Putting Pelotonia Dollars to Work
Pelotonia 16 is several months behind us, but time can’t dim the memory of an event so globally supported by thousands of people who share a single goal: to end cancer.

Financial projections indicate that Pelotonia 16, the eighth installment of this annual grassroots bicycle tour that raises money for cancer research at Ohio State, will likely yield another record yearly fundraising amount, elevating the eight-year total to well above the more than $106 million it generated in its first seven years.

The Pelotonia 16 tour consisted of 275 registered pelotons, or riding groups, that collectively contained 7,749 riders from 40 states and eight countries. It also benefited from more than 2,600 virtual riders and more than 2,700 volunteers. At last report in early October, Pelotonia 16 had raised more than $17 million and counting. It’s anticipated that the organization’s eight-year total amount raised will be boosted to more than $125 million this year.

Thanks to Pelotonia’s major funding partners—including L Brands, Huntington, and Richard and Peggy Santulli—every cent raised by riders, virtual riders and donors goes to cancer research at the OSUCCC – James to help our more than 330 researchers translate scientific discoveries to innovative patient care and prevention strategies that contribute to Pelotonia’s goal of ending cancer.

I extend my boundless praise and gratitude to the thousands of people who work hard to make this event a tremendous success. It bears repeating that without fundraising efforts such as Pelotonia—which has become the nation’s largest single-event cycling fundraiser based on ridership—many promising ideas for cancer research would go nowhere, since government grants are often difficult to obtain.

This investment report summarizes, on the facing page, how Pelotonia funds have been distributed over the event’s first seven years (money from Pelotonia 16 has not yet been allocated). It also shows how the money you raise benefits such key areas as Stimulating New Ideas (grant allocations to teams of faculty scientists), Investing in the Next Generation (our Pelotonia Fellowship Program for student researchers), New Recruit Research Support (bringing top scientists to Ohio State and helping them further their work), and Providing Tools for Discovery (purchasing equipment for use in cancer research and supporting the development of drugs for cancer treatment).

Thanks again for supporting our cause. To echo the sentiments of our keynote speaker during the Pelotonia 16 opening ceremony (see story, inside), we’re collectively sending a message to cancer that this disease is in trouble as we relentlessly ride to end it.

Michael A. Caligiuri, MD
Director, The Ohio State University Comprehensive Cancer Center
CEO, James Cancer Hospital and Solove Research Institute
John L. Marskas Nationwide Insurance Enterprise Foundation Chair in Cancer Research

7-Year Pelotonia Financial Summary

Pelotonia, the annual grassroots bicycle tour that started in 2009 to raise money for cancer research at the OSUCCC – James, generated more than $106 million in its first seven years through rider pledges and donations. Thanks to the event’s major funding partners, every dollar raised by riders, virtual riders and donors from 2009-15 has been 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

Since it began in 2010, the Pelotonia Fellowship Program has awarded $11 million in funding for 399 peer-reviewed cancer research projects by Ohio State students working in the labs of faculty mentors. The trainees are in multiple disciplines and at all levels of scholarship: undergraduate, graduate, medical school, postdoctoral and international scholars.
Pelotonia 16 Riders May Push 8-Year Fundraising Total Past $125 Million

The thousands of riders, virtual riders and volunteers who attended the Aug. 5 opening ceremony for Pelotonia 16—the annual grassroots bicycle tour that raises money for cancer research at Ohio State—saw living proof that Pelotonia is paying off.

For 16 years, Susan Davenport of northern Virginia has been battling cancer, first stage IV lymphoma, then sarcoma and now leukemia. When OSUCCC Director and James CEO Michael A. Caligiuri, MD, called her to center stage and introduced her as a special guest, she told the audience that, after 16 years of fighting—and enduring some difficult cancer treatment during that span—she was tired in body and spirit and had decided to stop all therapy.

“I was just tired…sick and tired of feeling sick and tired,” she recalls. “So I made the decision to quit treatment, and it changed my life.”

In 2014 by the U.S. Food and Drug Administration (FDA) for certain patients with chronic lymphocytic leukemia (CLL). Much of the clinical and basic science research that led to FDA approval of ibrutinib for treating CLL was conducted at the OSUCCC – James under the leadership of John C. Byrd, MD, Amy Johnson, PhD, and their colleagues, and much of their ibrutinib research was supported by Pelotonia funds.

Caligiuri had called Byrd and Johnson to the Pelotonia 16 opening-ceremony stage moments before summoning Davenport. He prefaced their arrival by noting that ibrutinib—the first drug designed to target a protein that is essential for CLL-cell survival and proliferation—leads to durable remissions with tolerable side effects in most patients who receive it.

“More than 90 percent of the people who take this pill go into remission and stay in remission,” Caligiuri said.

Davenport told the audience that it wasn’t until after she and her partner Gary registered to ride in Pelotonia 16, their first time participating in this internationally renowned event, that she learned about Ohio State’s extensive role in research leading to FDA approval of “my miracle drug…the drug that completely changed my cancer experience” and “literally gave me my life back.”

She added that, before registering for Pelotonia, “I had absolutely zero idea of the personal debt that I owe to Pelotonia and the OSUCCC – James. I’m here on this stage because of you. A decision you made to get on a bicycle and go for a ride, and raise a few dollars for a great cause while you were at it, is responsible for saving a life—my life.”

“How can I put into words what this ride and each of you…mean to me?” Davenport continued. “Saying ‘thank you’ doesn’t seem like enough, but it’s all I have, so thank you, each of you, from the bottom of my heart and those of my family and friends.

“Next year, five years, 10 years from now,” she predicted, “someone else will be standing on this stage telling the story of a life saved because of what this community of people accomplished this weekend.”

At this writing, riders, virtual riders and donors in Pelotonia 16 had raised more than $17 million, a total that continued to rise until fundraising ended on Oct. 7. At last report in early October, it was anticipated that funds generated by this year’s tour will boost the eight-year Pelotonia total to more than $925 million, every dollar of which directly supports cancer research thanks to the event’s major funding partners, including L Brands, Huntington, and Peggy and Richard Santulli.

Pelotonia 16, which encompassed assorted bike routes between the Columbus area and Kenyon College in Gambier, Ohio, consisted of 275 registered pelotons (riding groups) that collectively contained 7,449 riders from 40 states and eight countries. It also benefitted from more than 2,600 virtual riders and over 2,700 volunteers.

The audience at the opening ceremony also heard from keynote speaker Chris Draft, a former National Football League player whose wife Lakeshia Rutledge Draft died of lung cancer in 2011 at age 38.

Chris and Lakeshia created Team Draft during her year-long battle with cancer, according to the Team Draft website, “in hopes that her valiant fight to live, love, laugh and smile will give hope and comfort to people around the world. Team Draft is working to save lives by changing the face of lung cancer.”

Chris Draft, who rode 50 miles in Pelotonia 16, emphasized the importance of investing in cancer research because this disease is in its many forms “can happen to anyone. And you guys are doing something about it. By raising money for research, you are giving people more time, more hope, and a whole bunch of life.

“You’re sending a strong message to cancer—that cancer is in trouble, that the people who came here today aren’t playing…They came here to end cancer.”
From Ideas to Impact
Discoveries & Initiatives Supported by Pelotonia

Pelotonia funds support far-reaching initiatives and groundbreaking preliminary studies at the OSUCCC — James that produce data and publications that can lead to grants from external sources for larger studies. On average, about one in five preliminary Pelotonia funding awards has led to a grant from the National Institutes of Health (NIH), which is impressive since the NIH currently funds only about one of every 10 grant applications it receives. Also, more than 105 publications have appeared in scientific journals in relation to Pelotonia-funded projects. Thus, Pelotonia funds help advance cancer treatment and improve patient care. Here are two examples of innovative initiatives, followed by three examples of impactful research projects.

Statewide Project to Save Lives Sees Enduring Success
A statewide Pelotonia-funded screening initiative for colorectal cancer (CRC) patients and their relatives has been highly successful in saving lives — enough so that Ohio State University President Michael V. Drake, MD, featured it in a June 24 panel discussion during his Summer Tour stop in Cincinnati.

The event included representatives of TriHealth Good Samaritan Hospital, the OSUCCC — James and a patient in the Ohio Colorectal Cancer Prevention Initiative (OCCPI), a project led by the OSUCCC — James, to screen newly diagnosed CRC patients and their biologic relatives for Lynch syndrome (LS). LS is a cancer-causing condition that occurs when a person inherits a mutation in one of four genes. Individuals with LS are very likely to develop CRC, uterine, ovarian, stomach or other cancers.

If a CRC patient is found to have LS, the patient’s relatives are at-risk relatives. Some $4 million in Pelotonia funds support far-reaching initiatives and groundbreaking preliminary studies at the OSUCCC — James that produce data and publications that can lead to grants from external sources for larger studies.
“The effort has helped many people lose weight, enabling them to discontinue some medications,” says Electra Paskett, PhD, MPH, associate director for population sciences at the OSUCCC – James. “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.”

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 a funding initiative to test the idea why nearly a 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. They 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.

They also believe their research is the first to test the idea that Inflamed neurons contribute to the development of cognitive impairments in chemotherapy patients. The data from their Pelotonia-supported studies enabled them to obtain a multi-investigator, four-year, $2.15 million 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 the 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.

The grant led to a five-year, $31 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—oral microbiome—might influence the effect of the berries.

“Learning Whether Black Raspberries Can Inhibit Oral Cancer

An Idea Grant awarded in 2012 has helped a multidisciplinary team of OSUCCC – James researchers led by Yeal 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.

The researchers studied the use of a highly concentrated form of black raspberries, which research has shown have significant antitumor activity. The team’s Pelotonia-funded 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 the trial participants found most palatable.

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The Pelotonia Fellowship Program provides funds to train promising and accomplished undergraduate, graduate, medical and postdoctoral students from any discipline at Ohio State who have the potential to become independent cancer researchers.

The Fellowship Program, which started in 2010, has awarded 399 student fellowships through an annual allocation of $2 million in Pelotonia revenue that enables these students to conduct cancer research in the labs of faculty mentors. To date, scholarship recipients include 172 undergraduates, 114 graduates, six medical students, 86 postdoctoral fellows and 14 international scholars.

From October 2015-October 2016, the program awarded 65 fellowships to students at all levels of scholarship for conducting cancer research in the labs of faculty mentors. These recipients included 25 undergraduates, 16 grad students, 17 postdoctoral fellows, two medical students and four international scholars.

The awards are made by a Pelotonia Fellowship Committee that oversees the program and includes some of Ohio State’s most distinguished basic, translational and clinical researchers from many disciplines. The committee is chaired by Fellowship Program Director Gustavo Leone, PhD, associate director for basic research at Ohio State’s Comprehensive Cancer Center – James Cancer Hospital and Solove Research Institute (OSUCCC – James). Janice Kiecolt-Glaser, PhD, a Distinguished University Professor and member of the Cancer Control Program at the OSUCCC – James, is co-chair.

“External grants are very difficult to obtain, especially for students,” says OSUCCC Director and James CEO Michael A. Caligiuri, MD, “so it’s important for us to support the next generation of promising young cancer researchers if we are to keep working effectively toward our goal of ending this disease.”

Leone says the program is truly multidisciplinary, noting that fellowship students have been awarded to students working with mentors in multiple colleges and over 50 departments at Ohio State.

The Fellowship Program website (cancer.osu.edu/pelotoniaresearch) includes photos of all funded fellows, their project titles and mentors, and a lay summary and one-paragraph lay abstract describing their work. Here’s a look at three recent Pelotonia fellowship recipients and their project.

Pelotonia Fellowship Program Funds Next Generation of Cancer Researchers

Sophia Maharry

An undergrad majoring in biomedical science and French, Sophia Maharry studied the impact of the 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 S, in AML,” Maharry says, noting that her mentor for this work was Ann-Kathrin Eisfeld, MD, a postdoctoral fellow and 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, 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 marked 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.”

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.” Cahoun rode 100 miles in Pelotonia 15 and 18 in 16. “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 16. “I will continue to raise money for years to come for Pelotonia because it is an excellent organization and cause,” he says.

Teaming Up Against Cancer
Pelotonia-Funded Grants Support Key Collaborations

Pelotonia Funds Support 10 More Cancer Research Projects

Another 10 compelling cancer research studies being conducted by teams of Ohio State faculty scientists received grant funding in summer 2016 from Pelotonia. All 10 were funded by the OSUCCC – James Intramural Research Program (IRP), which is supported by Pelotonia. IRP funding comes in several forms, including:

- Idea Grants, which support high-risk, high-payoff research for which government grants are difficult to obtain;
- Community Partnership Awards, which support investigators who team with a community entity on a cancer-focused study;
- Clinical Trial Awards (protocol-specific research support), which support studies that seek ways to prevent, diagnose and treat cancer and provide participating patients with some of the most advanced treatments available anywhere;
- Bridge Funding Awards, which help researchers with competitive renewal applications for National Cancer Institute (NCI) grants that were not funded on their first submission, or for grants whose initial funding has expired.

This Pelotonia-supported funding is vitally important at a time when government funding is hard to obtain for the early pursuit of promising studies.

“The creative projects funded by this program involve ideas from scientists who are ‘thinking outside the box’ and need support for gathering early data that will enable them to apply later for larger external grants from entities such as the National Cancer Institute,” says OSUCCC Director and James CEO Michael A. Caligiuri, MD. “Our scientists could not pursue these innovative projects without funding raised by the thousands of riders in Pelotonia.”

In the past six years, 89 OSUCCC – James research teams have received Pelotonia-funded IRP grants awarded through a peer-review process conducted by both internal and external scientists who are not competing for grants in the current funding year. This latest round of grants totals $948,348. Here are summaries of each project:

**IMAGE-GUIDED, CATHETER-DELIVERED RADIOTHERAPY TO TREAT LOW-RISK PROSTATE CANCER**

(Investigator: Michael Tweedle, PhD, College of Medicine)

Men diagnosed with low-risk, localized prostate cancer have multiple choices for treatment, ranging from surveillance—which involves frequent monitoring for disease via blood tests and clinical evaluations—to surgery to remove the entire prostate gland, to targeted radiation treatments. Removing the prostate carries a high risk of impotence, incontinence and gland function. About 80 percent of men diagnosed with prostate cancer have gland-localized, early-stage disease that could theoretically be treated with cancer-targeted drugs if the exposure of normal tissues to these drugs could be eliminated. This preclinical study will evaluate a gland-sparing alternative to treat prostate cancer. Researchers hypothesize that an image-guided, super-selective micro catheterization of the prostate arteries could be used in combination with a novel peptide receptor radionuclide therapy to treat prostate cancer confined to the gland using 1000th of the expected intravenous dose. They will assess therapeutic outcomes along with sexual and urinary side effects.

**MECHANISMS BEHIND PREGNANCY-LACTATION CYCLE AND TRIPLE-NEGATIVE BREAST CANCER**

(Investigator: Bhuwaneswari Ramaswamy, MD, College of Medicine)

Previous studies suggest that giving birth and breastfeeding lower a woman’s overall risk of developing breast cancer, with the most recent data pointing to breastfeeding being protective specifically against triple-negative breast cancers. African-American/ black women have a disproportionately high rate of developing aggressive triple-negative breast cancer while also having higher birth rates and lower rates of breastfeeding. Research has also shown that women native to Africa have higher rates of breastfeeding and lower rates of breast cancer. The reasons that childbirth and breastfeeding affect breast cancer risk remain
remains the gold standard chemotherapy treatment for adriamycin in combination with ifosamide (HD-AIM) disease surviving less than 15 months. High-dose mortality rates, with most patients who have metastatic in the United States and are associated with very high Soft tissue sarcomas affect about 12,000 adults annually and Ewy Mathe, PhD, all from the College of Medicine) (Investigators: James Chen, MD, David Liebner, MD, Ewy Mathe, PhD, and John C. Byrd, MD, both of the College of Medicine) Acute myeloid leukemia (AML) is a complex form of blood cancer characterized by the rapid accumulation of neoplastic myeloid cells in the bone marrow, a soft fatty substance inside bones that is responsible for producing blood cells. The complexity of gene abnormalities involved in disease development—as well as the tumor microenvironment—makes it a challenge to identify potential therapeutic targets. This preclinical study will test a new inhibitor agent for the treatment of AML. The treatment agent is based on translational research discoveries made at the OSUCCC – James and may provide important insights into the effects of this class of inhibitors on AML. ELY BIOMARKERS OF TREATMENT EFFECTIVENESS, TOXICITY IN SARCOMA (Investigators: James Chen, MD, David Liebner, MD, and Ewy Mathe, PhD, all from the College of Medicine) Soft tissue sarcomas affect about 12,000 adults annually in the United States and are associated with very high mortality rates, with most patients who have metastatic disease surviving less than 15 months. High-dose adriamycin in combination with ifosamide (HD-AIM) remains the gold standard chemotherapy treatment for sarcoma, but just 30-40 percent of patients respond to the therapy. The combination frequently has life-threatening side effects. Identifying patients most likely to benefit from HD-AIM will improve effectiveness of this therapy and reduce deaths due to drug toxicity. In this clinical study, researchers will use metabolomics—a comprehensive quantification of small molecules from the tumor and drugs found in bodily fluids—to identify prognostic biomarkers in sarcoma. Based in the medical oncology sarcoma program, this clinical study seeks to identify early changes in urine and blood metabolites of soft tissue sarcoma patients undergoing HD-AIM therapy to determine whether these biologic measures can predict treatment response and toxicity. USING HERPES VIRUS TO TRAIN IMMUNE SYSTEM TO DESTROY CANCER CELLS (Investigator: Jianhua Yu, PhD, College of Medicine) Despite two decades of research, few treatment advances have been made for glioblastoma (GBM), a rare but deadly form of primary brain tumor with a median overall survival of less than 15 months. Oncolytic (cancer-killing) viral therapy is an emerging concept for new anticancer treatments that uses naturally occurring, replicating viruses engineered to infect and destroy cancer-specific cells. OSUCCC – James researchers have engineered an oncolytic virus based on the herpes simplex virus 1 designed to emit a “don’t eat me” signal to the immune system so the virus can infect/destroy the targeted cancer cells. Researchers hypothesize that the protein K1F11 plays a direct role in the radiotherapy response, and that therapy targeting K1F11 given in conjunction with radiotherapy would be more effective for overcoming treatment resistance. Researchers hypothesize that the protein K1F11 plays a direct role in the radiotherapy response, and that therapy targeting K1F11 given in conjunction with radiotherapy would be more effective for overcoming treatment resistance, therefore improving patient outcomes. ACHILLES’ HEEL FOR CANCER STEM CELLS (Investigator: Monica Venere, PhD, College of Medicine) All cells in the body start as stem cells that differentiate into other cells that serve specific functions. Some resemblance of this cellular hierarchy exists in malignant tumors like glioblastoma (GBM), which are believed to have a subpopulation of cancer stem cells, or cells that harbor the malignant characteristics of the disease and cause it to resist radiotherapy and chemotherapy. This basic science study will explore the role of cancer stem cells in the development of radiotherapy resistance with the aim of finding an ‘Achilles’ heel’ for cancer stem cells. Researchers hypothesize that the protein K1F11 plays a direct role in the radiotherapy response, and that therapy targeting K1F11 given in conjunction with radiotherapy would be more effective for overcoming treatment resistance, therefore improving patient outcomes.
LUNG TOXICITY FROM ELECTRONIC CIGARETTES AND TOBACCO PRODUCTS

(Investigator: Peter Shields, MD, College of Medicine)

Up to 40 percent of patients have a clinically actionable genomic alteration, but only 10 percent of patients go on to receive treatment due to limited availability of therapies or clinical trials targeting their gene mutations. Several barriers to cancer genomic testing in patients exist, including easy access to tumor specimens that may represent the patient’s current metastatic disease, and limitations to DNA sequencing lack of clinical-grade RNA sequencing. In this clinical study, researchers will use liquid biopsy to test for DNA and RNA through routine blood and urine samples. They hope to establish a foundation for implementing liquid biopsy in the clinic to help characterize drug resistance in patients. This would enable oncologists to better match patients with drug therapies that are more likely to achieve cancer control or reduction.

LUNG TOXICITY FROM ELECTRONIC CIGARETTES AND TOBACCO PRODUCTS

(Investigator: Peter Shields, MD, College of Medicine)

Electronic cigarettes (e-cigs), which deliver aerosolized nicotine and flavorings through a battery-operated device, have gained rapid popularity, particularly among never-smokers and youth users. Although they are touted as smoking-cessation tools, there is no scientific evidence to support this claim and very little data describing the health effects of using e-cigs as compared with the use of other tobacco products. This grant expands the scope of two ongoing research studies to evaluate the differences in lung toxicity between smokers and e-cig users, and to see how this compares to never-smokers of any product. Researchers hypothesize that e-cig constituents will induce lung inflammation and alter genomic and metabolic gene expression pathways. The pilot study will also establish the feasibility of using bronchoscopy as a way to measure lung toxicity and identify candidate genes for biomarker development.

DECODING GENETIC MUTATION’S ROLE IN PanCREATIC CANCER

(Investigators: Denis Guttridge, PhD, and Michael Ostrowski, PhD, both of the College of Medicine)

Although there have been advances in abdominal imaging, surgical techniques and chemotherapy regimens for pancreatic cancer, the death rates for the disease have not decreased significantly since the 1940s. Of the 53,000 people diagnosed with the disease annually, just 7 percent are expected to live five years after diagnosis. This basic science study will help researchers understand the relationship between Kras—one of the most common gene mutations found in human pancreatic cancer—and disruptions in the cellular checkpoints for inflammation that would normally serve to stop cancerous tumors from developing and growing. Data gathered in this study could provide insight on the role of an inflammation-regulator called NF-kB in pancreatic cancer and identify new targets for treating this disease.

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 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 investigator Gregory Behbehani, MD, PhD, assistant professor 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 seven to 10 markers just to identify them. That doesn’t leave much room for asking questions when using traditional flow cytometry.”

Providing Tools for Discovery

Pelotonia-Funded Super Cytometry Enhances Cancer Research

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

In mass cytometry, the same antibodies are 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 to 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 difficult to cure.

“In the future,” he says, “we hope to use instruments like this one to further personalize treatments and care more patients.”
Pelotonia Dollars Support Innovative Clinical Trials

Clinical trials improve cancer care by demonstrating the safety and effectiveness of new treatments, examining treatment strategies and probing problems associated with therapies so refinements can be made. Here are summaries of two Pelotonia-supported clinical trials at the OSUCCC – James. To learn more about these and other trials, call The James Line at 800-293-5066 or visit cancer.osu.edu

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 an oncolytic (cancer-killing) virus that selectively destroys cancer cells while doing little damage to healthy cells. The virus replicates in cancer cells and causes them to burst, killing those 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 U.S. 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 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 treating 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,” he adds. “We are the only ones in the world using this virus systematically. We’re hoping it will open an entirely new era of cancer therapy that is more effective and safe.”

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 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 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 65 and older, who often develop subtypes of AML that make it harder to achieve remission and more likely to recur. Also, older patients often face 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 colleagues 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; and several doses of a drug that stimulates NK-cell growth.

The researchers hypothesize that the fludarabine will help the patients’ 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 trial, Pelotonia funds helped Vasu, Williorn 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 over 60.

Using donated samples from patients who participated in 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 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.
Drug Development Institute

Pelotonia Funds Translating OSUCCC – James Discoveries Into New Cancer Treatments

The Drug Development Institute (DDI) at Ohio State is a biotech-like institute embedded in the OSUCCC – James. Its mission is to identify promising anticancer agents discovered by OSUCCC – James researchers and advance them through the pharmaceutical development process for potential partnering with industry to deliver new therapies to patients.

The DDI was founded in 2010 by OSUCCC Director and James CEO Michael A. Caligiuri, MD, and Timothy Wright, a former executive of several pharmaceutical companies and chair of the DDI External Advisory Board. It was founded 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 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 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.

Having shown that these B cells can attack tumors and dramatically decrease their size, the researchers next want to establish that the B cells promote the resection of established tumors and tumors that generate a poor immune response. They believe that their approach can overcome the limitations of related immune therapies currently on the market or in clinical trials testing.

A Novel MRI Imaging Agent

A practical and safe method for expanding the use of magnetic resonance imaging (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 selfassemble 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.

Bringing the Best to Ohio State

The OSUCCC – James attracts some of the brightest minds in cancer research, and Pelotonia dollars help them continue their research when they arrive. Among those recruited since last year’s investment report are these four prominent senior researchers:

CHERYL TAYLORE LEE, MD, is professor and chair of the College of Medicine’s Department of Urology. An expert in outcomes research and comparative studies, she was recruited from the University of Michigan to lead Ohio State’s urology, urogynecology and uro/oncologic programs. As a member of the University of Michigan Comprehensive Cancer Center, she cared primarily for patients with bladder cancer. Having been a principal investigator (PI) or co-PI on numerous clinical trials, Lee focuses her research on strategies to improve patient outcomes and quality of life after surgical treatments.

TIMOTHY PAWKILK, MD, MPH, PHD, is professor and chair of the College of Medicine’s Department of Surgery. Pawlik, a liver cancer expert, came to Ohio State from Johns Hopkins Hospital, where he was chief of the Division of Surgical Oncology, program director of the Surgical Oncology Fellowship and director of the Johns Hopkins Liver Tumor Center. He has authored or co-authored more than 600 published articles and over 50 book chapters, and he has edited five surgical textbooks. His primary interests include alimentary tract surgery with a special interest in hepatic, pancreatic and biliary diseases.

KAREN PATRICIA WILLIAMS, PHD, is a Nursing Distinguished Professor of Women’s Health and director of the Center for Women, Children and Youth at The Ohio State University College of Nursing. She came to Ohio State from MD Anderson Cancer Center in Houston as director of the Cellular Therapy and Cancer Immunotherapy Program for Nationwide Children’s Hospital’s Division of Hematology/Oncology/BMT and Center for Childhood and Blood Diseases. Lee, who also serves as director of cellular therapy at the OSUCCC – James, specializes in care for children undergoing stem cell transplantation. His research focuses on clinical trials of adoptive immune therapy with natural killer cells.

In addition, Pelotonia dollars have supported the work of 15 mid-level and junior oncology scientists and physicians recruited to Ohio State.

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