Pedaling Research

No matter how you spin it, our Pelotonia bicycle tour has hit the big time by becoming, in just four years, the nation’s largest single-event biking fundraiser as measured by riders.

Pelotonia 12 drew 6,212 riders from 43 states and three countries, as well as 3,141 virtual riders. Collectively these individuals, along with more than 80,000 donors, raised nearly $16.9 million to bring our four-year fundraising total to more than $42 million for cancer research at The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James).

That sounds extraordinary, but it’s exactly the kind of financial support that we must generate to bridge the funding gap we face amid ever-dwindling government allocations for cancer research, which ultimately holds the keys to curing this disease in its many forms. And thanks to Pelotonia’s generous underwriters, every cent raised by riders and donors goes directly to cancer research at Ohio State.

Funds from the 2012 Pelotonia have not been totally allocated, but in this special issue of Frontiers – devoted entirely to our still-young cycling extravaganza – we recap the 2012 event (page 4) and summarize how revenue raised by Pelotonia has been devoted to such areas as student fellowships for cancer research, Idea Grants to teams of faculty cancer researchers, purchases of sophisticated equipment for use by our researchers, and the recruitment and retention of brilliant cancer scientists to our faculty (page 5).

We also offer: closer looks at a few of the students and faculty who have received Pelotonia allocations and the important work that those dollars are supporting (pages 6-11); an “Ideas to Impact” story showing two examples of how projects supported by Pelotonia are already helping to reduce cancer risk in the community (pages 12-13); a story about two innovative, Pelotonia-supported clinical trials that are generating new hope (pages 14-15); a profile of a cancer survivor who rides in and also leads a rider group in Pelotonia (page 16); and a glimpse at gene sequencing technology purchased with Pelotonia funds and the impact it will have on cancer treatment (pages 17-18).

This issue closes with biosketches of gifted scientists who have joined our faculty in the past year or so with the help of Pelotonia money, and information about how to register as a rider, donor or volunteer for Pelotonia 13, which will unfold from Aug. 9-11. Please join us if you can. The more riders we have, the more money we will raise toward a cancer-free world.
BOOSTING BRILLIANCE
Pelotonia Fellowships sponsor young cancer researchers.

GIVING TRACTION TO GOOD THINKING
Pelotonia funds help bright ideas become breakthroughs.

FROM IDEAS TO IMPACT
Two examples of discovery and promise show how Pelotonia dollars are making a difference.

CLINICAL RESEARCH
NEW HOPE FROM THE CLINIC AND RESEARCH LABORATORY
Pelotonia funds support clinical and translational research with the goal of improving cancer care.

SURVIVOR/RIDER
CANCER SURGEON & SURVIVOR SET TO CYCLE IN HER FOURTH CONSECUTIVE PELOTONIA

EQUIPMENT UPGRADE
TECHNOLOGICAL ADVANCES MAKE GENOME SEQUENCING MORE EFFICIENT AND FASTER

BRINGING THE BEST TO OHIO STATE
Money raised by Pelotonia riders and donors has been committed to recruiting and retaining some of the brightest minds in cancer research to Ohio State.
Riders, virtual riders and donors in Pelotonia 12, the annual grassroots bicycle tour that generates money for cancer research at the OSUCCC – James, raised a record $16,871,403, a 28-percent increase over the Pelotonia 11 total of $13.1 million.

The Pelotonia 12 tally brought the four-year fundraising total for Pelotonia, which began in 2009, to more than $42 million. Pelotonia 12 drew a record 6,212 riders from 43 states and three countries, as well as 3,141 virtual riders and more than 2,000 volunteers. The riders were supported by more than 80,000 donors.

The routes for Pelotonia 13, scheduled for Aug. 9-11, will be virtually the same as they were for Pelotonia 12.

Measured by riders, Pelotonia 12 became the nation’s largest single-event biking fundraiser. Among the riders were a record 1,635 members of Team Buckeye, the official superpeloton (riding group) of The Ohio State University – a team that included 1,198 riders, 336 virtual riders and 101 volunteers. Team Buckeye comprised 84 pelotons that collectively raised more than $2.1 million of the Pelotonia 12 total.

Thanks to the event’s generous sponsors – Huntington Bank, Limited Brands Foundation, Richard and Peggy Santulli, American Electric Power Foundation, Nationwide Insurance, Cardinal Health Foundation, JP Morgan Chase and The Scotts Miracle-Gro Company – Pelotonia can direct every dollar raised by riders, virtual riders and donors to the OSUCCC – James for cancer research.
Pelotonia Financial Summary

In its first four years, Pelotonia has generated more than $42 million for cancer research at the OSUCCC – James through rider pledges and donations. Each of the bicycle tour’s first four years saw an increase in riders, volunteers and dollars raised: 2009 – 2,250 riders, 1,200 volunteers, $4.5 million; 2010 – 4,047 riders, 1,600 volunteers, $7.8 million; 2011 – 4,986 riders, 1,700 volunteers, $13.1 million; 2012 – 6,212 riders, 2,000 volunteers, $16.9 million. Thanks to the event’s generous underwriters, every dollar raised by riders and donors has been or will be committed to research-related expenditures. Funds raised in Pelotonia 12 have not yet been totally allocated. The chart shown to the left reflects funding allocations from Pelotonia 09, 10 and 11.

INVESTING IN THE NEXT GENERATION:
PELOTONIA FELLOWSHIP PROGRAM

To date, $5 million has been allocated to the Pelotonia Fellowship Program, which provides research money for Ohio State students at all levels of scholarship – undergraduate, graduate, medical school and postdoctoral fellows – who want to conduct cancer research in the labs of faculty mentors.

SPANNING THE UNIVERSITY

Pelotonia fellowship recipients may be from any discipline of study. Students from eight colleges and 38 departments at Ohio State have received fellowships funded by money raised in Pelotonia. The above chart shows a breakdown of colleges receiving fellowship grants.
In today’s economy, students with bright ideas for cancer research have virtually no hope of obtaining government grants to support their work.

OSUCCC Director and James CEO Michael A. Caligiuri, MD, says this could discourage the next generation of great scientists from pursuing careers in cancer research that could lead to cures.

But the Pelotonia Fellowship Program gives Ohio State students at all levels of scholarship a chance to start their projects in the labs of faculty mentors.

Administrative Director Jeff Mason says $5 million in Pelotonia funds has been committed to date to the program, which has awarded 173 grants to 74 undergrads, 44 graduate students and three medical students, as well as 10 international scholars and 42 postdoctoral fellows from around the world.

The grants go to students in any discipline who want to conduct cancer research under the guidance of an Ohio State faculty mentor.

Grants are awarded by a faculty committee chaired by Gustavo Leone, PhD, associate director for basic research at the OSUCCC – James. Awards are based on each applicant’s strengths and research potential, the mentor’s qualifications and training record, and the potential impact of the project.

Leone is impressed by the program’s track record. “I’m particularly inspired by how many accomplishments our Pelotonia Fellows have had in such a short time,” he says. “They are making discoveries, publishing their work, receiving larger awards and moving on to productive careers in research. It’s amazing how much they can accomplish at such a young age when given the right tools.”

Here are profiles of three Pelotonia fellowship recipients – an undergraduate, a graduate and a postdoctoral fellow.

**TAYLOR BROOKS**

Earning a Pelotonia fellowship enabled Taylor Brooks, a senior in Molecular Genetics, to leave his part-time job and devote that time to research that may translate to immunological therapeutic strategies for pancreatic cancer.

“My experiments focus on pancreatic cancer due to its poor prognosis, with less than five percent of patients surviving longer than five years,” says Brooks, who works in the lab of William Carson III, MD, associate director for clinical research at the OSUCCC – James.

Brooks says one possible cause of poor outcomes is the inhibition of the body’s natural immune response by an overabundance of myeloid-derived suppressor cells (MDSCs).

“MDSCs constitute less than five percent of circulating cells in healthy individuals but are increased in blood, lymph nodes and tumors of patients with pancreatic cancer,” he says, explaining that these cells promote cancer spread by inhibiting other cells that would normally destroy tumors.

“Dr. Carson’s team is studying ways to inhibit MDSCs, but it is difficult to obtain enough of these cells to conduct even the most basic experiments,” Brooks says.

Since starting his fellowship, Brooks has employed a cell culture system capable of generating a continuously dividing population of MDSCs. “We are generating these suppressive cells and immortalizing them. Immortalizing MDSCs allows us to study them and understand their role in pancreatic cancer. This may enable researchers to develop drugs that deplete these cells or inhibit their function.”

Brooks, who rode in Pelotonia 12 and plans to ride this year, aspires to attend medical school and pursue a career in oncology and translational research.

He describes his fellowship opportunity as transformative. “I spend time in a lab doing real science that may one day go toward helping a person.”

**KARA KLIEWER**

Some 30 percent of cancer patients in the United States experience cachexia, a severe wasting of body
fat and muscle that indicates poor tolerance to treatment and a higher risk of death.

Kara Kliewer, a graduate student in Ohio State’s Nutrition PhD program, is using her Pelotonia fellowship to study how body fat is lost in cancer and to understand changes in metabolism that occur with this disease. Her mentor is Martha Belury, PhD, of the Molecular Carcinogenesis and Chemoprevention Program at the OSUCCC – James.

“Many researchers studying cachexia focus on mechanisms of wasting within muscle tissue,” Kliewer says. “However, a recent study of cachexia using genetically altered mice showed that inhibiting the breakdown of fat preserved muscle mass.

“This suggested to me that cachexia may originate in fat tissue, that cross-talk between fat and muscle tissue is important to maintaining body mass, and that pharmacological inhibition of fat breakdown may be a therapeutic strategy to ameliorate wasting in some cases of cachexia.”

Kliewer is using an animal model of cancer-induced cachexia to characterize mechanisms of fat loss. She hopes her findings will lead to therapies for treating cachexia and extending survival.

After she earns her PhD, she wants to continue studying fat metabolism as a postdoctoral researcher and later in a government lab or industry.

“I am grateful to have received a Pelotonia fellowship,” says Kliewer, who has ridden in the past two Pelotonia and plans to ride this year. “Studies like mine are often poorly funded by government agencies. But decades of research have shown that weight loss affects survival and tolerance to cancer treatments, so studies like this can help improve patients’ lives.”

YUH-YING YEH, PHD

Although promising therapies are arising for chronic lymphocytic leukemia (CLL), the disease remains incurable as patients eventually develop drug resistance and have no good treatment options.

Yuh-Ying Yeh, PhD, a postdoctoral researcher in the lab of John C. Byrd, MD, director of the Division of Hematology, is using her Pelotonia fellowship to understand a natural process called autophagy as a mechanism of drug resistance in CLL.

Autophagy literally means “to eat the self.” It is a process that cells use during periods of starvation to derive energy by breaking down unneeded or dysfunctional components. It also plays an important role in cell growth and development and helps cells maintain a balanced life.

But Yeh says evidence has shown a link between autophagy and multiple human diseases, including cancer. One of her projects involves studying drug action and resistance of flavopiridol, which is under phase I/II clinical trial development for treating CLL.

“Our data showed that flavopiridol induced autophagy in CLL B cells and that inhibition of autophagy can enhance flavopiridol cytotoxicity in CLL,” Yeh says. “I’m investigating the molecular mechanisms of flavopiridol-activated autophagy to develop therapeutic agents for better clinical outcomes.”

Her work is making an impact.

“Combined with microarray data and molecular biology validation, we have found that an autophagy protein could provide us with a therapeutic target to specific autophagy inhibitors,” Yeh explains. “We also have generated flavopiridol-resistant cell lines to assist our in vitro studies in understanding drug resistance.”

Yeh, a native of Taiwan, says her goal is to become an independent translational researcher either in academia or industrial settings.

She has become more passionate about her research while participating in Pelotonia events, from fundraising to the bike ride itself. “I have met so many people who devote themselves to fighting cancer in different ways, and we all share one goal: to end cancer.”
GIVING TRACTION to Good Thinking

Pelotonia Idea Grants jump-start insightful OSUCCC – James research that can lead to breakthroughs in cancer prevention and treatment.

The grants provide $100,000 of research funding spread over two years. Proposals are selected for funding through a peer-review process that considers the study’s potential for discovery and publication, whether it will lead to a clinical trial and the likelihood of subsequent funding from the National Cancer Institute.

Applicants also provide a “commitment to ridership” stating that they will participate in Pelotonia to help raise money for cancer research at the OSUCCC – James.

Here are three examples of Pelotonia Idea Grants that were awarded in 2012. For information on the remaining 10 projects, visit cancer.osu.edu/pelotonia.

By Darrell E. Ward

Chemotherapy and the Brain

Nearly one-third of breast-cancer patients who receive chemotherapy report problems with memory, concentration, attention and understanding during and after treatment. Sometimes called “chemo brain,” chemotherapy-induced cognitive deficits can also be a problem for patients treated for other malignancies, including ovarian and prostate cancers.

The cause of these cognitive problems is poorly understood, and currently there is no treatment for them. Through a Pelotonia Idea Grant, Maryam Lustberg, MD, assistant professor of Medical Oncology and an OSUCCC – James breast-cancer specialist, and Courtney DeVries, PhD, professor of Neuroscience and Psychology, are investigating both a possible cause and a possible treatment in an animal model.

Lustberg and DeVries have evidence linking the cognitive difficulties to the overactivity of a particular type of immune cell in the brain. They also have identified an anti-inflammatory drug that might calm the overexcited cells and ease the symptoms.

“Our data from an animal model suggests that certain chemotherapy can overactivate brain cells called microglia, and that this contributes to localized inflammation and changes in brain cells,” Lustberg says.

She notes that microglia are involved in neurological disorders such as multiple sclerosis and other neuroinflammatory conditions. “But we believe we are the first to tie them to chemotherapy-induced cognitive deficits,” Lustberg says.

Normally, microglia move through the brain to rid it of damaged neurons, infectious agents and debris from dead cells. “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.

“The Pelotonia funding will help us tease out the biological mechanism,” she 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.”

Having a mechanistic explanation for the problem is essential for developing targeted therapies to treat it, she says. Until then, the Ohio State investigators have evidence that a widely available drug called minocycline might help control the inflammation and calm the overactivated microglia cells.

“The drug minocycline works well in our mouse model,” DeVries says. “With the help of Pelotonia funds, we will further define how it works and the best schedule for administering it.”

The researchers are using experimental conditions that closely mimic the therapy women receive, DeVries says. “We’re using the same chemotherapy drugs and similar doses, and we administer the treatment intravenously. A mouse model is not the same as a (continued on page 10)
Community Enthusiasm Helps Propel Research Couple’s Ride

Jerneja Tomsic, PhD, and her husband Enrico Caserta, PhD, came to Ohio State from Italy in 2005 to work as postdoctoral researchers in Ohio State’s Department of Microbiology. In 2008, they accepted research positions at the OSUCCC – James.

Tomsic, who is originally from Slovenia, works in the laboratory of Albert de la Chapelle, MD, PhD, professor of Medicine and the Leonard J. Immke Jr. and Charlotte L. Immke Chair in Cancer Research, and co-leader of the Molecular Biology and Cancer Genetics Program. She studies genetic factors that predispose people to cancer, particularly colorectal and thyroid cancers.

Her journey to Pelotonia began with the Livestrong Summit at The Ohio State University in summer 2008. “That made me realize how many people are affected by cancer,” she says. “When Pelotonia started in 2009, I had to be a part of it.”

She volunteered the entire weekend at the inaugural event. “I saw the community that came together, and it was an awesome experience,” she says.

She teamed up with a friend the second year and rode 50 miles. In 2011, she signed up for the 100-mile route, but circumstances prevented her from riding, so she volunteered again. In 2012, she tackled the 100-mile ride, and she plans to challenge herself with it again this year.

Riding is an emotional experience, she says. “Yes, you need to train for the ride,” she acknowledges, “but the encouragement of all riders around you, and the people along the road holding signs and cheering you on, carries you through to finish.”

As she rode last year, Tomsic kept in mind two people she’d never met who’d died of cancer and who she’d followed on social networking sites. One was a 12-year-old girl who died in January after a long battle with brain cancer. The other was a young woman who never smoked but died of lung cancer at age 37.

“I knew that the OSUCCC – James had recruited Dr. David Carbone, an important lung cancer scientist, with the help of Pelotonia funds (see page 19),” Tomsic says. “A lot is not known about lung cancer that develops in people who have never smoked.”

Tomsic describes Pelotonia as a “very important” event because it brings badly needed funds to the OSUCCC – James for cancer research, and for the way it brings the community together.

“People who participate include doctors and researchers, but also people who are not in research, people who are battling cancer or have relatives who battled cancer, and people in the community who have never had cancer. We’ve seen it grow from 2,000 riders in 2009 to 6,212 last year, they’re expecting 7,000 this year.”

Tomsic especially enjoys the final day of the event and meeting the people who finish the two-day ride. “I have been meeting the oldest Pelotonia rider, Leland, an 83-year-old rider and his wife He was riding the 180-mile ride, and when they parted, Tomsic told him she would be there to greet him at the end. “We said a kind of goodbye,” she recounted. The next day she was at the finish line.

“He was thrilled to see me, and I was thrilled to see him,” she says.

Enrico Caserta, Tomsic’s husband, got involved in the bike event after seeing Michael A. Caligiuri, MD, director of the Comprehensive Cancer Center and CEO of The James Cancer Hospital and Solove Research Institute, at a Pelotonia celebration.

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Martha at the 180-mile finish every year, and he’s now a good friend,” she says.

While riding in 2012 she met a man who was riding in memory of his brother, who’d died of colon cancer.

“It was an emotional discussion,” Tomsic says.

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Caserta worked as a volunteer during Pelotonia 10, rode 100 miles in Pelotonia 11 and rode 180 miles in Pelotonia 12. He plans to ride 180 miles again in Pelotonia 13.

Caserta is a postdoctoral researcher in the laboratory of Gustavo Leone, PhD, professor of Molecular Virology, Immunology and Medical Genetics, and associate director for basic research at the OSUCCC – James, where he is also a member of the Molecular Biology and Cancer Genetics Program.

In 2010, Caserta received a two-year Pelotonia postdoctoral fellowship to study the role of a gene that protects against the development of cancer in the body. “I am grateful to Pelotonia because that grant was really important for my research,” he says.

Riding in Pelotonia is an extraordinary experience, he says.

“The enthusiasm of the people pushes you forward. You may be out of energy. You may be hungry and thirsty. Then you reach a rest point, and you feel it. It’s also there along the road, and it enables you to keep going.

“That was especially true for me when I rode 100 miles for the first time in Pelotonia 11. I was exhausted, but when I got to the finish line and there was this row of people cheering, I got emotional. It was something. It was really something.”
human, but we believe it is a good model that will be useful for testing additional agents for this problem.”

Next, the researchers want to evaluate minocycline in a clinical trial of women with breast cancer. “We could do this relatively quickly because this drug is already approved by the Food and Drug Administration and is available,” Lustberg says.

**BLACK RASPBERRY CONFECTIONS TO INHIBIT ORAL CANCER**

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 42,250 Americans were expected to develop cancer of the mouth, and 7,850 were expected to die of the disease. The malignancy’s 50-percent five-year survival rate has remained largely unchanged for decades, so new ways to prevent and treat the disease are needed.

A Pelotonia Idea Grant awarded to Yael Vodovotz, PhD, professor of Food Science and Technology, and a multidisciplinary team of OSUCCC – James researchers might help meet both needs.

The scientists are developing a food-based approach for preventing oral cancer in people at high risk for the disease and for improving the treatment for people who have the disease. Their study uses highly concentrated black raspberries, which research has shown have significant anticancer activity.

The team’s Pelotonia grant will support a two-week clinical trial of 60 healthy adult volunteers who will consume black raspberry confections at two doses and in three forms. One form resembles a hard candy and releases the phytochemicals slowly; the other two forms have gummy consistencies that provide intermediate and fast release rates.

“The confections are a way to incorporate a substantial amount of black raspberry phytochemicals into the diet in a more directed way,” Vodovotz says.

The study will show which form most effectively releases the berries’ natural cancer-fighting phytochemicals into the mouth. To learn that, the researchers will take mouth swabs from each participant before, during and after the trial. This collects mouth cells that will be analyzed for certain phytochemicals or their metabolites and for the activation of certain genes.

Research by team member Christopher Weghorst, PhD, has found that black raspberry phytochemicals turn up the activity of certain genes and turn down the activity of others. “His evidence suggests that changes in these genes might improve the effectiveness of therapy for these cancers,” Vodovotz says.

The study should also reveal whether the phytochemicals are taken up better when released in the mouth slowly or quickly as a burst.

Team member Steven Schwartz, PhD, director of the OSUCCC – James Nutrient and Phytochemical Analytics Shared Resource, will oversee analysis of the biological samples, which include urine samples that are examined in part to monitor consumption levels of the confections by trial participants.

In the end, the phytochemical absorption information and gene expression data will determine which dose and form of confection best deliver the anticancer agents in black raspberries to cells that line the mouth. That knowledge, in turn, will guide the design of a future phase II study in people at high risk for oral cancer. That study will evaluate whether the confections can prevent oral cancer or improve therapy in cancer patients.

“This crops-to-clinic initiative is a marriage of food science and medicine,” Vodovotz says. “To my knowledge, our collaborative team is unique in the way we approach functional food to fight cancer, and Pelotonia will have played an important role in making it happen.”

Other OSUCCC – James investigators involved in this study are Steven Clinton, MD, PhD, and Dennis Pearl, PhD.

**TARGETING MICRO MESSENGERS**

Multiple myeloma (MM) is currently an incurable cancer of the blood that affects 21,700 people in the United States and kills about 10,700 Americans annually. The malignant cells survive and grow in part by triggering the release of growth factors and other substances from normal cells in the bone marrow.

How the cancer cells cause the normal cells to release those factors isn’t understood, but OSUCCC – James researchers Don Benson, MD, PhD, and Flavia Pichiorri, PhD, have evidence that an unusual mechanism is involved, and they have been awarded a Pelotonia Idea Grant to pursue their suspicions. If they are correct, it would lead to a better understanding of the disease and perhaps to new ways to diagnose and treat it.

Their evidence indicates that myeloma cells shed tiny spheres called microvesicles into the blood. The spheres are packed with regulatory molecules called microRNA. Bone marrow cells take up the spheres and respond to the regulatory molecules by producing factors that help the cancer cells grow and proliferate. In addition, the spheres influence the behavior of immune cells called natural killer cells.
“It was first believed that microvesicles were bits of cell membrane or pieces of dead cells floating around in the bloodstream,” Pichiorri says. “Then we looked at them more closely in blood from myeloma patients and found that they contain a rich repertoire of signals that other cells can take up.”

Preliminary work by the investigators has shown that MM microvesicles include microRNAs that can influence cancer development and immune responses.

“Microvesicles have been reported in a number of cancers, but MM seems to make a lot of microvesicles relative to other cancers, and they are jam-packed with potential cell signals,” Benson says.

Their Pelotonia-funded research will analyze the contents of microvesicles from MM patients and explore how the vesicles might communicate with other cells and whether the vesicles help suppress the body’s immune response to the disease.

The findings could lead to a novel form of therapy.

“If we knew more about how microvesicles facilitate the disease, we might make synthetic microvesicles and pack them with signals that help control the disease,” Benson says.

The project is emblematic of the concept behind Idea Grants: a neat idea that no one has yet explored very deeply. “If what we expect is true, it will put us in a competitive position for obtaining larger grants,” Benson says. “It’s high-risk and high-reward research. It’s the kind of idea that would be sitting on the shelf without the Idea Grant mechanism.”

**Riding for the HEALTH of it**

**Joel Mayerson, MD,** director of Musculoskeletal Oncology at the OSUCCC – James, had ridden a bike as a teenager, and every so often after that. He made the decision to ride when the first Pelotonia ride was announced in 2009. “I got out the mountain bike that I’d had as a teenager and rode the 50-mile route,” Mayerson says.

“It was fantastic being out there and seeing colleagues, staff and even patients riding,” he says. But Mayerson is a big guy, and he was bigger then, weighing some 325 lbs. “I completed the 50 miles, but I about died. It was really challenging.”

Mayerson had another reason for getting his bike out and riding, too. His son, Drew, 13, had been diagnosed with type 1 diabetes earlier that year. “I wanted to set a good example for him,” Mayerson says.

He resolved to get into shape. He went on a low-carbohydrate diet, and, after trading his mountain bike for a hybrid model, he began training and trimming down for his son and for Pelotonia 2010.

He rode about 1,500 miles in training rides and lost 80 pounds. The 50-mile Pelotonia route was no problem in 2010. He also organized a sarcoma peloton, or riding group, of four or five people.

Looking ahead to Pelotonia 11, he set out to tackle the 100-mile ride. He clocked about 3,000 miles in training rides in preparation. When the time came, he succeeded with little problem and repeated the ride for Pelotonia 12.

But his 2011 century ride was especially memorable, Mayerson says. “It was fantastic. It was the first time in my life I’d ridden a hundred miles. I was 42 years old, I’d trained for it, and I kept up with my partner who was eight years younger.” His sarcoma peloton had grown to 18 members and included two patients and a cancer survivor.

The community support was energizing, he says. “The ride is amazing. Sixty and seventy miles out, you pass people along the road with signs that say things like ‘Thanks for riding’ and ‘Thanks for making a difference.’

“It’s a six-and-a-half or seven-hour ride, and when you’re tired, it’s pretty cool to see those signs and the people cheering you on.”

Pelotonia is meaningful in many ways for Mayerson.

From a personal standpoint, it helped him adopt a healthy lifestyle. “I’ve ridden close to 8,000 miles since I began training,” he says. “It’s gotten many people involved in a healthier lifestyle and gotten corporations involved in getting their employees out and exercising.”

And it brings the community together to fight cancer. “One of every two or three of us is going to get cancer. Pelotonia raises cancer awareness – thousands of people may have learned about sarcoma who otherwise might not have – and it raises dollars to cure cancer so that maybe someday we won’t have to worry about it.”

It’s good for the city’s economy, he says, and it raises awareness about the city of Columbus. “People who pass through Port Columbus see the Pelotonia banners and want to know more about it. They will learn something about the city that might bring them back.”

Even the word “Pelotonia” stirs curiosity. “I’ve worn my Pelotonia shirt to scientific meetings in San Francisco and elsewhere, and I can be at Starbucks and someone will ask me what it means. It’s an interesting word,” he says.

“I think what’s most amazing is the community spirit that in four years has created the largest charity bicycle event in terms of riders in the United States. We’ve gone from 2,250 riders to 6,200 riders in four short years. It shows how wonderful our community is.”
From Ideas to Impact

The impact of Pelotonia dollars is realized most dramatically in discoveries made by teams of researchers funded through this event. Here are two examples of impact, discovery and promise.

BY BOB HECKER

STATEWIDE SCREENING INITIATIVE HAS LIFE-SAVING POTENTIAL

Pelotonia funds have helped the OSUCCC – James launch a statewide initiative to screen newly diagnosed colorectal cancer (CRC) patients and their biological relatives for Lynch syndrome (LS), a major cause of inherited colorectal, ovarian and uterine cancer. The effort will reveal others who may be at risk of developing these cancers so they can take precautionary measures.

The Ohio Colorectal Cancer Prevention Initiative (OCCPI) is led by Heather Hampel, MS, CGC, associate director of the Division of Human Genetics. Hampel says that about 3 percent of CRC cases result from Lynch syndrome, which is characterized by inherited mutations in one of four genes for DNA-repair proteins. Each CRC patient with LS has, on average, three relatives with the syndrome, heightening their risk for CRC.

Based in large part on research conducted at the OSUCCC – James from 1999-2008, the Centers for Disease Control and Prevention recommends that all newly diagnosed CRC patients be screened for LS. The OSUCCC – James has done this since 2006 to help reduce morbidity and mortality in CRC patients and their at-risk relatives, who can also be screened and advised of increased surveillance methods if they too are found to have LS.

The OCCPI includes 42 hospitals from throughout Ohio that will implement the LS screening program at their own institutions. Partner hospitals will advise patients and their physicians of the results, offer genetic counseling and make high-risk cancer surveillance recommendations to patients and family members found to have LS.

“If you find people with LS before they get cancer, you have the potential to really save lives,” Hampel says. LS patients can take precautionary measures by having colonoscopies earlier and more frequently, starting at age 20 to 25 and performed every one to two years so precancerous polyps can be detected and removed, or so that cancer can be detected in an early stage when it is more treatable.

And to prevent ovarian and uterine cancers, she adds, women with LS may choose to have an oophorectomy and hysterectomy once they are finished having children.

“If you find people with LS before they get cancer, you have the potential to really save lives.”
“An obesogenic environment promotes obesity by encouraging physical inactivity and limiting healthy food choices.”

ELECTRA PASKETT, PHD, MSPH  
associate director for population sciences

FAITH-BASED FIGHT TO REDUCE OBESITY SPANS FIVE APPALACHIAN STATES

A transdisciplinary health-disparities team led by Ohio State and supported in part by Pelotonia dollars is partnering with churches in a five-state region to refine and test a previously piloted faith-based intervention program to promote health and reduce cancer risk by addressing obesity.

Electra Paskett, PhD, MSPH, associate director for population sciences at the OSUCCC – James, where she also leads the Cancer Control Program, is principal investigator for the project, which is the research component of the larger Appalachian Community Cancer Project (ACCN) funded at $6.13 million over five years by the National Cancer Institute (NCI) – including $2.7 million for the research component.

The intervention uses community-based participatory research strategies aimed at two behavioral causes of obesity: sedentary lifestyle and unhealthy diet. The target region is mainly rural and contains medically underserved populations characterized by low income, education deficits, poor health, increased rates of obesity and high cancer incidence.

“An obesogenic environment promotes obesity by encouraging physical inactivity and limiting healthy food choices,” Paskett says. “This project is testing a faith-based intervention in 10-15 churches compared with a program in 10-15 additional churches where participants will receive only information and cancer-screening tests.”

Participants in the intervention churches receive help in increasing physical activity and consuming healthier foods, including more fruits and vegetables daily.

Paskett says part of the intervention also involves a two-year e-health computer program that tracks the number of steps taken per day by participants and gives them tailored messages about increasing physical activity and changing their diets. The e-health program is supported by a $100,000 Pelotonia Idea Grant – money allocated to teams of scientists who need funds to start working on innovative ideas that may initially have difficulty getting funds elsewhere. Paskett says the Idea Grant “helped us secure NCI funding to do the whole research study in the 20-30 churches throughout the ACCN region.” The full-scale study is under way.

“We believe this project is having an immediate impact among members of the churches that are involved with the intervention,” Paskett says. “These successful strategies could be used to improve the health of residents throughout Appalachia in the future.”
New Hope
From the Clinic and Research Laboratory

Pelotonia funds support clinical and translational research with the goal of improving cancer care

BY DARRELL E. WARD

“A clinical research” is research that involves patients, and it usually refers to clinical trials. “Translational research” encompasses studies that use genes, cells, and animal models to solve problems related to medical treatment. The two types of investigation are closely linked: The ultimate goal of translational research is to apply the findings to humans in a clinical trial.

Pelotonia funds support both clinical and translational studies at the OSUCCC – James. We present an example of each below. The first is a clinical trial proposed by an OSUCCC – James physician researcher to evaluate a new drug for chronic lymphocytic leukemia (CLL). CLL is the most common form of leukemia in the nation, with about 15,000 new cases and 4,400 deaths occurring annually. It is currently incurable.

Second is an example of translational science by OSUCCC – James researchers working to improve the treatment of tamoxifen-resistant breast cancer.

A CLINICAL TRIAL THAT MET TWO NEEDS

Ibrutinib is an experimental drug that works by inhibiting a chemical pathway that CLL cells need to survive. The drug was tested in phase I and phase II clinical trials at Ohio State and a few other centers with exciting results.

“Early ibrutinib trials indicated that the agent was highly active in CLL and well-tolerated by patients, with many durable responses and few serious side effects,” says Kami Maddocks, MD, assistant professor in the Division of Hematology and a CLL specialist.

The success of the early trials prompted Pharmacycics, Inc., the biopharmaceutical company that developed the drug, to plan a phase III trial, which is needed for the drug to earn approval by the U.S. Food and Drug Administration.

Between the close of the early trials and the start of the phase III trial, however, the drug would be unavailable to those relapsed CLL patients. To cover that period, Maddocks proposed a new phase II trial to answer an important question while also making ibrutinib available to more patients.

Maddocks worked with OSUCCC – James CLL specialist John C. Byrd, MD, director of the Division of Hematology, professor of Medicine, Medicinal Chemistry and Veterinary Biosciences, and the D. Warren Brown Designated Chair in Leukemia Research.

The new trial focused on patients with a particular cytogenetic abnormality in their CLL cells. Patients with this “17p deletion” don’t respond well to standard treatment. They have shorter remissions and a decreased survival. Maddocks’ trial would compare CLL patients with the deletion to patients without it.

“The company generously agreed to provide the drug for this trial, but we had to provide the funding for the trial,” Maddocks says. “That’s where the Pelotonia funds came in. They made this trial possible.”

Her trial – A Phase 2 Study of the Bruton’s Tyrosine Kinase Inhibitor, PCI-32765, in Relapsed and Refractory Patients with Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma and B-cell Prolymphocytic Leukemia – opened in May 2012. By March 2013, it had accrued 67 of the target 68 participants.

“This trial gave almost 70 more patients, many without any other treatment options, access to a drug that’s been very effective and that otherwise would not have been available during that time frame,” Maddocks says.

“Clearly, along with the important data it will provide, this trial has made a huge difference in the lives of several patients by making this drug available to them,” she says, “and Pelotonia funds played a huge part in our ability to open that trial here.”
Breast cancer was expected to strike some 230,000 women in the United States in 2012 and to kill almost 40,000 of them. More than two-thirds of breast cancer cases show high levels of the estrogen receptor (ER).

Doctors treat these ER-positive tumors in part using the drug tamoxifen. “Tamoxifen has improved the disease-free survival of people with ER-positive breast cancer by 50 percent,” says OSUCCC – James breast cancer specialist and medical oncologist Bhuvana Ramaswamy, MD, “but 30 to 40 percent of patients who take tamoxifen become resistant to it after about five years.

“Currently, treatment options for patients with tamoxifen-resistant breast cancer are very limited, and most end up receiving chemotherapy, which can have significant side effects,” she says. But Pelotonia funds are supporting work by Ramaswamy and collaborator Sarmila Majumder, PhD, research assistant professor in the Department of Molecular and Cellular Biochemistry at Ohio State, to better understand tamoxifen-resistant breast cancers and to develop targeted therapies that effectively treat them.

In 2012, Ramaswamy, Majumder and a group of colleagues published findings in the journal Cancer Research showing how tamoxifen-resistant breast-cancer cells grow and proliferate. They also identified an experimental agent that might offer a new therapy for these tumors.

Cells transmit signals from the outside world to the inside of the cell using biochemical pathways. When estrogen contacts an ER-positive cancer cell, it activates a particular pathway that causes the cells to proliferate.

Majumder and Ramaswamy discovered that when tamoxifen shuts down the pathway activated by estrogen, a different pathway, called hedgehog (Hhg), takes over. When the Hhg pathway turns on, tamoxifen therapy stops working, and the tumor grows in spite of it. Another signaling pathway, called PI3K/AKT, is also involved.

By analyzing more than 300 human tumors, the researchers also learned that patients with an active Hhg pathway in their tumor cells had worse outcomes.

Finally, Majumder, Ramaswamy and colleagues showed that an experimental drug called vismodegib, which blocks the Hhg pathway, inhibits the growth of tamoxifen-resistant human breast tumors in an animal model. The drug is in clinical trials testing for other types of cancer.

“Using this drug to target the hedgehog pathway alone or in combination with the PI3K/AKT pathway could be a novel therapeutic option for treating tamoxifen-resistant breast cancer,” says Majumder.

With this body of laboratory and animal evidence in hand, Ramaswamy and Majumder are preparing to complete the translational-research circle. “We now want to organize a clinical trial to evaluate vismodegib in patients with tamoxifen-resistant breast cancer,” Ramaswamy says.

The researchers are working with the National Cancer Institute (NCI) to design a clinical trial using the hedgehog inhibitor in patients with tumors resistant to hormone therapies such as tamoxifen, aromatase inhibitors and faslodex.

“Pelotonia funding helped support many of our laboratory and preclinical studies,” Ramaswamy notes. “Now we are using Pelotonia funds to study this target in triple-negative breast cancer (TNBC).” TNBC typically strikes younger women and has few treatment options and poor outcomes.

“Pelotonia support has been crucial in helping us understand this potential therapy, first in estrogen-resistant patients, and now Pelotonia funds are helping us obtain the data and translate the findings for a clinical trial in triple-negative breast cancer.”
Cancer Surgeon & Survivor Set to Cycle In Her Fourth Consecutive Pelotonia

BY BOB HECKER

If preparing to take her surgical recertification board exam in late 2009 weren't stressful enough for Doreen Agnese, MD, she now had a lump on her neck.

Her primary care doctor found it when Agnese, a surgical oncologist and clinical geneticist at the OSUCCC – James, was having a routine physical. An endocrinologist later biopsied it. While awaiting the results, Agnese managed to pass her exam.

Almost immediately afterward, she learned that she had papillary thyroid cancer. In January 2010 she had surgery at the OSUCCC – James to remove the tumor, which fortunately had been detected before spreading to her lymph nodes.

Her surgery was followed by radioactive iodine therapy that lasted about a week and had mild but lingering effects on her voice and sense of taste. But Agnese, whose clinical specialties include breast cancer, melanoma and general surgery, is not complaining.

"It was a weird time with a strange mix of feelings for me," she recalls. "I felt sad and concerned about my cancer diagnosis, but I also felt 'survivor guilt' because so many of my patients have worse prognoses and more severe side effects from treatment."

Agnese remains cancer-free, but like other survivors she faces the fear of recurrence. Her determination to quell that, and all other cancer fears, propels her participation in Pelotonia.

"I want to help take the power out of the words, 'You have cancer,'" she says. "When people get into a car, they don't usually wonder if they're going to die in a crash. But when they hear that they have cancer, dying is a sudden concern."

"It would be so nice to find cures for the many forms of cancer so that we could at the least manage them like a chronic illness," Agnese adds. "We've made a lot of strides, but people still die of their cancers. Only through continued research will we find cures, but with government money for research dwindling, we need other ways to fund it."

Like Pelotonia. She worked as a volunteer for the inaugural event in 2009 (before her diagnosis), but she has ridden 50 miles in each of the three subsequent Pelotonias and will do it again in Pelotonia 13. Her participation has required rigorous training.

"I rode bikes as a kid back in New Jersey, but I hadn't ridden much at all since then," Agnese says. "Preparing to ride was a major ordeal. For a non-athlete like myself, the couch is always calling. I come from a long line of couch potatoes."

But she thinks the work, both training and fundraising, is worth it. She is the captain of the OSU Surgical Oncology Peloton, a riding group that is part of Team Buckeye, Ohio State's official superpeloton.

"Pelotonia is a great community event that brings thousands of people together for a common cause that benefits everyone by funding cancer research," Agnese says. "And since I'm so busy clinically and as an educator that I can't do the lab research myself, I feel this is a way I can contribute to that too."
Cancer is a disease written in code. That code is represented by four letters – A, C, G and T – with each letter corresponding to one of the four building blocks of DNA. The sequence of these four DNA building blocks, called bases, encodes our genetic information.

Changes in that sequence in individual cells can, over time, cause cells to become cancerous. Rather than dying as they should, the damaged cells live on, proliferate and form tumors. Finally, they acquire the ability to migrate to other organs, where they form metastatic tumors.

Understanding the DNA changes that cause cells to become cancerous is critical for developing new and more effective therapies, overcoming treatment resistance and discovering prognostic biomarkers.

DNA sequencing is a vital technology for identifying the gene changes that occur in cancer cells, and Pelotonia funding has enabled The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James) to keep pace with important advances in sequencing technology.

The human genome is made up of three billion base pairs divided into 23 chromosomes. Each is a ribbon of bases. The longest of these, chromosome 1, is a string of 246 million base pairs; the shortest, the Y chromosome, has 50 million base pairs. The task of gene sequencing is to identify each base in the chain in the order in which it occurs.

The Human Genome Project used gene sequencing to identify all of the 3 billion bases in the normal human genome. The project ended in 2003, lasted 13 years and involved 18 countries. The sequencing alone cost $400 million.

In 2012, Pelotonia funds enabled the OSUCCC – James to upgrade to a second-generation gene sequencer called the HiSeq 2000 from an older, slower predecessor, the GenomeAnalyzer IIA. This year, Pelotonia funding is permitting the upgrade of that system to the HiSeq 2500.

“Pelotonia funding has allowed us to keep up with the latest technology and to democratize high-throughput sequencing by lowering the sequencing cost.”

PEARLLY YAN, PHD, technical director of the next-generation sequencing core
“The robot runs nonstop and can prepare up to 96 samples at once. . . It is not fast, but it is precise and reproducible. And it leaves personnel free to do other things.”

“Pelotonia funding has allowed us to keep up with the latest technology and to democratize high-throughput sequencing by lowering the sequencing cost,” says Pearly Yan, PhD, technical director of the OSUCCC – next-generation sequencing core. “It also provides options for longer runs and fast turnaround time when they are needed.”

For example, the HiSeq 2500 can operate in regular or in fast mode. In regular mode, the technology can sequence five to six human genomes in about 11 days at 30-fold coverage (a measure of sequencing depth to increase confidence in identifying base alterations), much like the HiSeq 2000. In fast mode, the machine can sequence one human genome in 27 hours at that coverage.

“The upgrade gives us the option to run samples fast, such as the sequencing of clinical samples that need timely results,” Yan says. “The upgrade enables the sequencer to read longer DNA fragments, collecting up to 300 base pairs of data right after the upgrade and 500 base pairs of data in the near future. This is really powerful,” Yan says.

Longer reads during sequencing are important for identifying features such as gene insertions and deletions or major chromosomal changes, but longer reads require more reagent and instrument time, so they are more expensive.

Preparing samples for sequencing is called making DNA or RNA “libraries,” and it is a laborious, time-consuming task when done manually. It involves turning DNA or RNA (which is first converted into DNA) collected from a research model or a patient sample into high-quality DNA fragments that can be sequenced.

Pelotonia funding enabled the OSUCCC – James to purchase a robotic device, called a SciClone, to automate the preparation of DNA libraries for larger sequencing projects, such as transcriptome or exome sequencing or whole genomes.

“The robot runs nonstop and can prepare up to 96 samples at once,” Yan says. “It is not fast, but it is precise and reproducible. And it leaves personnel free to do other things.

“The robotic system enables us to generate DNA libraries efficiently and reproducibly, and with the HiSeq upgrade, we can produce highly consistent data faster. It truly speaks highly of the importance of Pelotonia funding to OSUCCC – James research.”
Bringing the Best to Ohio State

Money raised by Pelotonia riders and donors has been committed to recruiting and retaining some of the brightest minds in cancer research to Ohio State. Among those recently recruited with the help of Pelotonia dollars are:

**DAVID CARBONE, MD, PhD**, an internationally renowned lung cancer specialist recruited from Vanderbilt University to establish and lead a thoracic oncology center at the OSUCCC – James. Carbone is an expert in the molecular biology of lung tumors, which includes understanding the genetic, proteomic and metabolic features of each patient's cancer and developing drugs to optimally target tumors.

**PAUL GOODFELLOW, PhD**, professor of Obstetrics and Gynecology. Goodfellow was recruited from Siteman Cancer Center, Barnes Jewish Hospital, at Washington University School of Medicine in St. Louis. His research focuses on identifying and characterizing genetic events important in tumor initiation and progression, and on understanding molecular events that can help develop approaches to preventing and treating uterine and breast cancers.

**SAMEEK ROYCHOWDHURY, MD, PhD**, a specialist in genomics and tumor sequencing whose research focuses on personalized approaches to patient treatment through genomics. He was recruited from the University of Michigan as an assistant professor in Ohio State's Department of Internal Medicine, Division of Medical Oncology, and in the School of Biomedical Science, Department of Pharmacology.

**THEODORE BRASKY, PhD**, recruited from Fred Hutchinson Cancer Research Center as an assistant professor in Ohio State’s Department of Internal Medicine, Division of Cancer Prevention and Control. Brasky works to better understand the association of inflammation and cancer by studying substances and genes hypothesized to affect inflammation. He also studies non-steroidal anti-inflammatory drugs and cancer risk.

**NICHOLAS DENKO, MD, PhD**, associate professor in the Department of Radiation Oncology. Recruited from Stanford University, Denko studies how stressors within the tumor microenvironment can influence tumor cell progression and the response of solid tumors to therapeutic interventions. He currently is investigating the role of reduced oxygen and nutrient stress on gene expression and cellular metabolism.

**JOHN HAYS, MD, PhD**, recruited from the National Cancer Institute (NCI) as an assistant professor in Ohio State’s Department of Internal Medicine, Division of Medical Oncology. His work furthers the understanding of protein-signaling networks and how they can guide the design of personalized therapies for cancer patients. His clinical interests include drug development for gynecologic cancers and rare gastrointestinal malignancies.

**JAY HOLlick, PhD**, associate professor in the College of Arts and Sciences, Department of Molecular Genetics. Recruited from the University of California at Berkeley, Hollick is interested in biological mechanisms that generate and maintain inherited genetic variations in physical and other traits. These studies shed light on chromosome evolution and gene function.

**THOMAS LUDWIG, PhD**, associate professor in the Department of Molecular and Cellular Biochemistry. Ludwig was recruited from the Institute of Cancer Genetics at Columbia University in New York City. He studies biological functions of the BRCA1 and BRCA2 tumor-suppressor genes and some of their interacting partners in normal and malignant development. Mutations in these genes predispose carriers to certain cancers.

**SUSAN OLIVO-MARSTON, PhD, MPH**, recruited from the NCI as assistant professor of Epidemiology in Ohio State’s College of Public Health. She is interested in how early-life conditions such as obesity and asthma, and exposure to second-hand smoke, may affect adult cancer risk, and which biological pathways are involved.
Registration Open for PELOTONIA 13

Anyone wanting to participate in Pelotonia 13 as a rider, virtual rider or volunteer should visit [http://pelotonia.org/register](http://pelotonia.org/register) and sign up for this year’s tour, to be held Aug. 9-11. Riders may choose from among routes of varying distances, with the longest extending from Columbus to Gambier, Ohio – home to Kenyon College. There also will be second-day return routes for those who wish to ride even farther.

The Pelotonia website above offers details and online forms for registering as an adult (16 or older), as a minor (those of age 14 or 15 may ride the 25- or 50-mile routes), as a virtual rider or as a volunteer. Riders must agree to raise the amount of funds specified for their chosen route. Thanks to generous event sponsors, all money raised by riders, virtual riders and donors will go directly to cancer research at the OSUCCC – James.

Pelotonia 12 attracted 6,212 riders from 43 states and three countries, as well as 3,141 virtual riders and more than 2,000 volunteers. The event raised a record $16.87 million, bringing the four-year total for Pelotonia to more than $42 million. Questions? Contact Karl Koon, director of development/Pelotonia at the OSUCCC – James, at karl.koon@osumc.edu.

Apply Now for Pelotonia Post-Doc Fellowships

The Pelotonia Fellowship Program at Ohio State provides two-year research fellowships to promising postdoctoral candidates from any discipline – from the traditional sciences to such fields as history, business, engineering and humanities – who want to help cure cancer. These fellowships pay a competitive annual stipend based on National Institutes of Health (NIH) guidelines for postdoctoral fellows. Applications are scored on:

- Applicant strengths and research potential (emphasis is given to clinical fellows and to applicants who received their doctorate within the past year and will be new to Ohio State, or who have been at the University less than one year, and who have the potential to become independent scientists);
- Mentor/adviser qualifications and training record;
- Innovativeness and impact of the project on cancer research.

Applications are due three times per year. For more information, including eligibility guidelines and an application, visit [http://cancer.osu.edu/go/pelotoniafellowship](http://cancer.osu.edu/go/pelotoniafellowship) or send an email to Jeffrey.Mason@osumc.edu.

MELANOMA RESEARCH AND CARE

Under the leadership of medical oncologist Kari Kendra, MD, PhD, the expanding OSUCCC – James melanoma program is using a multidisciplinary, science-based approach to innovative patient care that involves targeted therapies, immunotherapeutic techniques and agents with novel mechanisms of action. The program has seen increases in patient volume, in clinical trials and in the number of patients enrolled in these studies.

SYNERGISTIC SCIENCE

Research findings by OSUCCC – James investigators contribute to clinical trials designed by other OSUCCC – James investigators. OSU-1080 evaluates a DNA-damaging agent plus a PARP inhibitor in women with triple-negative breast cancer and certain women with ER+/PR+ breast tumors. Three areas of OSUCCC – James research contributed to this innovative trial.