. OSUCCC – James researchers are learning how cancer cells metabolize amino acids and glucose differently to survive and to make the molecules needed for rapid cell division and tumor growth. Their work is identifying potential new therapeutic targets for treating currently intractable cancers such as glioblastoma.