INVESTING IN A CANCER-FREE WORLD 2015

Putting Pelotonia Dollars to Work

The James

The Ohio State University
Comprehensive Cancer Center

We at The Ohio State University Comprehensive Cancer Center – James Cancer Hospital and Solove Research Institute (OSUCCC – James) envisioned great things for Pelotonia when we launched it in 2009.

Thanks to all who have embraced our cause, we have not been disappointed.

Pelotonia 15, the seventh installment of this annual grassroots bicycle tour that raises money for cancer research at Ohio State, produced still another ridership record and will likely yield another record yearly fundraising amount, elevating the overall seven-year total to well above the $82.34 million it generated in its first six years.

The Pelotonia 15 tour consisted of 277 registered pelotons, or riding groups, that collectively contained 7,981 riders from 40 states and 10 countries. It also benefited from more than 3,800 virtual riders (the exact total has yet to be announced) and over 2,700 volunteers.

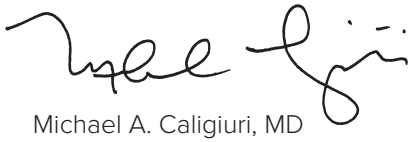
Fundraising for Pelotonia 15 officially ended on Oct. 9, and we'll soon learn this year's final dollar total. At last report in early September, it was above $15 million and rising, a figure that had boosted the seven-year total to more than $97.41 million.

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 300 researchers translate scientific discoveries to innovative patient care and prevention strategies that contribute to Pelotonia's single goal of ending cancer.

I can't express gratitude enough to the thousands of people from near and far who make this incredible event such a huge success. 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, and the field would languish, since government grants are often difficult to obtain.

This investment report briefly summarizes (on the facing page) how Pelotonia funds have been distributed over the event's first six years. It also offers a look at our Pelotonia Fellowship Program for student researchers, our Idea Grant allocations of the past year to teams of faculty scientists, our most recent equipment purchases with Pelotonia support, findings from selected Pelotonia-supported studies, a couple of clinical trials boosted by Pelotonia dollars, and five recently recruited scientists whose work has received Pelotonia support.

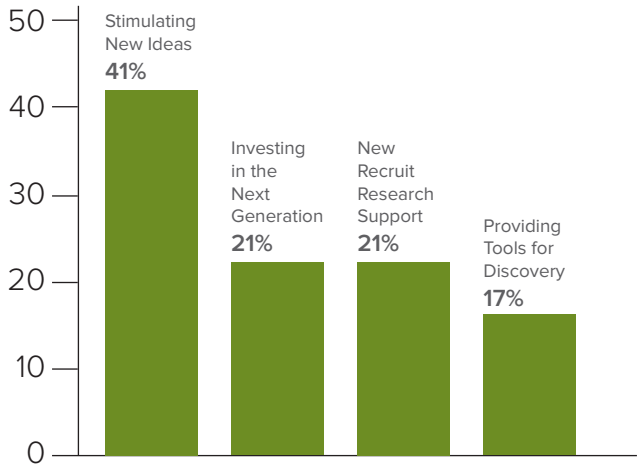
I hope this report helps assure you that the money we are raising for Pelotonia is being put to good use in our continuing pursuit of a cancer-free world.



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

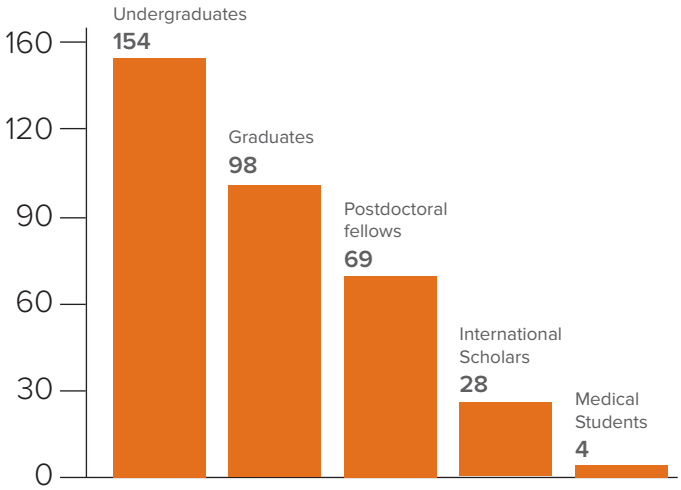
Six-Year Pelotonia Financial Summary

Allocations of Funding From Pelotonia 2009-2014



Pelotonia, the annual grassroots bicycle tour established in 2009 to raise money for cancer research at the OSUCCC – James, generated more than $82 million in its first six years through rider pledges and donations. Thanks to the event's Major Funding Partners, every dollar raised by riders, virtual riders and donors since Pelotonia began has been used to advance cancer research as shown in the bar graph to the left.

Fellowship Grants Awarded



Investing in the Next Generation: Pelotonia Fellowship Program

Since it began in 2010, the Pelotonia Fellowship Program has awarded $11 million in funding for 353 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.

Bringing All 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. Ohio State colleges that have received Pelotonia money include:

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

Pelotonia Fellowship Program Overview

Students from any discipline and level of scholarship at Ohio State who want to conduct cancer research with faculty mentors can receive the funding boost they need to get started through the Pelotonia Fellowship Program.

Since the program began in 2010, it has received $11 million in Pelotonia funds to support the award of 353 student fellowship grants to 154 undergraduates, 98 graduates, four medical students, 69 postdoctoral fellows and 28 international scholars who likely would have received no other funding opportunities.

“External grants are very hard to come by, especially for students,” says OSUCCC Director and James CEO Michael A. Caligiuri, MD, “so it’s important for us to fund the next generation of promising young cancer researchers and maintain our momentum toward ending this disease.”

In its most recent allocation (spring of 2015), the program awarded 55 new fellowships to students, including 25 undergraduates, 21 graduates, two postdoctoral fellows and seven international scholars, bringing the six-year total to 353.

A 46-member committee containing some of Ohio State’s top cancer researchers reviews all Pelotonia fellowship applications and issues the awards. The committee is chaired by Fellowship Program Director Gustavo Leone, PhD, a professor in Ohio State’s Department of Molecular Virology, Immunology and Medical Genetics, and associate director for basic research at the OSUCCC – James. Janice Kiecolt-Glaser, PhD, a Distinguished University Professor in Ohio State’s Department of Psychiatry and Behavioral Health, and a member of the Cancer Control Program at the OSUCCC – James, is co-chair.

Leone says fellowship award decisions are based on quality of applications rather than a set number to be issued each year. “This program is truly multidisciplinary,” he adds. “We have awarded fellowships to students working with mentors in 10 colleges and 48 departments at Ohio State, and also from applicants at Nationwide Children’s Hospital and Cincinnati Children’s Hospital Medical Center.”

The Pelotonia Fellowship Program website (**http://go.osu.edu/pelotoniafellowships**) includes photos of all funded fellows, their project titles and mentors, and a lay summary and one-paragraph lay abstract describing their work. In addition, several videos have been produced in which the fellows explain their projects and say what their funding means to them. These videos can be accessed from the funded fellows’ Web page.

Post-Fellowship Highlights

After completing their cancer research in the labs of Ohio State faculty mentors, many past Pelotonia fellows have continued to achieve and make a difference. Their pursuits include:

- Medical degrees at Ohio State
- Educational opportunities in other health-related areas at Ohio State, including graduate programs and postdoctoral fellowships in the Comprehensive Cancer Center and in the departments of Pathology, Molecular Genetics, Molecular and Cellular Biochemistry, Nutrition, Internal Medicine (divisions of Hematology and Medical Oncology), and Molecular Virology, Immunology and Medical Genetics, as well as in the College of Pharmacy
- Advanced studies in the health sciences at Ohio State, Harvard, Stanford, Johns Hopkins, Kentucky, Case Western Reserve, Toledo, Michigan, Duke, Baylor, Ohio University, Pittsburgh, Northwestern, Texas, UCLA, MD Anderson Cancer Center, the National Cancer Institute (NCI) at the National Institutes of Health, and the Government of India Institute of Life Sciences, to name a few
- Professional employment at Nationwide Children's Hospital, Cincinnati Children's Hospital Medical Center, Tufts University, University of California Helen Diller Family Comprehensive Cancer Center, Genentech, Medical University of South Carolina, University of Delaware, Ferris State University, University of Prince Edward Island (Canada), Birla Institute of Technology and Science (India), and Manchester Royal Infirmary Hospital (United Kingdom)

From Ideas to Impact

Pelotonia's impact is perhaps most obvious in discoveries made and published in scientific journals by teams of researchers who have received Pelotonia support over the past few years. Some examples:

CanDL Database Shines Light on Clinically Important Cancer Gene Mutations

Many clinical trials use genome sequencing to learn which gene mutations are present in a patient's tumor cells. The question is important because targeting the right mutations with the right drugs can stop cancer in its tracks.

But it can be difficult to determine whether there is evidence in the medical literature that particular mutations might drive cancer growth and could be targeted by therapy, or evidence showing which mutations are of no consequence.

To help molecular pathologists, laboratory directors, bioinformaticians and oncologists identify key mutations that drive tumor growth in tissues obtained during clinical studies, OSUCCC – James researchers, with support from Pelotonia and other funds, have designed an online database called the Cancer Driver Log, or CanDL.

The freely accessible database, described in a paper published in the *Journal of Molecular Diagnostics*, includes mutations in 60 genes, with 334 distinct variants and 169 unique matching literature references across multiple cancers as of October 2015.

"Currently, pathology laboratories that sequence tumor tissue must manually research the scientific literature for individual mutations to determine whether they are considered a driver or a passenger to facilitate clinical interpretation," says principal investigator Sameek Roychowdhury, MD, PhD. "CanDL expedites this time-consuming process by placing key information about known and possible driver mutations that might be effective targets for drug development at their fingertips. "CanDL does not tell doctors what to do—it places the evidence in the scientific literature at their fingertips, enabling them to read and interpret the information themselves," he adds.

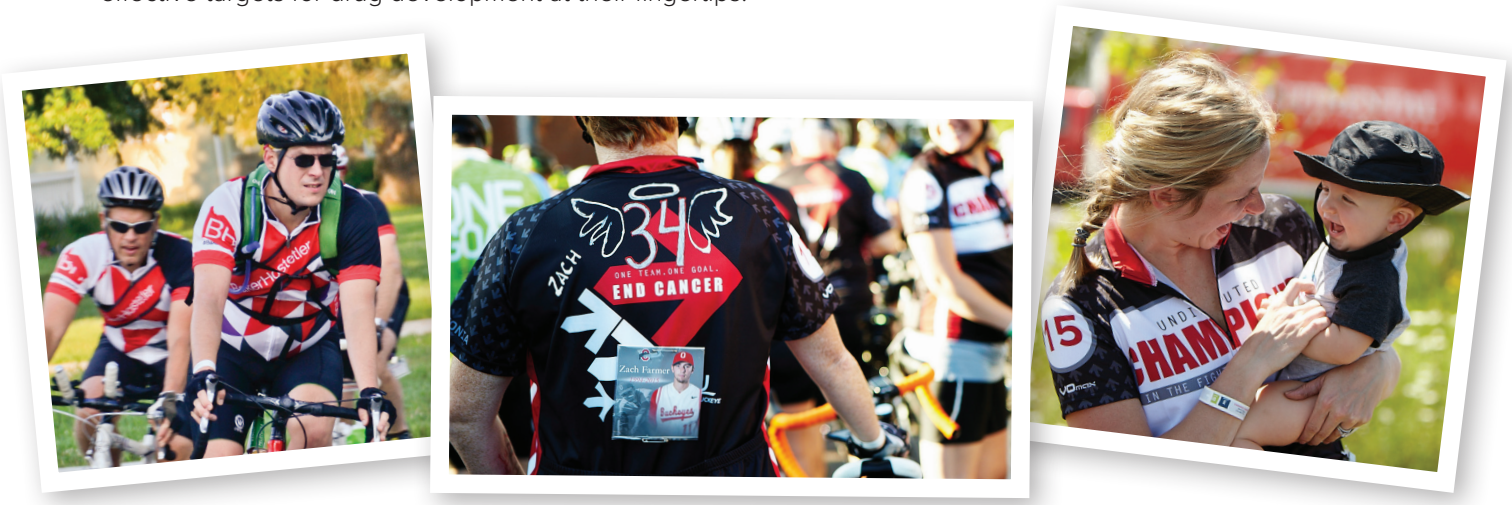
Identifying driver mutations in a patient's tumor cells can also help reveal why some patients in a clinical trial respond well to a novel agent while others do not respond. That information can help improve the effectiveness of existing anticancer drugs and identify patients who would benefit most from particular therapies.

Prostate Cancer Androgen Receptor Activates Different Genes When Bound to Antihormone Drugs

A 2011 Pelotonia Idea Grant helped OSUCCC – James researchers led by Qianben Wang, PhD, conduct research that produced a surprising finding about a key receptor for testosterone, a hormone that drives prostate cancer development and progression.

That key molecule in prostate cancer is called the androgen receptor (AR). When testosterone activates that receptor, it causes the receptor to activate a certain set of genes. However, a study published in 2015 in *The EMBO Journal* by Wang and his colleagues showed for the first time that when the receptor binds with certain drugs (bicalutamide and enzalutamide) used to treat prostate cancer, it activates a completely different set of genes, including some that promote cancer.

The researchers called these newly discovered AR binding sites on DNA "antiandrogen response elements" and showed that they activate genes that might enable tumor progression during antiandrogen treatment.



Their findings suggest that the treatment of prostate cancer with antiandrogenic drugs should include agents that target antiandrogen-regulated oncogenes.

"The discovery of antiandrogen response elements was completely unexpected," says Wang, noting that antiandrogen agents are known to work by competing with androgens to bind to AR, thus inhibiting androgen-induced gene expression.

"But we found that antiandrogens can also trigger AR to bind to DNA sequences that are distinctly different from androgen response elements, and thus regulate genes relevant to prostate cancer development," says Wang, a member of the Molecular Carcinogenesis and Chemoprevention Program at the OSUCCC – James.

Chitosan-Coated, Chemotherapy-Packed Nanoparticles May Target Cancer Stem Cells

Funds from a postdoctoral fellowship helped support a study led by OSUCCC – James researchers that indicated nanoparticles packed with a chemotherapy drug and coated with an oligosaccharide derived from the carapace of crustaceans might target and kill cancer stem-like cells.

Cancer stem-like cells have characteristics of stem cells and are present in very low numbers in tumors. Highly resistant to chemotherapy and radiation, they are believed to play an important role in tumor recurrence. This laboratory-and-animal study showed that nanoparticles coated with an oligosaccharide called chitosan, and encapsulating the chemotherapy drug doxorubicin, can target and kill cancer stem-like cells six times more effectively than free doxorubicin. The study appeared in the journal *ACS Nano*.

"Our findings indicate that this nanoparticle delivery system increases the cytotoxicity of doxorubicin with no evidence of toxic side effects in our animal model," says principal investigator Xiaoming (Shawn) He, PhD, a member of the OSUCCC – James Translational Therapeutics Program. "We believe chitosan-decorated nanoparticles could also encapsulate other types of chemotherapy and be used to treat many types of cancer."

This study showed that chitosan binds with a receptor on cancer stem-like cells called CD44, enabling the nanoparticles to target the malignant stem-like cells in a tumor.

The nanoparticles were engineered to shrink, break open and release the anticancer drug under the acidic conditions of the tumor microenvironment and in tumor-cell endosomes and lysosomes, which cells use to digest nutrients acquired from their microenvironment.

He and his colleagues conducted the study using models called 3D mammary tumor spheroids (i.e., mammospheres) and an animal model of human breast cancer.

OSU Co-Anchors National Precision Cancer Research Collaboration

Pelotonia funds have enabled the OSUCCC – James to extend its reach by helping to establish the Oncology Research Information Exchange Network (ORIEN).

Founded and co-anchored by Moffitt Cancer Center in Tampa, Fla., and the OSUCCC – James, ORIEN is a national collaboration involving nine cancer centers that are using a protocol called Total Cancer Care® (TCC) to hasten the development and delivery of more precise cancer treatments, diagnostic tools and prevention strategies through secure research-sharing of consented patient data.

Other ORIEN members are Rutgers Cancer Institute of New Jersey, University of Virginia Health System, Morehouse School of Medicine in Atlanta, University of New Mexico Cancer Center, University of Southern California (USC) Norris Comprehensive Cancer Center, City of Hope National Medical Center in Duarte, Calif., and University of Colorado Cancer Center.

The TCC protocol is a lifetime partnership between cancer patients and their treatment institution in which patients consent to donate their de-identified tissue and clinical data, including corresponding genomic data, for research. ORIEN member institutions then share that data to help them better understand cancer at the molecular level and accelerate the development of more targeted treatments for individual patients. As of last summer, more than 124,000 patients had consented to the TCC protocol.

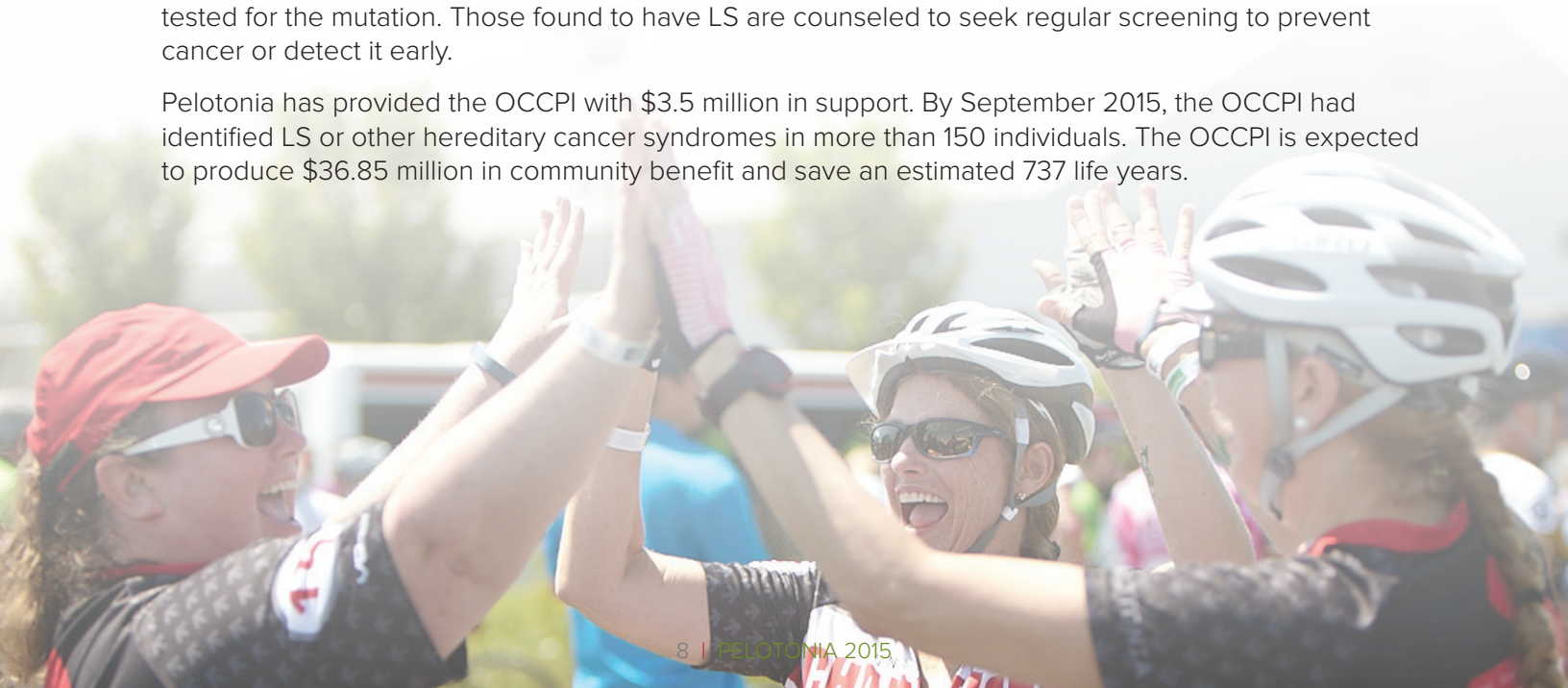
Saving More Lives Statewide: An Update

Through the Pelotonia-funded Ohio Colorectal Cancer Prevention Initiative (OCCPI), the OSUCCC – James is now working with 50 Ohio hospitals to reduce the number of deaths from colorectal cancer (CRC) in a statewide screening initiative.

The OCCPI, led by Heather Hampel, MS, LGC, of the OSUCCC – James, focuses on screening tumor samples from CRC patients to learn which ones also have Lynch syndrome (LS), a cancer-causing condition that occurs when a person inherits a mutation in one of four genes. Anyone who has one of those mutations is very likely to develop CRC, uterine, ovarian or other cancer.

First-degree relatives (parents, siblings and children) of someone with LS have a 50-percent chance of inheriting the same mutation. But when LS is identified in one family member, other members can be tested for the mutation. Those found to have LS are counseled to seek regular screening to prevent cancer or detect it early.

Pelotonia has provided the OCCPI with $3.5 million in support. By September 2015, the OCCPI had identified LS or other hereditary cancer syndromes in more than 150 individuals. The OCCPI is expected to produce $36.85 million in community benefit and save an estimated 737 life years.



Providing Tools for Discovery

Instruments of Progress

A Mass Spectrometry Upgrade

The Orbitrap Fusion™ and Quantiva mass spectrometers are among the newest equipment purchased with support from Pelotonia funds. The funds were contributed by the OSUCCC – James to an Ohio State and state of Ohio investment in a major upgrade and expansion of OSU's mass spectrometry and proteomics capabilities.

Mass-spectrometers are used in cancer research to better understand cancer-cell biology. The instruments are needed, for example, to identify the quantity and characteristics of proteins in tumor and normal tissues. The new mass spectrometers were purchased for the Proteomics Shared Resource (SR), which provides this critical technology and expertise for OSUCCC – James researchers and the cancer-research community across Ohio.

The Proteomics SR is part of the Campus Chemical Instrument Center that is managed by Ohio State's Office of Research and the OSUCCC – James.

Proteomics SR Director Michael Freitas, PhD, a member of the Molecular Biology and Cancer Genetics Program at the OSUCCC – James, says the sophisticated new mass spectrometers will enable researchers to identify compounds faster, more accurately and more thoroughly.

Vicki Wysocki, PhD, an Ohio Eminent Scholar in the Department of Chemistry and Biochemistry in Ohio State's College of Arts and Sciences, and senior faculty adviser to the Proteomics SR, says the ongoing mass spectrometry upgrade/expansion has involved the purchase of several state-of-the-art instruments for measurements, and they include sample robots for high-throughput applications.

These new instruments are housed in the Campus Chemical Instrument Center, which was founded in 1981 as a unit of the OSU Office of Research to provide research facilities for the entire campus in three areas: NMR spectrometry, mass spectrometry and proteomics, and macromolecular X-ray crystallography.

"The Center is an interdisciplinary unit serving faculty from the colleges of Arts and Sciences; Education and Human Ecology; Engineering; Food, Agricultural and Environmental Sciences; Medicine; Optometry; Pharmacy; Veterinary Medicine; and Ohio State's Comprehensive Cancer Center, to name a few," Wysocki says.

She notes that the Center also is a hub for the Ohio Nuclear Magnetic Resonance and Ohio Mass Spectrometry MR consortiums, providing researchers in colleges and universities throughout Ohio with access to the Center's facilities.

The Microscopy Shared Resource (MSR) at the OSUCCC – James also benefited from Pelotonia dollars in the same round of funding with the purchase of a $400,000 microscope to perform sophisticated live cell imaging. The MSR, part of the Campus Microscopy and Imaging Facility under the OSU Office of Research, is managed by the OSUCCC and located in Ohio State's Biomedical Research Tower. The MSR gives researchers access to state-of-the-art microscopes and services ranging from standard light and electron microscopy to live-animal, multiphoton microscopy. MSR experts support high-level cancer research with the latest microscopy techniques.

Thank You

Pelotonia Riders, Virtual Riders, Donors and Volunteers

Team Science

Pelotonia-Funded Grants Support Key Collaborations

Fifteen teams of faculty scientists received funding boosts through Pelotonia revenue for their innovative research projects during fiscal 2014-15. All 15 were funded by the OSUCCC – James Intramural Research Program (IRP), which is supported by Pelotonia dollars.

A dozen of the funding awards were Idea Grants, one was a Community Partnership Award, one was a Clinical Trial Award (protocol-specific research support) and one was a Bridge Funding Award. All of these grants, which are typically two-year awards of $50,000 per year, are especially important at a time when government funding is hard to obtain for the early pursuit of promising studies.

“There is no routine cancer research, and these creative projects which involve ideas from scientists thinking ‘outside the box’ would not be possible without the thousands of Pelotonia riders and donors who are bringing us closer each day to creating a cancer-free world,” says OSUCCC Director and James CEO Michael A. Caligiuri, MD.

In the past five years, 73 OSUCCC – James research teams have received Pelotonia-supported IRP funding awards totaling about $7.6 million. Awardees are selected through a peer-review process conducted by internal and external scientists not competing for grants in the current funding year. Here are the fiscal 2014-15 IRP awards:

IDEA GRANTS

(These grants provide early funding support for high-risk, high-payoff research for which external grants are difficult to obtain.)

IDENTIFYING AND DEVELOPING NEW IMMUNOAGENTS FOR CANCER DIAGNOSIS AND THERAPY

(PIs: Michael Tweedle, PhD, and Charles Hitchcock, MD, PhD)

This study will develop molecular tools for cancer diagnosis and therapy by targeting nucleoli, a marker abundantly present on the surface of cancer cells but not on normal cells. This research team recently identified an agent that blocks nucleolin, and now the team will investigate the therapeutic potential of this agent on several types of human tumors. The compound also will be attached to tracers that will help clinicians and surgeons identify the tumors, plan the surgical procedure and assess the complete removal of cancer cells from patients, which will improve their overall survival.

PROTEASOMAL PATHWAY REGULATES PTEN PROTEIN DEGRADATION AND PROMOTES CARCINOGENESIS

(PIs: Sarmila Majumder, PhD, and Michael Ostrowski, PhD)

Certain genes, known as tumor-suppressor genes, protect people from cancer and promote response to cancer therapy. *PTEN* is a tumor-suppressor gene, but it is lost due to the genetic changes that occur in many cancers. Recent studies by this research team suggest that in some breast cancer patients *PTEN* is lost because the *PTEN* protein is unstable. The researchers have identified several factors that promote *PTEN*-protein breakdown; now they will determine how these factors regulate *PTEN* protein stability and regulate breast cancer initiation and progression. Restoring *PTEN* protein by blocking these negative regulators could be a novel therapy for many cancers.

TRPV2/CANNABIDIOL AS A NOVEL THERAPEUTIC TARGET FOR TRIPLE-NEGATIVE AND METASTATIC BREAST CANCER

(PI: Ramesh Ganju, PhD)

The overall goal of this project is to develop therapies against highly aggressive and metastatic triple-negative breast cancers (TNBC), which are associated with poor prognosis due to early metastasis to other organs and a lack of targeted therapies. This team has preliminary data that shows TNBC growth and metastasis were inhibited in culture and mouse models by a plant-derived compound called cannabidiol, which has been shown to activate an ion channel, transient vanilloid-like receptor 2 (TRPV2). The researchers hypothesize that cannabidiol, upon binding to TRPV2, activates immune cells and increases immune response against tumors. This study will help them further determine the role of TRPV2/cannabidiol in inhibiting growth and metastasis of TNBC.

DEVELOP IL-27-BASED COMBINATIONAL IMMUNOTHERAPY OF CANCER

(PI: Xue-Feng Bai, MD, PhD)

Cancer immunotherapy has emerged as a major weapon in the war against cancer. The increase in response rates following treatment with anti-CTLA-4 antibodies and anti-PD1 antibodies shows the power of combining immune therapy agents. However, because severe autoimmune side effects limit the use of this combination, additional combinations are sought. This team will develop therapeutics that have the potential to boost the effectiveness of cancer immunotherapies, including antibody-based agents and cancer vaccines. The researchers hypothesize that combining IL-27 with anti-PD1 antibodies or cancer vaccines can enhance the effectiveness of those immune therapies while avoiding serious autoimmune side effects.

CERAGENIN-BASED THERAPY FOR MULTIPLE MYELOMA

(PI: Don Benson, MD, PhD)

Myeloma is an incurable form of blood cancer affecting more than 75,000 patients in the United States. Novel treatments that extend patient survival, in part through the body's immune system, have provided new opportunities to harness the immune system to fight cancer. Recent discoveries suggest that tiny proteins called antimicrobial peptides in the immune system might also have anticancer properties. This grant will enable researchers to learn whether artificial peptides that are based on the naturally occurring immune proteins might offer an entirely new myeloma treatment.

DEFINING THE ROLE OF AUTOPHAGY IN ANOIKIS RESISTANCE AND IN PERITONEAL CARCINOMATOSIS/SARCOMATOSIS

(PIs: James Chen, MD, and John Hays, MD, PhD)

Many cancers can spread throughout the abdomen in a pattern known as carcinomatosis or sarcomatosis. This type of spread indicates the cancer is highly aggressive, but the mechanisms involved in these processes are poorly understood. These researchers have developed a laboratory model that mimics carcinomatosis or sarcomatosis and have shown that, across multiple cancers, a process called autophagy, which can cause cells to self-destruct, is dysregulated. Their initial experiments showed that, by altering the mechanism of autophagy, they can lower the number of cancer cells that survive. This grant will help them study more drugs and cancers to see if they can repeat these effects.

TUMOR SUPPRESSION AND GENOME STABILITY

(PIs: Kay Huebner, PhD, and Daniel Schoenberg, PhD)

Tumor-suppressor genes protect cells from developing into cancer. When these genes are mutated or silenced, they can no longer protect the cell, and this contributes to cancer development. *Fhit* is a tumor-suppressor gene that is lost in most human cancers, but scientists do not completely understand how or why its loss contributes to cancer. In this study, researchers will identify *Fhit*-regulated genes that control cell survival, proliferation and invasiveness with the goal of identifying new targets for drugs that might help treat more than 50 percent of all cancer cases.

IMPROVING CHEMOTHERAPY EFFECTIVENESS IN BREAST CANCER

(PI: Alo Ray, PhD)

Many kinds of chemotherapy kill cancer cells by damaging the DNA of rapidly dividing tumor cells. However, some cancer cells survive the treatment due to their ability to repair DNA damage and their use of checkpoint signaling pathways. This study will examine ways to disrupt or block DNA repair and cell-signaling pathways that enable cancer cells to survive chemotherapy and radiotherapy treatments. It could define whether blocking a certain signaling pathway in the presence of chemotherapeutic agents improves chemotherapy effectiveness in breast cancer.

STEM CELL RESISTANCE IN CHRONIC LYMPHOCYTIC LEUKEMIA (CLL)

(PIs: Natarajan Muthusamy, MPH, PhD, and L. James Lee, PhD)

Stem cells are cells that give rise to other cells in tissue. A small proportion of cancer cells also has qualities of stem cells and is thought to play a role in cancer development and resistance to chemotherapy. Leukemia-generating stem cells are widely accepted in myeloid leukemia, but little is known about their role in the most common form of adult leukemia, CLL. These researchers will evaluate a new technology for identifying potential stem-like CLL cells, determining whether they are true leukemia stem-like cells, and then learning more about their biology. Findings could lead to new and more effective CLL treatments.

DEFINING PROSTATE CANCER AGGRESSIVENESS THROUGH DNA SEQUENCING

(PIs: Qianben Wang, PhD, and Steven Clinton, MD, PhD)

Research has demonstrated that male hormones called androgens are necessary for the development and progression of prostate cancer. Antiandrogen hormone therapy has been a critical intervention in prostate cancer treatment. Although dramatic responses are often seen, the therapy ultimately fails as the cancer evolves to a treatment-resistant state. How androgens stimulate cancer growth and how resistance to antiandrogens occurs are poorly understood. This study will improve understanding of the molecular and genetic events involved in these processes while helping to define markers that enhance choices of antiandrogens for treating patients. This knowledge could result in the identification of androgen-regulated targets and the development of better treatments.

STEM CELLS' ROLE IN BRAIN TUMOR DEVELOPMENT AND SPREAD

(PI: Susan Cole, PhD)

Gliomas are the most common tumor of the central nervous system and are difficult to treat, resulting in overall poor treatment outcomes. Researchers at the OSUCCC – James believe that populations of cancer stem-like cells cause these tumors to be resistant to therapy. This project will take a closer look at the tumor microenvironment and cell communication pathways that support these clusters of stem-like cells in an effort to better understand how regulating these pathways could lead to treatments for gliomas.

RESISTANCE OF LIVER CANCER TO SORAFENIB: MECHANISMS AND DEVELOPMENT OF STRATEGIES TO COMBAT RESISTANCE

(PI: Samson Jacob, PhD)

Liver cancer is the fifth most prevalent cancer in the world and the second leading cause of cancer-related death (particularly in men), with the annual death rate exceeding 500,000. The incidence of liver cancer and mortality is increasing rapidly in the United States. A major problem in treating this cancer is its late diagnosis. Currently, sorafenib is the only approved drug for treating these patients. However, patients quickly develop resistance to sorafenib, which impedes the effectiveness of therapy and results in death shortly after initiating treatment. Therefore, it is important to develop new therapeutic strategies to further extend the survival of these patients. This study will address that issue.

CLINICAL TRIAL AWARD (PROTOCOL-SPECIFIC RESEARCH SUPPORT)

(Clinical trials not only help develop ways to prevent, diagnose and treat cancer, but they also give participating patients access to some of the most advanced treatments available anywhere. Awards in this category support such studies.)

HERPES-BASED VIRUS TO ATTACK SOLID TUMORS

(PI: Timothy Cripe, MD, PhD)

This team will test a new therapy for treating childhood and young-adult cancer. Oncolytic virus therapy uses live viruses to selectively infect and kill cancer cells with minimal damage to normal tissue. Once inside cancer cells, the anticancer virus is designed to kill those cells as it replicates and spreads to adjacent tumor cells. The goal is more complete and precise treatment of the tumor. This project is a first-in-human study of a locally developed oncolytic virus based on the herpes simplex virus-1. It is the first step toward determining whether the virus can shrink solid tumors outside the central nervous system.

COMMUNITY PARTNERSHIP AWARD

(This category supports investigators who partner with a community entity to conduct a cancer-focused study.)

MOBILE HEALTH INTERVENTION FOR HPV VACCINATION

(PIs: Mira Katz, PhD, MPH, and Paul Reiter, PhD, MPH)

Human papillomavirus (HPV) vaccination in young adults of ages 18 to 26 is an effective strategy for reducing the burden of HPV-associated diseases like cervical cancer; however, vaccination rates are suboptimal among this population. In a new pilot study, researchers at the OSUCCC – James, in collaboration with the Wilce Student Health Center, will test a mobile health intervention (i.e., a targeted HPV vaccine narrative on a mobile-friendly website) to communicate with young adults about HPV-associated diseases and the HPV vaccine in an effort to increase uptake of the vaccine in this high-risk population. The study also will obtain preliminary data on whether the narrative format increases HPV vaccine initiation in this age group.

BRIDGE FUNDING AWARD

(These funds assist researchers with competitive renewal applications at the level of an NCI R01 grant or equivalent that were not funded on their first submission. IRP Bridge Funding is also available for competitive renewal of grants whose initial funding has expired.)

A MASS-SPECTROMETRY APPROACH TO MAPPING HISTONE MODIFICATION CROSSTALK

(PIs: Michael Freitas, PhD, and Mark Parthun, PhD)

Histones are proteins that help package DNA in cells. Specific histone modifications can influence the modification of other histones, generating complex networks of histone-modification crosstalk. This research team will combine a molecular genetics and a mass-spectrometry approach to produce the most comprehensive view of histone cross-interactions to date.

New Hope

Pelotonia Dollars Support Innovative Clinical Trials

Clinical trials improve cancer care by demonstrating the safety and effectiveness of new treatments, examining treatment strategies and looking at problems associated with therapies so refinements can be made. Here are two examples of Pelotonia-supported clinical trials at the OSUCCC – James. For more information about these and other trials, call The James Line at 1-800-293 5066 or visit ***cancer.osu.edu****.*

Researchers Detail Reasons for Discontinuing Ibrutinib Therapy in Some CLL Patients

Basic and clinical research at Ohio State and elsewhere has shown the drug ibrutinib to be highly effective among certain patients with chronic lymphocytic leukemia (CLL), but a study at the OSUCCC – James shows that about 10 percent of patients stopped taking the drug because their disease progressed.

Although CLL, the most common form of adult leukemia, remains incurable, advances in therapy have been made, notably in the emergence of kinase inhibitors such as ibrutinib for patients whose disease has recurred or is resistant to other therapies.

Ibrutinib is the first drug to target a protein called Bruton tyrosine kinase that is essential for CLL cell survival and proliferation. Studies by OSUCCC – James researchers played a key role in gaining FDA approval of ibrutinib to treat certain patients with CLL or mantle cell lymphoma.

Clinical studies of this drug have continued, including a Pelotonia-supported study by Ohio State hematologists Kami Maddocks, MD, Jennifer Woyach, MD, and their colleagues, that described outcomes of patients who discontinued ibrutinb therapy during four sequential clinical trials involving over 300 patients at the OSUCCC – James. The study was published in the *Journal of the American Medical Association Oncology*.

At a midpoint follow-up of 20 months, the study showed that of 308 patients, 232 remained on ibrutinib, 45 stopped using it due to infection or other adverse events, and 31 stopped using it due to disease progression.

The study concluded that this single-institution experience with ibrutinib confirms it to be an overall highly effective therapy and identifies, for the first time, baseline factors associated with ibrutinib therapy discontinuation.

"These data enhance our understanding of how patients do on ibrutinib long-term and who is likely to relapse," says Woyach, the study's senior author and a member of the Leukemia Research Program at the OSUCCC – James. "Understanding which patients are at higher risk helps us select who might benefit from clinical trials on other new agents and combination therapies rather than starting ibrutinib treatment by itself."

Learning What Works From Women Coping With Chemotherapy

A Pelotonia Idea Grant awarded to OSUCCC – James researcher Kristen Carpenter, PhD, is supporting a clinical trial designed to identify strategies used by women who cope well with harsh chemotherapy side effects during treatment.

"Historically, health psychology focused on bad things that happen to people during cancer treatment—variables that make their outcomes worse," says Carpenter, a member of the Cancer Control Program at the OSUCCC – James. She notes that her team wants "to learn what helps folks who do well during treatment."

"Results from several studies in breast cancer have suggested that optimistic patients do a bit better through treatment," Carpenter says. "Our goal is to investigate the role of optimism and other dispositional variables to ascertain what kinds of things they do that might facilitate better outcomes."

She and her collaborators also hope to gain insight into whether coping strategies that work well for optimistic people work as well for those who are less optimistic.

"What excites me about this study is that we have an opportunity to look at what patients do naturally to help them through treatment," she says. "We will look for patterns that we hope will help us develop more individualized, targeted interventions."

The researchers will assess patients before they begin chemotherapy and several times during treatment to learn which symptoms they experienced and how they coped.

In one phase of the study, patients will complete a daily "diary" of their symptoms and the strategies they use to make themselves feel better, distract themselves or otherwise offset the problem. "The closer we act to the time when something occurs, the more accurate patient reports are," Carpenter says.

The study will assess participants' personality, their tendency toward optimism and their general coping style, as well as the presence of depression, anxiety and stress, if any.

"We want to learn which strategies work best and for whom, and how we can develop an intervention that makes sense in the long run," she adds.

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 studies when they arrive. Among those recruited in 2015 are these five prominent senior researchers:

DANIEL JONES, MD, PHD, is professor, vice chair and director of molecular pathology in the Department of Pathology, as well as director of molecular pathology for the OSUCCC – James. Jones brings more than 15 years of combined experience in academic medicine and industry. He most recently was medical director of cancer diagnostics services at Quest Diagnostics Nichols Institute, where his group developed more than 100 oncology, genomics and pathology assays for the nation's largest reference laboratory. Previously, Jones was at The University of Texas MD Anderson Cancer Center as a tenured professor overseeing a research laboratory and a clinical molecular diagnostics team that served 13 cancer care centers.

ANIL PARWANI, MD, PHD, MBA, is professor, vice chair and director of anatomic pathology in the Department of Pathology. He also directs a new shared resource/core facility focused on digital pathology imaging and pathology informatics. Within the OSUCCC – James, he directs the digital pathology service that will enable the expansion of precision cancer diagnostics and treatment. Parwani came to Ohio State from the University of Pittsburgh, where he was a professor of pathology and biomedical informatics as well as director of the Division of Pathology Informatics. His research focuses on diagnostic and prognostic biomarkers in bladder and prostate cancer, and on molecular classification of renal cell carcinoma.

SHARYN BAKER, PHARMD, PHD, is professor and chair of the Division of Pharmaceutics and Pharmaceutical Chemistry in the College of Pharmacy, and she holds the Gertrude Parker Heer Chair in Cancer Research. She also is a member of the Leukemia Research Program at the OSUCCC – James. Baker came to Ohio State from St. Jude Children's Research Hospital, where she directed the pharmacokinetics shared resource. Her cancer-relevant research interests broadly cover translational and clinical pharmacology of anticancer agents. More specifically, her interests include developmental therapeutics for acute myeloid leukemia (AML), translational pharmacology of tyrosine kinase inhibitors, and investigational anticancer drug development.

ALEX SPARREBOOM, PHD, who also came from St. Jude Children's Research Hospital, is a professor in the College of Pharmacy's Division of Pharmaceutics and Pharmaceutical Chemistry, and a member of the Translational Therapeutics Program at the OSUCCC – James. Sparreboom's research examines the contribution of solute carriers to chemotherapy-induced toxicity profiles, identifies chemical inhibitors of critical transporters, translates the findings to clinical trials, and ultimately improves the long-term outcome of patients with cancer by modulating the therapeutic window of widely used chemotherapeutics. His lab is developing transport modulators for use in connection with platinum-based drugs and tyrosine kinase inhibitors.

RAJGOPAL GOVINDARAJAN, DVM, PHD, an associate professor in the College of Pharmacy's Division of Pharmaceutics and Pharmaceutical Chemistry, was recruited to Ohio State from the University of Georgia, where he was an associate professor in the Department of Pharmaceutical and Biomedical Sciences. One of his lab's primary research goals is to understand how the solute carrier group of transporters modulates tumor cell sensitivity or resistance to chemotherapeutics. His lab also investigates: nucleoside and oligonucleotide (miRNA) drug sensitivity in cancer cells; epigenetic alterations in pancreatic cancer; and small molecule manipulations of epigenetic changes in pancreatic cancer cells.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